CLEVELAND HIGH SCHOOL STUDENT SCIENTIFIC ENRICHMENT & OPPORTUNITY PROGRAM AND YOUTH ENGAGED IN SCIENCE PROGRAM

2021 STUDENT RESEARCH VIRTUAL PRESENTATION

CASE WESTERN RESERVE UNIVERSITY SCHOOL OF MEDICINE

Participating High Schools

Andrews Osborne Academy, Avon HS, Beachwood HS, Bedford HS, Brecksville-Broadview Heights HS, Campus International HS, Charles F. Brush HS, Cleveland Heights HS, Cleveland School of Science and Medicine, Cumberland Valley HS, Euclid HS, Ginn Academy, Glean Academy, Hathaway Brown School, John F. Kennedy HS, Lakeridge Academy, Laurel School, Mayfield HS, Nathan Hale HS, Nordonia HS, Orange HS, Padua Franciscan HS, Revere HS, Saint Edward HS, Saint Ignatius HS, Saint Joseph Academy, Shaker Heights HS, Shaw HS, Solon HS, St Villa Angela-St Joseph HS, Stow Munroe Falls HS, The Lawrenceville School, Twinsburg HS, University School, Westlake HS

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CWRU Center for Science, Health and Society

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SCHOOL OF MEDICINE
CASE WESTERN RESERVE UNIVERSITY

July 29, 2021

WELCOME

Welcome to the eighteenth annual Scientific Enrichment and Opportunity (SEO) and Youth Engaged in Science (YES) Program - High School Student Research and Poster Capstone Presentation sponsored by the Case Western Reserve University School of Medicine, Center for Science, Health and Society. This year has been filled with challenges presented by the COVID-19 pandemic, yet one in which we saw the triumph of scientific research over disease, and one in which we witnessed the importance of unique, innovative approaches with the development of the mRNA vaccines, all emphasizing the importance of our summer student research program to promote diversity in biomedical research and healthcare practice. It is noteworthy that while many summer programs closed down due to the pandemic, our full program was adapted to a virtual and in-person, hybrid and delivered to over 100 high school students and six high school teachers.

The SEO Program was initiated in 2004 to focus on connecting students from the Cleveland Metropolitan School District with outstanding research and clinical faculty and staff at the CWRU School of Medicine. Over the years, the program has expanded to more broadly include students from a greater area of northeast Ohio. In 2018, with support from the National Cancer Institute Youth Engaged in Science (YES) grant, the program further increased to specifically include underrepresented minority students interested in cancer research and health care.

The SEO and YES programs provide Cleveland H.S. students with a unique opportunity to engage in biomedical research under the supervision of expert CWRU Medical School and Case Comprehensive Cancer Center faculty, to mentor and motivate students to complete H.S., attend college, and pursue careers in the biomedical sciences and health professions, and to enrich Cleveland by transforming students into enlightened members of the community who are prepared, enthusiastic and eager to participate in the growth of the biomedical sciences, the health care delivery systems and the elimination of health care disparities. Those students that have completed high school are currently enrolled in college, most are pursuing studies in science and some have now advanced to biomedical and healthcare schools.

We gratefully acknowledge the help of the dedicated counselors and leadership from the Cleveland area High Schools who guided the application process and worked along with committed CWRU faculty members to complete the student selection process.

This program would not be possible without the dedication of the faculty and staff of CWRU School of Medicine and the Case Comprehensive Cancer Center, who have volunteered their time as seminar speakers, mentors and coordinators, taking the high school students into their labs to show them the excitement associated with scientific investigation and discovery. We hope that their efforts will contribute to the students' success and to the future of health, health care and biotech development in Cleveland and around the globe.

We extend our special compliments to the students, who have worked diligently on their research projects, to understand the scientific method and to contribute their talents to solving a variety of fundamental and clinical biomedical challenges. We also extend our appreciation to the students' families for supporting and encouraging their engagement in these academic pursuits.

In addition to the abstracts in this book, this year's presentations of the SEO & YES student research projects are available at the URL at the bottom of this page. We thank all of you for your support, your participation, and your encouragement. It is our hope and expectation that, in the near future, we all will benefit from what you have enabled these students to accomplish this summer.

Nathan A. Berger, M.D.
Distinguished University Professor
Hanna-Payne Professor of Experimental Medicine
Professor, Medicine, Biochemistry, Oncology, Genetics & Genome Sciences
Director, Center for Science, Health & Society

2021 student presentation videos are available at:
https://youtube.com/playlist?list=PLU-Y99ofM6bqEzG4t63WpQU_ry6q9-R5Z

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ACKNOWLEDGEMENTS

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Mei Zhang, PhD, Department of Biomedical Engineering
Xiongwei Zhu, PhD, Department of Pathology

ACKNOWLEDGEMENTS—Continued

2021 SEO/YES Lunch & Learn and Career Café Seminar Speakers

Derek Abbott, MD, PhD, Department of Pathology
Eberechi Agwa, MD, Oncology
Mel Berger, MD, PhD, Pediatric Allergy and Immunology
Nathan Berger, MD, Case Comprehensive Cancer Center
Ronald Conlon, PhD, Department of Genetics
Jennifer Cullen, PhD, MPH, Department of Population and Quantitative Health Sciences
Navid Faraji, MD, Department of Radiology
Charles Hoppel, MD, Department of Pharmacology
Alex Huang, MD, PhD, Department of Pediatrics/Pathology/Immunotherapy
Mark Jackson, PhD, Department of Pathology
Natalie Joseph, MD, Department of Surgical Oncology/MetroHealth
Damian Junk, PhD, Case Comprehensive Cancer Center
Smitha Krishnamurthy, MD, Department of Hematology & Oncology
Hillard Lazarus, MD, Professor Emeritus, School of Medicine
Mike Lederman, MD, Professor Emeritus, School of Medicine
Rodrigue Lembvem, Undergraduate Admissions
Anant Madabhushi, PhD, Department of Biomedical Engineering
Lina Mehta, MD, Department of Radiology, SOM Admissions
Michelle Merrill, LCGC, Department of Genetics and Genome Sciences
Lalitha Nayak, MD, Department of Medicine, Hematology & Oncology
Nancy Oleinick, PhD, Department of Radiation Oncology
Andrew Sloan, MD, Department of Neurological Surgery
Kurt Stange, MD, PhD, Center for Community Health Integration
Aaron Weinberg, DMD, PhD, Dental Medicine

2021 SEO/YES Near Peer Mentors

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Oscar Bautista
Yuri Buckley
Michelle Alexis Cruz
Razaq Durodoye
Marc Ferrell
Leandre Glendenning
Allison Grenell
Emma Kundracik
Adam Lauko
Kate Letai
Sara Mason
Kimberly Parker
Otis Pinkard
Stephanie Swedik

2021 Participating High Schools

Andrews Osborne Academy
Avon High School
Beachwood High School
Bedford High School
Brecksville-Broadview Heights High School
Campus International High School
Charles F. Brush High School
Cleveland Heights High School
Cleveland School of Science and Medicine
Cumberland Valley High School
Euclid High School
Ginn Academy
Glean Academy
Hathaway Brown School
John F. Kennedy High School
Lakeridge Academy
Laurel School
Mayfield High School
Nathan Hale High School
Nordonia High School
Orange High School
Padua Franciscan High School
Revere High School
Saint Edward High School
Saint Ignatius High School
Saint Joseph Academy
Shaker Heights High School
Shaw High School
Solon High School
St Villa Angela St Joseph
Stow Munroe Falls High School
The Lawrenceville School
Twinsburg High School
University School
Westlake High School

SEO & YES ALUMNI and COLLEGES

Student	High School	College
Marie Abdul-Karim	James F. Rhodes High School	Cuyahoga Community College Case Western Reserve University Cleveland State University
Nichele Abeyesundere	Shaker Heights High School	
Amal Aboumerhi	Westlake High School	
Henrietta Abrams	East Technical High School	Cuyahoga Community College
Nneka Adigwe	John F. Kennedy High School	Cuyahoga Community College Kent State University
Nassim Aidja	Mayfield High School	
Jordan Alexander	John F. Kennedy High School	
Manal Alkabani	Cleveland School of Science and Medicine	
Raneem Almhana	Saint Joseph Academy	
Dominic Anderson	John F. Kennedy High School	Cuyahoga Community College
Anushree Aneja	Solon High School	University of Pennsylvania
Katherine Antepara	James F. Rhodes High School	Cuyahoga Community College
Marangely Aponte	James F. Rhodes High School	Cuyahoga Community College
Shruthika Araselvan	Hathaway Brown School	
Alexis Armstead	Glenville High School	Cuyahoga Community College Hiram College
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Shay McDermott	Shaker Heights High School	
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DeVaughn McNary	Glenville High School	ITT Technical Institute
Akhil Medarametla	University School	
Arul Mehta	St. Ignatius High School	Case Western Reserve University
Ira Mehta	Lakeridge Academy	
Rafael Mercado	James F. Rhodes High School	
Beverly Mercedes	James F. Rhodes High School	Kent State University
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Toussaint Miller	University School	Harvard University
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Jaida Motley	John F. Kennedy High School	
Nathan Mu	University School	
Patrick Murphy, Jr.	John F. Kennedy High School	Cleveland State University
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Ogechi Muruako	Cleveland School of Science and Medicine	
George Nageeb	University School	Harvard University
Mary Nazimiec	Cleveland School of Science and Medicine	Cleveland State University
Tina Nguyen	Mayfield High School	
Antoine Nichols	Cleveland School of Science and Medicine	The Ohio State University
Kiana Nicholson	Glenville High School	University of Phoenix
Sullymar Nieves	Facing History New Tech	Cuyahoga Community College
Eric Nouafo	Solon High School	University of Pennsylvania
Micha Nouafo	Solon High School	
Fata Nyei	Cleveland School of Science and Medicine	
Gile Nzitunga	Glenville High School	University of Dayton
Ayonitemi Odukoya	Solon High School	
Jesutomi Odukoya	Solon High School	Yale University

Student	High School	College
Oyinkansola Odukoya	Solon High School	Case Western Reserve University
Richard Ojo	Eleanor Roosevelt High School	University of Maryland
Andrea Okocha	Bedford High School	
Aida Omoijuanfo	Glean Academy	
Ebahi Omoijuanfo	Glean Academy	
Ese-Onosen Omoijuanfo	Glean Academy	University of Notre Dame
Jason Ong	Solon High School	University of Pittsburgh
Meredith Onnie	James F. Rhodes High School	Cuyahoga Community College Kent State University
Angel Ononogbo	Orange High School	
Ogechi Onyeukwu	Cleveland School of Science and Medicine	Cuyahoga Community College Cleveland State University
Kwabena Owusu	Solon High School	Cuyahoga Community College
Nana Owusu	Solon High School	Yale University
John Pape	University School	
Gabriel Papell	Shaker Heights High School	The Ohio State University
Taniya Parker	Glenville High School	
Chantae Parsons	John F. Kennedy High School	University of Dayton
Kaitlyn Pawul	James F. Rhodes High School	Cuyahoga Community College
Rica Payne	Glenville High School	Cleveland State University
Shaquona Pearsall	Glenville High School	Kent State University
Haridu Peiris	Twinsburg High School	
Angelica Pickett	John F. Kennedy High School	Ohio State University
Eric Pieper	Shaker Heights High School	
Justin Pieper	Shaker Heights High School	

Student	High School	College
Chad Porter	Villa Angela/St. Joseph High School	The Ohio State University
Ta'Shiyah Porter	Cleveland School of Science and Medicine	
Bre-Shay Potts	John F. Kennedy High School	Cleveland State University
Adrien Powell	New Tech East	
Trinity Pruitt	Cleveland School of Science and Medicine	
William Qu	Solon High School	Case Western Reserve University Emory University
Riley Rainey	Glenville High School	University of Phoenix John Carroll University
Keyvon Rashidi	University School	Case Western Reserve University
Gabrielle Raymont-Scott	Cleveland School of Science and Medicine	Miami University
Amaya Razmi	Hathaway Brown	Harvard University
Logan Readinger	James F. Rhodes High School	Bryant & Stratton College
Jessenia Rebello	James F. Rhodes High School	Case Western Reserve University
Anika Rede	Hathaway Brown	UC Berkeley
Shantall Reece	John F. Kennedy High School	Cuyahoga Community College
Angela Richmond	John F. Kennedy High School	American Intercontinental University
Martina Richter	Shaker Heights High School	
Krystle Rivera	James F. Rhodes High School	John Carroll University Cleveland State University
Tai Roberts	Andrews Osborne Academy	
Kala Rodriguez	James F. Rhodes High School	
Sophia Rose	Shaker Heights High School	

Student	High School	College
Shira Rosenberg	Hathaway Brown	
Imani Rucker	Hathaway Brown	Kenyon College
Jacob Rudin-Luria	Hawken School	
Nichelle Ruffin	John Hay High School	Case Western Reserve University
Jonica Rutledge	John F. Kennedy High School	Lakeland Community College Western Governors University
James San	John Hay High School	Case Western Reserve University
Brittany Sanders	John F. Kennedy High School	Cleveland State University
Yaritizy Santizo	Cleveland School of Science and Medicine	
Samantha Schall	Cleveland School of Science and Medicine	Case Western Reserve University
Leo Schirokauer	Shaker Heights High School	Harvard University
Samuel Schlang	Hawken School	University of Chicago
Ariel Scott	John F. Kennedy High School	Coastal Carolina Community College
Heather Scott	James F. Rhodes High School	Ursuline College Chamberlain University
Joseph Scott	Cleveland School of Science and Medicine	
Danae Seals	St. Villa Angela-St. Joseph High School	
Khadijah Seay	John Hay High School	Bryn Mawr College Temple University
Vishal Sentilkumar	Brunswick High School	Case Western Reserve University
Aaron Sepulveda	James F. Rhodes High School	Case Western Reserve University
Cesar Sepulveda	James F. Rhodes High School	John Carroll University
Soham Shah	St. Ignatius High School	

Student	High School	College
Sorina Shahadeh	James F. Rhodes High School	Bryant & Stratton College Baldwin Wallace University
Yasmeen Shahadeh	James F. Rhodes High School	Kent State University
Kulthoom Shaheed	Campus International High School	
Zaynab Shaheed	Campus International High School	Case Western Reserve University
Zayne Shaheed	Campus International High School	
Sidney Sheppert	Stow Munroe Falls High School	
Sandy Shen	Solon High School	University of Akron Swarthmore College
Shannon Shih	Downington STEM Academy (PA)	
Lashaune Short	John F. Kennedy High School	California College
Channell Shoulders	Glenville High School	Cuyahoga Community College
Dylan Siegler	University School	
Layce Simbeck	Facing History New Tech	Cuyahoga Community College
Jasmine Sims	James F. Rhodes High School	The Ohio State University
Tarini Singh	Berea Midpark High School	Caltech
Erica Smith	Glenville High School	Lakeland Community College Cleveland State University
Kayla Smith	Cleveland School of Science and Medicine	
Maya Smith	Cleveland School of Science and Medicine	The Ohio State University
Sherry Smith	Glenville High School	
She'Rise Thompson-Smith	Glenville High School	Case Western Reserve University
Asaan Snipes-Rea	University School	Oberlin College
Pranav Sompalle	Mayfield High School	

Student	High School	College
Summer Sorrell	James F. Rhodes High School	Cuyahoga Community College Cleveland State University
William Spears	James F. Rhodes High School	Cuyahoga Community College Cleveland State University
Anaya Spencer	Cleveland School of Science and Medicine	Cuyahoga Community College
Terrah Spencer	Glenville High School	Bryant & Stratton College Tuskegee University
Kristen Stash	James F. Rhodes High School	Cuyahoga Community College Ursuline College
Charnae Steward	John F. Kennedy High School	University of Toledo Tiffin University
Ryckia Sutton	Cleveland School of Science and Medicine	
Diya Swain	Shaker Heights High School	
Hans Swain	University School	
Ian Swain	University School	
Eric Swander	James F. Rhodes High School	Cuyahoga Community College Hiram College
Josea Switzer	Glenville High School	Akron University
Maheera Syed	Strongsville High School	
Rubab Syed	Strongsville High School	Case Western Reserve University
Kamar Taweel	Cleveland School of Science and Medicine	
Aliysha Taylor	James F. Rhodes High School	Chattahoochee Technical College
Mackensie Thompson	Andrews Osborne Academy	
David Tibbitts	James F. Rhodes High School	Cleveland State University
Dashiell Tidrick	Saint Ignatius High School	

Student	High School	College
Owen Tolbert	Shaker Heights High School	
Lauren Torres	Facing History New Tech	
Tavaris Tucker	John F. Kennedy High School	Cuyahoga Community College Cleveland State University
Igor Tuteleman	Solon High School	Case Western Reserve University
Mythili Ungarala	Shaker Heights High School	
Zoie VanHuffel Gouldlock	Bedford High School	
Mantas Viazmitinas	Westlake High School	
Marcela Villegas	James F. Rhodes High School	Copper Mountain College
Damon Wallace	Nordonia High School	Walsh University
Kennon Walton	University School	
Chougyu Wang	St. Ignatius High School	
Lindsey Wang	Orange High School	
William Wang	Orange High School	
Yinyin Wang	Shaker Heights High School	
Janiece Warfield	Glenville High School	Cleveland State University
Gwen Weagraff	Avon High School	
Bianca West	Glenville High School	Baldwin Wallace University
Isaiah Whatley	Mayfield High School	The Ohio State University
Lawrence White	Glenville High School	Akron University
Alexandria Williams	James F. Rhodes High School	Cleveland State University
Chanelle Williams	Glenville High School	Bowling Green University
Denyse Williams	Glenville High School	Lakeland Community College
Lauren Williams	John F. Kennedy High School	Cuyahoga Community College
Dianea Willis	Glenville High School	University of New Mexico

Student	High School	College
Allan Willmon, Jr	Cleveland School of Science and Medicine	Case Western Reserve University
Emily Wilson	Hathaway Brown School	
Isaiah Wilson	Cleveland School of Science and Medicine	
Matthew Wilson	Solon High School	The Ohio State University
Gavyn Woo	Cleveland School of Science and Medicine	
Alice Wu	Solon High School	Duke University
Daisy Wu	Solon High School	Case Western Reserve University University of Toledo
Tionna Wynn	Glenville High School	Cuyahoga Community College Akron University
Victor Xie	Solon High School	
Weixiong Xu	Cleveland School of Science and Medicine	Ohio State University
Maggie Yang	Solon High School	
Chasity Young	John F. Kennedy High School	Kent State University
Adam Yu	Solon High School	
Kimberly Zarczynski	James F. Rhodes High School	Hiram College
Chelsea Zheng	Beachwood High School	Case Western Reserve University
Kevin Zhou	Solon High School	
Yong Liang Zhou	Cleveland School of Science and Medicine	John Carroll University

SEO & YES COLLEGE STUDENT ALUMNI

STUDENT	COLLEGE
Cassidy Abdeen	Case Western Reserve University
Dylan Arnold	Case Western Reserve University
Ramon Correa	Case Western Reserve University
Nikita Davidenko	Case Western Reserve University
Zain Khawaja	Case Western Reserve University
Jesutomi Odukoya	Yale University
Richard Ojo	University of Maryland College Park
Ese Omoijuanfo	University of Notre Dame
Samantha Rodriguez	Case Western Reserve University
Maya Smith	The Ohio State University
Esmeralda Terrazas	Case Western Reserve University
Luis Tirado	Case Western Reserve University

YES TEACH TO BEAT CANCER TEACHER ALUMNI

TEACHER	HIGH SCHOOL
Angela Augustus	CMSD Mentor K 12 Fuel
Billy Augustus	CMSD Substitute Teacher
Gregory Archer	James F. Rhodes High School
April Archer-Bailey	Euclid Middle School
Wilmarie Busher-Betancourt	Cleveland School of Science and Medicine
William Dunn	Glenville High School
Michael Ford	Andrews Osborne Academy
Sharita Hill	Shaker Heights High School
Sergey Kolomiyets	Facing History New Tech
Deepshikha Paul	Max Hayes High School

2021 SEO/YES STUDENT RESEARCH POSTERS

Poster #	Student and High School	Title	Advisor	Department
1.	Nichele Abeyesundere Shaker Heights High School	Young Adult Substitution of Flavored Cigarillos with Menthol Cigarettes	Erika Trapl, PhD	Department of Population and Quantitative Health Sciences
2.	Amal Aboumerhi Westlake High School	COVID-19 and Transplant Patients: Covid Vaccine Hesitancy Among Adult Kidney Transplant Recipients	Kenneth Chavin, MD, PhD	Department of Surgery
3.	Nassim Aidja Mayfield High School	Characterization of the Role of Smooth Muscle Jagged1 in Modulation of Myogenic Tone	Aaron Proweller, MD, PhD	Department of Medicine
4.	Jordan Alexander John F. Kennedy High School	Lymphatic Filariasis	Christopher King, MD, PhD	Department of Pathology
5.	Manal Alkabani Cleveland School of Science and Medicine	Examining if *Candida auris* species generate more mutations for resistance when challenged with antifungal treatment compared to other species of candida	Thomas McCormick, PhD	Department of Dermatology
6.	Raneem Almhana Saint Joseph Academy	Comparison of Lymphatic Filariasis Antigen Diagnostic Assay: Extended Read vs per Protocol Read	Daniel Tisch, MPH, PhD	Department of Population and Quantitative Health
7.	Rithvik Ayyagari Saint Ignatius High School	Pathophysiology of α-Synuclein In The Eye	Neena Singh, MD, PhD	Department of Pathology
8.	Anusha Bangalore Westlake High School	Post-Translational Modification of JAB1: A Newly Identified Proto-Oncogene in Prostate Cancer Cells	David Danielpour, PhD	Case Comprehensive Cancer Center
9.	Rhycordia Barner John F. Kennedy High School	COVID-19 and Damage to the Lungs	Debora Bruno, MD	Department of Medicine
10.	Rachel Bart Cleveland School of Science and Medicine	The Trends Found by Counties with Obesity with Certain Cancers	Siran Koroukian, PhD	Department of Population and Quantitative Health
11.	Anna Beck Laurel School	The Effect of NK Cells on Neuroendocrine Tumors	David Wald, MD, PhD	Department of Pathology
12.	Julian Berger University School	A Novel Fluorescent Dye Based Method for Detecting Autophagy	Zhenghe Wang, PhD	Department of Genetics and Genome Sciences

13.	Joshua Bickerstaff University School	Effects of Processed and Red Meat on Blood Sugar Levels	Thomas LaFramboise, PhD	Department of Genetics and Genome Sciences
14.	Thomas Blossom University School	The Effect of Diet on Aviator Performance	Michael Decker, PhD, RN	Department of Physiology and Biophysics
15.	Emily Boron Shaker Heights High School	Excess Dietary Iron and Intestinal Cancer	James Swain, PhD, RDN	Department of Nutrition
16.	Luke Brandon University School	Dietary Restrictions to Improve the Imbalance of Autism Spectrum Disorder (ASD) Microbiome	Mahmoud Ghannoum, PhD	Department of Dermatology
17.	Anaria Britt Hathaway Brown School	African American Screening Guidelines and Reasonings for a Different Set of Guidelines for African Americans	Erika Trapl, PhD	Department of Population and Quantitative Health
18.	Janae Camargo Andrews Osborne Academy	Nanoscale Protein Delivery Implementation and Obstacles	John Tilton, MD	Department of Nutrition
19.	Neha Chellu Beachwood High School	The Efficacy of Using Deep Learning Algorithms to Assess Epicaridial Fat in CT Calcium Score Exams	David Wilson, PhD	Biomedical Engineering
20.	Maia Childress Nathan Hale High School	The Effects of Targeted Marketing on Tobacco use in Youth and Minority Populations	Erika Trapl, PhD	Department of Population and Quantitative Health
21.	Desire Clark Cleveland School of Science and Medicine	Can Kidney, Bladder and Lung Cancer Deaths be linked to Smoking?	Siran Koroukian, PhD	Department of Population and Quantitative Health
22.	Javan Cobb University School	IL-33: Discovering the Calcium Dependent Mechanism of Release in Response to Allergens in Airway Epithelial Cells	George Dubyak, PhD	Department of Physiology and Biophysics
23.	Nikita Davidenko CWRU	A systematic review of metastatic spinal melanoma	Adrienne Callahan, MD	Department of Dermatology
24.	Landon Dawson Avon High School	Comparing Intracortical Microelectrode Tissue Staining Methods	Jeffrey Capadona, PhD	Biomedical Engineering
25.	Manzili Denis University School	Identifying Target of Selective Cancer-targeting Small Molecules	Drew Adams, PhD	Department of Genetics and Genome Sciences
26.	Claire Dunn Shaker Heights High School	How Electronic cigarettes and other tobacco products affect your lungs	Erika Trapl, PhD	Department of Population and Quantitative Health

27.	Thomas Dunn Shaker Heights High School	The Biological Process of Transfection and Western Blotting	Can Shi, PhD	Cardiovascular Research Institute
28.	Adrik Dutta Shaker Heights High School	Photobiomodulation: Investigating the effect of light on the progression of Alzheimer's Disease using the Drosophila model	Masashi Tabuchi, PhD	Department of Neurosciences
29.	Le'Aona DySart Cleveland School of Science & Medicine	What are the differences between signet-ring & colorectal cancer	Stephen Fink, PhD	Case Comprehensive Cancer Center
30.	Chloe Echols Hathaway Brown School	Resiliency in African Americans and the Impact of Potentially Traumatic Events	Peter Hovmand, PhD	Center for Community Health Integration
31.	Ahmed Elsharkawy Saint Edward High School	Comparison of MRI CT, and Ultrasound for assessing cartilage grafts	Bryan Carroll, MD, PhD	Department of Dermatology
32.	Karim Elsharkawy Saint Edward High School	Evaluating the effects of exercise on muscle metabolism and insulin sensitivity	Xin Yu, ScD	Biomedical Engineering
33.	Kaitlyn Ernst Laurel School	BG34-200 Engagement with Integrin CD11b for Modulating Tumor-Associated Myeloid Cells in Pancreatic Cancer	Mei Zhang, PhD	Biomedical Engineering
34.	Mary Estafanous Laurel School	The Abundance of PML in Estrogen Receptor Alpha Breast Cancer	Hung-Ying Kao, PhD	Department of Biochemistry
35.	Adora Ezepue Campus International High School	In what ways does CDK5 inhibit immune evasion of tumor cells?	Alex Huang, MD, PhD	Department of Pediatrics
36.	Jenny Fan Revere High School	The Impact of VCAM-1 on Tumor Associated Macrophages	Alex Huang, MD, PhD	Department of Pediatrics
37.	Abem Fetene University School	An evaluation of the efficacy of Bax inhibiting small compounds to prevent iBax cell death	Shigemi Matsuyama, PhD	Department of Pathology
38.	Dennae Foster, Jr. Ginn Academy	Degradation of mutant P53 in HPV- in Head and Neck Cancer	Quintin Pan, PhD	Department of Otolaryngology
39.	Fahness Freeman Cleveland Heights High School	Determining the pathways for transmembrane water and CO_2 flux via AQP5	Walter Boron, MD, PhD	Department of Physiology and Biophysics
40.	Benjamin Frostino Padua Franciscan High School	A pathway enrichment analysis of genes that modify tobacco smoking risk for multiple sclerosis	Farren Briggs, PhD	Department of Population and Quantitative Health

41.	My'Desire George-Wiggins Shaw High School	Flavored Tobacco Product Use Amongst the Younger Population	Erika Trapl, PhD	Department of Population and Quantitative Health
42.	Isaiah Gilbert University School	Role of RNA binding proteins dysregulation in cancer development and progressions	J. Alan Diehl, PhD	Department of Biochemistry
43.	Nalin Gupta Solon High School	Proximity Labeling to Identify Protein Interactions Involving the Nonsense-mediated mRNA decay proteins UPF2 and UPF3	Kristian Baker, PhD	Department of Genetics and Genome Sciences
44.	Hannah Holt Charles F. Brush High School	Association between Pediatric Brain Cancer and Learning, Sleep Quality, and Myelination: A Systematic Review	Sarah Markt, PhD	Department of Population and Quantitative Health
45.	Manith Humchad Brecksville-Broadview Heights High School	Blood Vessel Extraction from Retinal Images	Anant Madabhushi, PhD	Department of Biomedical Engineering
46.	Ahmad Islambouli Cleveland School of Science and Medicine	Tumor-Associated Macrophages: Contributing to Therapy Resistance in Breast Cancer	John Letterio, MD	Department of Pediatrics
47.	Ta'nea Jackson Shaw High School	Cytokeratin Profile Of Human Oral Mucosa	Aaron Weinberg, DMD, PhD	Department of Biological Sciences, Dental Medicine
48.	Rohan Jaiswal Solon High School	Comparing the Predicted Secondary and 3D Structures of Betacoronavirus Stem-Loop 1s	Blanton Tolbert, PhD	Department of Chemistry
49.	Anu Jakate Solon High School	Identifying Targeted Therapies for Treating TGF β-Resistant Esophageal Adenocarcinoma	Andrew Blum, MD, PhD	Case Comprehensive Cancer Center
50.	Jonathan Jang University School	Investigating Immunotherapy Treatment Methods for Metastatic Melanoma	Bethany Rohr, MD	Department of Dermatology
51.	Davionna Johnson Euclid High School	Triple Negative Breast Cancer in African American Women	Jennifer Cullen, PhD	Department of Population and Quantitative Health
52.	Rohan Kumar University School	EPHRINB2 In Esophageal Adenocarcinoma	Kishore Guda, DVM, PhD	Case Comprehensive Cancer Center
53.	Adlai Kwofie Cleveland School of Science and Medicine	Sighs: A Biomarker Inflammation in the Circuitry of Respiratory Control	Ted Dick, PhD	Department of Neurosciences
54.	Arthur Li The Lawrenceville School	Immunohistochemistry Staining of Colorectal Cancer Tissue to Confirm the Liver Microenvironment's Paracrine Activation of the HER3-Akt Pathway	Jordan Winter, MD	Department of Surgery

55.	Kate Lindley Cumberland Valley High School	P7C3-A20 Treatment Protects Against Neurodegeneration and Neurobehavioral Deficits After Whole-Brain Radiation Therapy	Andrew Pieper, MD, PhD	Department of Pathology
56.	Karis Liu Solon High School	PTPmu Fluorescent Imaging Agents for the Detection and Treatment of Glioblastoma	Susann Brady-Kalnay, PhD	Department of Molecular Biology and Microbiology
57.	Andrew Loney Shaker Heights High School	Cloning Truncations Mutants of CHMP5 to Investigate Thymocyte Selection	Stanley Adoro, PhD	Department of Pathology
58.	Ivana Macazana Bedford High School	The role of a cytoskeletal protein (CP) in hair cell mechanotransduction	Brian McDermott, PhD	Department of Otolaryngology
59.	Sarisha Mahajan Revere High School	Cellular Adaptation to Osmotic Stress	Maria Hatzoglou, PhD	Department of Genetics and Genome Sciences
60.	Shay McDemott Shaker Heights High School	Glial Cells in the Nervous System	Paul Tesar, PhD	Department of Genetics and Genome Sciences
61.	Ira Mehta Lakeridge Academy	The effectiveness of apigenin as a potential histone deacetylase inhibitor	Sanjay Gupta, PhD	Department of Urology
62.	Arul Mehta Saint Ignatius High School	Quantitative MRI Assessments of Kidney Disease Progression in Patients with Autosomal Recessive Polycystic Kidney Disease (ARPKD)	Chris Flask, PhD	Department of Radiology
63.	Kyimani Miller Beachwood High School	Inflammatory Bowel Disease: Crohn's Disease and Ulcerative Colitis	Fabio Cominelli, MD, PhD	Department of Medicine
64.	Janailyn Morris Cleveland School of Science and Medicine	The Effects of Inhibitors of Uracil DNA Glycosylase on Cancer Cell Growth	Stan Gerson, MD	Case Comprehensive Cancer Center
65.	Jaida Motley John F. Kennedy High School	An Understanding of Protein Aggregation	Helen Miranda, PhD	Department of Genetics and Genome Sciences
66.	Nathan Mu University School	Developing an Autoencoder to Improve the Efficiency of QSAR Modeling	Horst von Recum, PhD	Department of Biomedical Engineering
67.	Tina Nguyen Mayfield High School	An Evaluation of the Role of Tumor-Associated Macrophages and CD59 Membrane Proteins in the Advancement of Pancreatic Cancer	John Letterio, MD	Department of Pediatrics

68.	Andrea Okocha Bedford High School	Vitamin E and the effects of Oxidative Stress on Fertility	Danny Manor, PhD	Department of Nutrition
69.	Ebahi Omoijuanfo Glean Academy	Determination of Prostate Specific Membrane Antigen (PSMA) expression in Prostate Cancer Cells	James Basilion, PhD	Department of Biomedical Engineering
70.	Aide Omoijuanfo Glean Academy	Using Quantitative PCR and Western Blot to Explore FXII Expression in Glioma Cells	Andrew Sloan, MD	Department of Neurological Surgery
71.	Angel Ononogbo Orange High School	The Role of the MIZ1 gene in Triple-Negative Breast Cancer in Cell Proliferation and 3D-growth	William Schiemann, PhD	Case Comprehensive Cancer Center
72.	Kwabena Owusu Solon High School	African American male screening results will show greater risk for prostate cancer at a younger age	Erika Trapl, PhD	Department of Population and Quantitative Health
73.	Haridu Peiris Twinsburg High School	Lung Airway Segmentation: An Automated Algorithm Approach	Anant Madabhushi, PhD	Department of Biomedical Engineering
74.	Eric Pieper Shaker Heights High School	The effect of temperature on acoustic stability and movement of nanobubble ultrasound contrast agents	Agata Exner, PhD	Department of Radiology
75.	Justin Pieper Shaker Heights High School	Assessment of CT Calcium Score Images Using Deep Learning	David Wilson, PhD	Department of Biomedical Engineering
76.	Ta'Shiyah Porter Cleveland School of Science and Medicine	CITED2 limits LPS-induced pro-inflammatory macrophage activation	Ganapathi Mahabaleshwar, PhD	Department of Pathology
77.	Trinity Pruitt Cleveland School of Science and Medicine	Chromosome Therapy For Large Chromosomal Aberrations	Anthony Wynshaw-Boris, MD, PhD	Department of Genetics and Genome Sciences
78.	Martina Richter Shaker Heights High School	Prostate Cancer Screening and Screening Guidelines Incorporating Biological and Sociological Factors Affecting African American Men with Prostate Cancer	Erika Trapl, PhD	Department of Population and Quantitative Health
79.	Tai Roberts Andrews Osborne Academy	The Effect & Possible Solutions of Wearable Devices on Gynecological Cancer	Stefanie Avril, MD	Case Comprehensive Cancer Center
80.	Sophia Rose Shaker Heights High School	Identification of P7C3-S321 Associated Neuroprotective Pathways in a Rodent Model of Alzheimer's Disease	Andrew Pieper, MD, PhD	Department of Medicine
81.	Yaritizy Santizo Cleveland School of Science and Medicine	Melanoma: Pathophysiology, Risk Factors, and Treatments	Sonal Shah, MD	Department of Dermatology

82.	Joseph Scott Cleveland School of Science and Medicine	The Impact of Prescription Drugs on Cancer Risk	Fred Schumacher, PhD	Department of Population and Quantitative Health
83.	Danae Seals St. Villa Angela-St. Joseph High School	Tissue macrophages promote the progression and therapy resistance in breast cancer	John Letterio, MD	Department of Pediatrics
84.	Soham Shah St. Ignatius High School	CITED2 attenuates IRF1 signaling in macrophages	Ganapathi Mahabaleshwar, PhD	Department of Pathology
85.	Sidney Sheppert Stow Munroe Falls High School	Environmental Risk Factors of Lung Cancer in Ohio	Cheryl Thompson, PhD	Department of Nutrition
86.	Pranav Sompalle Mayfield High School	Organization and Quality Control of Large-Scale Prostate Medical Imaging Datasets for Machine Learning Research	Rakesh Shiradkar, PhD	Department of Biomedical Engineering
87.	Diya Swain Shaker Heights High School	Effects of PGC-1alpha modulation in Alzheimer's Mice model	Xiongwei Zhu, PhD	Department of Pathology
88.	Hans Swain University School	Does treatment for psoriasis decrease the risk of developing comorbidities, such as cardiovascular disease?	Neil Korman, MD, PhD	Department of Dermatology
89.	Abdurrahman Tamim Westlake High School		Lin Mei, MD, PhD	Department of Neurosciences
90.	Mackensie Thompson Andrews Osborne Academy	BV and THRIVE	Adam Burgener, PhD	Department of Pathology
91.	Owen Tolbert Shaker Heights High School	Analyzing the Impact of Pc 4-PDT on Candida Auris	Thomas McCormick, PhD	Department of Dermatology
92.	Mythili Ungarala Shaker Heights High School	The Positive Aspects of Sunscreen in Regards to the Benzene Contamination	Christina Wong, MD	Department of Dermatology
93.	Zoie VanHuffel Gouldlock Bedford High School	Optimizing Cytarabine and BAFF Doses to Maximize the Reduction of Cytarabine's Effect on JEKO Proliferation	Reshmi Parameswaran, PhD	Case Comprehensive Cancer Center
94.	Mantas Viazmitinas Westlake High School	Substrate Charge Distribution Modulates the Activity of the GalNAc-Transferase-Catalyzed Initial Mucin-Type O-Glycosylation	Thomas Gerken, PhD	Department of Biochemistry
95.	Damon Wallace Nordonia High School	Comparing Serous of Endometrioid Tumors	Mark Cameron, PhD	Department of Population and Quantitative Health

96.	Lindsey Wang Orange High School	Risk, incidence, and disparities of COVID-19 vaccine breakthrough infection among patients with multiple myeloma in the United States between December 2020 and July 2021	Nathan A. Berger, MD	Case Comprehensive Cancer Center
97.	William Wang Orange High School	COVID-19 Vaccine breakthrough infection among vaccinated patients with colorectal cancer in the United States between December 2020 and July 2021: a retrospective cohort study using electronic health records	Nathan A. Berger, MD	Case Comprehensive Cancer Center
98.	Gwen Weagraff Avon High School	Manipulation of gut-resident bacteria to influence changes in gut microbiota within the brain tissue	Jeffrey Capadona, PhD	Department of Biomedical Engineering
99.	Isaiah Whatley Mayfield High School	Does cholesterol depletion alter the size of lipid raft microdomains of T-Cell signaling proteins in Jurkat T Cells	Alan Levine, PhD	Department of Molecular Biology and Microbiology
100.	Matthew Wilson Solon High School	Family Income and its Impact on Family Resilience	Peter Hovmand, PhD	Center for Community Health Integration
101.	Gavyn Woo Cleveland School of Science and Medicine	Neural Components contributing to the formation of the Perineuronal Net	Lin Mei, MD, PhD	Department of Neurosciences
102.	Victor Xie Solon High School	Stability of Indocyanine Green-Loaded Nanobubbles for Multimodality Imaging Applications	Agata Exner, PhD	Department of Radiology
103.	Adam Yu Solon High School	Role of IL-33 in inflammatory bowel disease-related fibrosis	Theresa Pizzaro, PhD	Department of Pathology
104.	Chelsea Zheng Beachwood High School	Employing 3D Choropleth Geospatial Maps to Evaluate Colorectal Cancer Incidence Rates	Fred Schumacher, PhD	Department of Population and Quantitative Health

ABSTRACT #1

Young Adult Substitution of Flavored Cigarillos with Menthol Cigarettes

Nichele Abeyesundere, Shaker Heights High School; Christopher Otieno, University of Kentucky; Catherine Osborn, MA, Prevention Research Center for Healthy Neighborhoods, CWRU School of Medicine; Elizabeth Klein, PhD, MPH, Ohio State University; Amanda Quisenberry, PhD, Department of Health Behavior, Roswell Park Comprehensive Cancer Center; Erika Trapl, PhD, Department of Population and Quantitative Health Sciences, Case Western Reserve University

Background:
Flavored cigarillos are often used by young adults who smoke cigarillos. Young adult cigarillo users are also likely to use other tobacco products, such as cigarettes, E-cigarettes, hookahs and smokeless tobacco. Flavored cigarillo users may switch to these products if flavored cigarillos are banned.

Goals:
Evaluate the hypothesis that cigarillo smokers who have smoked menthol cigarettes would be more likely to substitute flavored cigarillos with menthol cigarettes when flavored cigarillos are not available. We sought to inform the FDA Center for Tobacco Products' policies on flavored cigarillos and menthol cigarettes.

Methods:
Young adults (21-28 years) who had used at least 2 cigarillos in the prior week were recruited through social media to complete an online survey. Participants reported self-identified gender, race/ethnicity, and current tobacco use behaviors, including ever and past 30-day use of menthol cigarettes. Participants were asked, "What would you do if you could not get flavored cigarillos?" with the option to choose all that apply from 15 options, such as quitting or substituting with another product. We conducted bivariate analyses on SPSS to assess whether substitution with menthol cigarettes varied based on whether a participant ever used or currently uses menthol cigarettes.

Results:
Overall, 586 individuals participated in the survey; 59% of the sample identified as female, and the mean age was 24.5 years. Nearly 43% identified as Black or African American and 39% identified as White. Overall, 77.9% of participants have ever smoked a menthol cigarette, and 49.6% smoked menthol cigarettes within the past 30 days. Over half (52.1%) of Black respondents reported past 30-day menthol cigarette use compared to 47.3% of White participants. Of current menthol cigarette users, 14.3% would switch to menthol cigarettes if they could not get flavored cigarillos, compared to 3.3% of non-current menthol users ($p<0.001$). Notably, 10.9% of ever menthol cigarette smokers would switch to menthol cigarettes if they could not get flavored cigarillos while none of the never users would do so.

Conclusions:
Although most cigarillo smokers would not choose menthol cigarettes when flavored cigarillos are not available, participants who had ever used or currently use menthol cigarettes were significantly more likely to substitute their flavored cigarillos with menthol cigarettes should flavored cigarillos be unavailable. The exclusion of menthol cigarettes from restrictions on flavored tobacco products could exacerbate nicotine dependence and disparities in tobacco use.

Nichele Abeyesundere is a Martha Holden Jennings Scholar

ABSTRACT #2

COVID-19 and Transplant Patients: Covid Vaccine Hesitancy Among Adult Kidney Transplant Recipients

Amal Aboumerhi, Westlake High School; Edmund Sanchez, MD; Meelie DebRoy, MD, Kenneth Chavin, MD, PhD, Transplant and Hepatobiliary Surgery, Case Western Reserve University

Background:
Rapid development and deployment of various vaccines against the SARS-Cov-2 virus has been instrumental in the management and containment of the current global pandemic. The virus, also known as COVID-19, is a deadly disease that causes primarily respiratory symptoms if contracted through airborne or surface transmission. Two covid vaccines administered by Pfizer-BioNTech and Moderna, have both been tested to be over 94% effective at preventing severe COVID-19 symptoms in the United States. However, many Americans remain skeptical or hesitant about receiving the vaccine, for a variety of reasons. Solid organ transplant recipients are at the highest risk for poor outcomes if they contract the disease. Transplant patients may choose not to receive the vaccine regardless of its benefits, as some are concerned of organ rejection or remain as a part of the population skeptical about the vaccine's effectiveness. In this study we will review the number of adult kidney transplant patients hesitant to receive the vaccine at the University Hospital Cleveland Medical Center in Cleveland, Ohio, and how their decision may affect their delay in immunization in the midst of the coronavirus pandemic.

Goals:
The goal of this literature review is to gain insight into the reasoning of the population of kidney transplant patients hesitant to receive the vaccine. This review will go into depth regarding the understanding of specific candidates in the study who chose to receive the SARS-CoV-2 vaccine or why they opted against it. We will attempt to determine if the willingness of our specific population of transplant patients to receive the vaccine is aligned with the general population's demographics regarding covid vaccine hesitancy.

Materials and Methods:
We gathered information from clinical databases of patients transplanted at University Hospitals, Cleveland, Ohio, specifically regarding vaccine status of adult kidney transplant patients. We compiled data regarding age and ethnicity in an effort to delineate possible reasons for decisions regarding vaccination.

Results:
In this study, 30 candidates provided responses regarding whether they received their COVID vaccine or not. The 30 candidates consisted of 18 males (age 21-73 years), and 12 females (age 32-69 years). The ethnicity of patients was ~56% White, ~36% Black, ~6% identified as either Middle Eastern or Asian. In this study, 14 patients are fully vaccinated, 2 are not vaccinated by choice, 3 received their first dose, and 10 patients were recorded for alternative reasons.

Conclusions:
When comparing the data extracted from our databases to the general population's demographics on COVID vaccine hesitancy, ~46% of our kidney transplant population is fully vaccinated. According to the CDC, 48.3% of Americans are fully vaccinated. These two populations contain similar results regarding vaccinated individuals, whether they be transplant patients or regular individuals. It may be concluded that transplant patients fall under the same category as the general population regarding their hesitancy for receiving the vaccine because of demographic factors such as age, race, or ethnicity.

ABSTRACT #3

Characterization of the Role of Smooth Muscle Jagged1 in Modulation of Myogenic Tone

Nassim Aidja, Mayfield High School; Sarah Hoffman; Aaron Proweller, MD, PhD,
Department of Medicine, Case Western Reserve University

Background:
More than 3 million people yearly are diagnosed with high blood pressure (BP) or hypertension, which is a major risk factor for myocardial infarction (MI), stroke, and death. Evidence suggests that the Notch signaling pathway may be involved in the regulation of normal blood pressure (BP), which relies on the myogenic function of arteries. Normal myogenic function features a constrictive vascular response to increase pressure, maintaining optimal blood flow and BP to vital organs. In the Notch pathway, ligands Jagged1 and Jagged2, and delta-like proteins D(11)1, D113, D114, attach to cell receptors Notch1-Notch4, to initiate the pathway which causes the expression of proteins involved in the Notch pathway. Depending on the ligand, the response may be an increase in myosin light chain kinase (MLCK) or myosin phosphatase (MP.) The Jagged1 ligand results in an increase in MLCK and related vasoconstriction. The reverse occurs with the Dll4 ligand, which causes an increase in MP and related vasodilation. Both MLCK and MP participate in the myogenic response. Presently, we are studying the involvement of the Notch pathway in myogenic response to better characterize the role of the pathway in BP regulation. Through intensive studies of the Notch pathway, we eventually aim to develop novel therapeutics with the potential to alleviate the risk of MI and stroke.

Goals:
The goal of this project is to characterize the involvement of elements of the Notch pathway, including the Jagged1 ligand, in regulating myogenic tone.

Materials And Methods:
3rd order mesenteric arteries were obtained from 8-12 week old littermate control mice (SM-J1 +/+), and 8-12 week old adult male SM-Jag1 -/- deficient mice. Vessels are placed onto the pressure myograph in physiologic saline solution (PSS). Pressure is applied onto the vessels in a graded fashion and myogenic tone is measured by diameter changes of the artery.

Results:
In the past, my lab has observed impaired vasoconstriction to chemical agonists or depolarization upon Jagged1 knockdown in vessels using wire myography and has also observed a decrease in MLCK protein as measured by a western blot. Using pressure as a stimulus, we expect to see a decreased myogenic response in arteries from SM-Jag1 -/ mice, a finding that would extend the role of the Jagged1/Notch as a regulator of vasoreactivity in response to agonists, depolarization, or even pressure stimulation. Optimization of the experimental protocol for pressure myography is in progress with results forthcoming.

Conclusions:
Should we see a decreased myogenic response in the Jagged1-deficient mice, this would further underscore our lab's view that Jagged1 is essential to vasoconstriction and overall vascular homeostasis. This would help to further characterize the Notch signaling pathway's role in modulating BP, which has the potential to lead to the development of novel alternative therapeutics for vascular hypertensive disease.

ABSTRACT #4

Lymphatic Filariasis

Jordan Alexander, John F. Kennedy High School, Krufinta Bun; Christopher King, MD, PhD, Department of Pathology, Case Western Reserve University

Background:
Lymphatic Filariasis (LF) is a tropical disease transmitted through mosquitoes that carry a parasite called nematodes, also known as roundworms. The nematodes begin to grow and live in a human's lymphatic system, which can be from 5-7 years and can cause damage and dysfunction in the lymph system. Medicines have been; recommended to help with LF by the Mass drug administration (MDA).

Goal:
The goal of this research/ project is to measure lymphatic Filariasis (LF) as well as see why some people who have received treatment have had reactions while others haven't.

Methods:
Literature; Study and time methods begin to show estimates globally of the prevalence of FL; brought estimated numbers of individuals from region to region.

Results:
I expect in about 5+ years that there will be a very effective treatment that works for the majority of people diagnosed with LF, believing that having a very effective treatment will lower the infection rate.

Conclusion:
I can conclude that with studies, the infection rate has declined, but help is necessary for large regions. In rural communities, there is ~~a lot of~~ miscommunications when it comes to the medicines.

Supported in part by R25 CA221718

ABSTRACT #5

Determining whether *Candida auris* species generate more mutations for resistance when challenged with antifungal treatment compared to other species of candida and whether more mutations in *C.auris* (as it becomes resistant to antifungal) will occur in hotspot 1 than in hotspot 2 of the FKS1 gene

Manal Alkabani, Cleveland School of Science and Medicine; Thomas McCormick, PhD, Department of Dermatology, Case Western Reserve University

Background:

Candida auris **(*C. auris*) is an emerging pathogen that has been gaining worldwide attention due to the serious global health threat and high mortality that it presents. This pathogen species was first identified in Japan in 2009, where it was isolated from the external ear canal of an infected individual. *C. auris* can easily colonize patients' skin and other body sites, including nails and wounds, and this colonization can lead to various invasive infections (candidiasis). The global health threat that this species presents is due to a major characteristic that this species acquires: *C.auris* is a multi-drug resistant pathogen. Approximately 90% of *C.auris* strains/isolates are resistant to one of the most common types of antifungal treatment for candida species, fluconazole. Other examples of antifungal drugs that a proportion of isolates of this species are resistant to include amphotericin B and echinocandins, both considered to be highly efficacious antifungal agents. Because of its resistance to multiple antifungal drugs, treatment options for *C.auris* are highly limited. Not only is resistance to antifungal drugs a major topic in regards to *C. auris*, but detection of this pathogen is difficult, as this candida species can sometimes be mistaken for other species of candida, particularly *Candida haemulonii*.**

Goals:

Ultimately, prove/disprove the hypothesis that *Candida auris* generates more (potentially resistant) mutations following an antifungal challenge compared to other species of *Candida*. The secondary goal of this study is that most mutations that will occur in C.auris (as it becomes resistant to antifungal) will occur in hotspot 1 of the FKS1 gene.

Materials and Methods:

Antifungal resistant liquid cultures of the candida species that were utilized (*c.auris, c.tropicalis, c.albicans*), were grown in RPMI 1640 supplemented with antifungal treatment - the 4 types of antifungal treatments this project utilized (this step was done multiple times, with a doubling of the antifungal supplementation for each challenge- starting with a supplementation of 0.0625 µg/ml and ending at a concentration of 1ug/ml). After each passage in RPMI 1640, the absorbance of each liquid culture was measured spectrophotometrically to monitor cell density, a reflection of cell growth. After each absorbance measurement, 1 x 106 cells (from the previous liquid culture) were selected, and were grown in RPMI 1640, with a doubled antifungal treatment supplement. After the last passage/growth with RPMI 1640 supplemented with 1 µg/ml of antifungal treatment, colonies of resistant organisms were grown on PDA agar plates and DNA was extracted from the colonies for genome sequencing of resistant (mutant) strains of the candida and from the control- antifungal susceptibility candida (wild type).

Results:

As demonstrated by the viability and growth graphs (OD 490 nm measurements), *C. auris* is the candida organism that showed the least decrease in the OD measurement magnitude throughout the RPMI 1640 growth passages, in the multiple types of antifungals used, and throughout the candida growths passages (even though a great decrease in OD measurements magnitude was seen towards the end of the passages of antifungal challenge, as the antifungal treatment magnitude increased) in comparison to the other types of candida organisms utilized. This observation correlates with the idea that *Candida auris* is the least susceptible *Candida* for anti-fungal treatment, and it may acquire greater resistance to these antifungal treatments, thus generating more mutations in response to being

ABSTRACT #5 CONTINUED

challenged with antifungal treatment compared to *C. albicans* and *C. tropicalis* (other strains of *Candida* also observed to be pathogenic in many patients). As the optical density changes illustrate, the density (of cell count) of the *Candida* liquid cultures was reflective of resistance at a higher level in the *C. auris* strain. The analysis of optical density (in regards to cell amount) demonstrates that the liquid cultures of the *Candida* formed resistance to the antifungal treatment- resistance which may be based on molecular (DNA) mutation, meaning that the candida organism generated mutations needed for generating antifungal resistance. The magnitude of the optical density (OD) measurement for each cell culture of candida correlates with susceptibility or resistance of the candida to the treatment. Whereas less OD measurement decrease after every increasing antifungal treatment, it is more likely that the candida in the corresponding liquid culture is not being affected (and therefore its less likely that the cells in that liquid culture are decreasing in amount) by the antifungal treatment, and this alludes to the resistance that the candida acquires against the antifungal drug. Even though extended research/research time was needed to complete all the genome sequencing, genome sequencing of c.auris was completed, and it was determined that hotspot 1 and hotspot 2 of the gene FKS1 acquired the same amount of mutations (a total of 37 mutations in each hotspot). However, HS1 mutations tended to have better consensus alignments to their predicted mutation sequence- meaning that they matched up more closely to the predicted mutations than those of HS2.

Conclusion:

PubMed, it was concluded that Candida auris is the candida species that has shown the most resistance to multiple types of antifungal treatments- indicating that a great magnitude of mutations have possibly occurred as the background for such great resistance; Having been defined as the most resistant type of specie, it can be presumed that it is, therefore, also the specie that generates the most resistance for mutations (since resistance correlates with the generation of mutations). In the project performed, The OD (490 nm) measurements of the candida organisms utilized, after each antifungal challenge growth passage, that were performed and analyzed in this study, allude to this conclusion as well. Even though extended research was needed to confirm the initial hypothesis/goal of this study, genome sequencing of C. auris was accomplished, and the results correlated with the secondary hypothesis.

Manal Alkabani is a Mort and Iris November Scholar

ABSTRACT #6

Comparison of Lymphatic Filariasis Antigen Diagnostic Assay: Extended Read vs per Protocol Read

Raneem Almhana, St. Joseph Academy; Daniel Tisch, MPH, PhD, Department of Population and Quantitative Health Sciences, Case Western Reserve University

Background:
Eliminating lymphatic filariasis relies on diagnostic tests that confirm infection, and efficient mass drug administration. In the past, multiple rounds of treatment have proven effective in lowering infection rates. In Papua New Guinea, the focus of this paper, the severity of the disease has largely been mitigated in several regions. However, variation in results of the antigen diagnostic test over time has warranted a need for further review of test scores.

Goals:
The goal of this research is to understand the numerous dimensions of lymphatic filariasis, including the complexity of testing for the disease.

Methods and Materials:
Literature from the PubMed database on lymphatic filariasis and surrounding topics was reviewed. Raw data from a field notebook in a study on lymphatic filariasis in Papua New Guinea was transcribed and organized in a dataset in Excel. The data was structured in a form that highlighted the changes over time that the tests had undergone. Tables were created with the 10 minute and 12 hour scores of the test results.

Results:
While the results are yet to be finalized, trends show that a small, but significant percentage of antigen tests changed over the 12-hour period.

Conclusions:
In an analysis of diagnostic tests, it was found that out of the results that changed after 12 hours, a majority intensified, indicating a stronger microfilariae presence than reported at 10 minutes. Per protocol, the result is provided after 10 minutes. This change from the original score indicated that test scores may also need to be reviewed after a longer period of time. Future implications of this data are improving prognosis in lymphatic filariasis patients and having more accurate infection rates in regions affected by the disease.

Raneem Almhana is a Sam Miller Scholar

ABSTRACT #7

Pathophysiology of α-Synuclein in the Eye

Rithvik Ayyagari, St. Ignatius High School; Ajay Ashok; Alex Kritikos; Suman Chaudhary; Neena Singh, MD, PhD, Department of Pathology, Case Western Reserve University School of Medicine

Background:

Synucleins are small, soluble proteins that are found most commonly in neural tissue while also being detected in other organs in the body. The synuclein family is comprised of three proteins: α-synuclein, β-synuclein, and ɣ-synuclein. Although the full functionality of the proteins has not been thoroughly discovered yet, it is known that α-synuclein functions in synaptic transmission in the brain and the retina. α-synuclein and β-synuclein are found primarily in brain tissue whereas ɣ-synuclein is found in the central nervous system and the retina. Each of these proteins have implications on the body in different ways. α-synuclein is implicated in the pathogenesis of Parkinson's Disease (PD), a neurodegenerative disorder of the elderly. Additionally, recent studies have shown that α-synuclein has implications in the retina; specifically, retinal degeneration that is associated with PD. This is attributed to the aggregation of α-synuclein in intracellular structures called Lewy Bodies. Physiologically, α-synuclein aids in the regulation of synaptic vesicle traffic as well as neurotransmitter release. The neurotransmitter release is through the effects on the SNARE complex which mediates vesicle fusion. The problems with α-synuclein arise when it misfolds and in beta-sheet rich aggregates. Furthermore, the protofibrils of α-synuclein are a toxic species that disrupt cellular homeostasis and mediate neuronal death and as a result, have an adverse effect on synaptic function.

Goal:

The goal of this project was to further the understanding of the pathophysiology of α-synuclein in the eye as well as to better understand the link between α-synuclein in the eye and the pathogenesis of PD-associated ocular disorders.

Materials and Methods:

We collected tissue lysates from knockout α-synuclein (KO) and wild-type (WT) mice eyes and conducted a Western blot comparing the expression of α-synuclein in the anterior and posterior segments of both the KO and WT mice. A sample from bovine aqueous and vitreous humor was analyzed in parallel as a control.

Results:

Results from the initial Western blot were inconclusive because bands corresponding to α-synuclein were detected in both KO and WT mice samples. We are in the process of conducting additional blots from WT and KO mouse brains and other tissues that are known to express α-synuclein.

Conclusion:

Further research is required to more clearly understand the presence of α-synuclein in KO and WT mouse samples.

Rithvik Ayyagari is a Sam Miller Scholar

ABSTRACT #8

Post-Translational Modification of JAB1: A Newly Identified Proto-Oncogene in Prostate Cancer Cells

Anusha Bangalore, Westlake High School; Leo Wu, Department of Biochemistry; Guang Zhou, PhD, Department of Orthopedics; David Danielpour, PhD, Case Comprehensive Cancer Center, Case Western Reserve University

Background:

C-Jun activation domain-binding protein-1 (JAB1) was first identified as a co-activator of the transcription factor c-Jun. Researchers later identified JAB1 as the fifth subunit of an eight multi-protein complex known as the COP9 signalosome whose primary function is to control the activity of Cullin E3 ubiquitin ligases through excision of a ubiquitin-like peptide called NEDD8 from Cullins. Neddylation is a type of post-translational modification that tags proteins with NEDD8, through a cascade involving E1, E2 and E3 enzymes distinct from protein ubiquitination. Removal of NEDD8 from proteins is known as de-neddylation, and JAB1 is the catalytically active subunit in COP9 critical to such de-neddylation. JAB1 controls many important cell functions, such as cell cycle, apoptosis, and DNA damage response. In cancers, such functions are deregulated, likely in part because of deregulation of JAB1. JAB1 is over-expressed in certain cancers. Dr. David Danielpour's laboratory recently found that JAB1 functions as an oncogene in prostate cancer cells. A recent study showed that JAB1 is phosphorylated, meaning a phosphate group is added to it, at serine and threonine residues, and that such post-translational modifications control the function of JAB1 in the COP9 signalosome. Therefore, it is important to investigate the phosphorylation of JAB1 as a potential cancer therapeutic target. Our bioinformatic data-mining of pulmonary and lymphocyte cell lines helped us predict JAB1 may be phosphorylated at tyrosine residues. By using immunoprecipitation and Western blot analysis, we are testing this prediction and studying the regulation and function of such phosphorylation using prostate cancer cell models.

Goals:

Our research aims to study the post-translational modification of JAB1 by its phosphorylation. We are testing the hypothesis that JAB1 undergoes phosphorylation at tyrosine residues and that this phosphorylation regulates JAB1's function using prostate cancer cell models.

Materials and Methods:

Western blot was used to analyze the change in global tyrosine phosphorylation and Neddylation of proteins in the PC-3 prostate cancer cell line treated with either epidermal growth factor (EGF), insulin, fetal bovine serum (FBS), orthovanadate, or a combination of all those growth factors. Rabbit anti-NEDD8 and mouse anti-phospho-tyrosine antibodies were used as the primary antibodies, and Donkey anti-Rabbit HRP and Donkey anti-Mouse HRP were used as the secondary antibodies. Jab1 was immunoprecipitated from cell lysates using an antibody against Jab1 and protein A immobilized to a matrix. Immunoprecipitated Jab1 was then eluted by heating with SDS and analyzed for tyrosine phosphorylation by western blotting.

Results:

Based on our analysis of the western blots, treatment of PC-3 prostate cancer cell line with EGF, insulin, FBS, orthovanadate, and the combination of all of those factors promoted protein neddylation, correlating with increased tyrosine phosphorylation. Such treatments promote the tyrosine phosphorylation of proteins that co-migrate with JAB1 on Western blots, consistent with a potential phosphorylation of JAB1. We are conducting immunoprecipitation experiments to test whether JAB1 is tyrosine phosphorylated in PC-3 cells treated with orthovanadate.

ABSTRACT #8 CONTINUED

Conclusion:

Data mining helped us to identify phosphorylation of JAB1 at tyrosine residues in various pulmonary lymphocyte cell lines. Our western blots results on PC-3 cells are consistent with the possibility that mitogens induce the tyrosine phosphorylation of JAB1 (based on protein size) and alter the neddylation of various proteins. However, we are not clear if such altered neddylation is due to JAB1, another unit of the COP9, or unrelated to COP9. Further research is still needed to determine if JAB1 is tyrosine phosphorylated, and if so, the specific tyrosine phosphorylation site on JAB1. The latter can be determined through mass spectrometry. Currently, our lab is working on generating a FLAG-tagged JAB1 overexpression vector to better observe the effect of tyrosine phosphorylation. Further work will be necessary to test the effect of tyrosine phosphorylation on the function of JAB1.

ABSTRACT #9

COVID-19 and Damage to The Lungs

Rhycordia Barner, John F. Kennedy High School; Debora Bruno, MD Department of Medicine, Case Western Reserve University School of Medicine

Background:
Since COVID-19 has surfaced, fourteen percent of cases have been severe and damaging to the lungs. Since covid-19 is a respiratory disease, it will infect the respiratory tract, including the lungs. Coronavirus can infect the upper or lower part of your respiratory tract. It travels down your airways. The lining can become irritated and inflamed. In some cases, the infection can reach all the way down into your alveoli.

Goals:
The goal of this research is to discover ways that covid-19 affects and damages the lungs

Materials and Methods:
literature

Results:
My expectations are that more research needs to be done on COVID-19 in the lungs and that a cure may be found to prevent or reverse damage to the lungs from Covid-19.

Conclusions:
Based upon research, COVID-19 has had a humongous negative effect on the lungs and the respiratory tract. Which means that more research should be done within the next couple of years.

Supported in part by R25 CA221718

ABSTRACT #10

The Obesity Trends Found by Ohio Counties with Certain Cancers

Rachel Bart, Cleveland School of Science and Medicine; Weichuan Doug; Siran Koroukian, PhD, Department of Population and Quantitative Health Sciences, Case Western Reserve University

Background:
Cancer is the leading cause of death in the United States. Some of these cancers are prostate, cervical, and breast. Breast cancer has been known to occur in one out of every three women within their lifetime. Some risk factors to getting breast cancer include getting older, mutations in genes like BRCA1 and BRCA2, and being obese and drinking alcohol. Cervical cancer is almost always caused by HPV which is transmitted through sexual contact. Just as with Breast cancer, the likelihood of getting prostate cancer in men increases as they age or if an individual has a family history as well as being obese. If people are regularly screened and know the risk factors that contribute to cancer, their prognosis can have a better outcome.

Goal:
The goal is to figure out, using scientific data, what Ohio counties have a higher percentage of cases and deaths from individuals with prostate, cervical, and breast cancers in the area and how much of it contributes to obesity.

Materials and Methods:
What is needed is a computer that is able to record the data and a program like Tableau that can take that data and turn it into a diagram so you can look at the trends. You will also need to look up reliable sources so you can get the data you need. Most of the data that I used was from the Ohio reports or from the CDC.

Results:
For each of the cancers they have a higher percentage of cases and deaths in different counties. However, in the county of Ottawa in all three cancers they had a higher percentage of cases and one of the lowest percentage of deaths. It has also been found that the link between obesity and these cancers are not directly linked with not much correlation with one another.

Conclusion:
Obesity and prostate, cervical, and breast cancer are not directly linked to one another in the cases or in the deaths in certain counties. Much more research needs to be done to determine the risk factors to get prostate, cervical, and breast cancer and why so many people in a certain county have a higher risk of death than others.

Rachel Bart is a Martha Holden Jennings Scholar

ABSTRACT #11

The Effect of NK Cells on Neuroendocrine Tumors

**Anna Beck, Laurel School; David Wald, MD, PhD, Department of Pathology,
Case Western Reserve University**

Background:
Natural killer cells are immune lymphocytes that play a critical role in the destruction of virally infected or cancerous cells. Like T lymphocytes (T cells), they can be isolated and expanded from peripheral venous blood and reinfused into a cancer patient for immunotherapy. Natural killer cell therapy is being investigated as an alternative to T cell therapy because NK cells are less expensive to obtain, easy to enhance, and do not have the side effects of T cell therapy in some cases. Recently a number of studies have demonstrated that NK cells are effective against many types of hematologic and solid tumors both in vitro and in mouse models. Neuroendocrine tumors are a rare, complex branch of tumors with many subtypes, including those that cause pancreatic islet cancer. Because they are so diverse, neuroendocrine tumors are difficult to diagnose and to treat. For pancreatic cancer patients, few treatment options are available, and they usually have poor prognosis. NK cell therapy could be examined as a possible treatment option.

Goals:
The goal of this project was to measure the effective cytotoxicity of peripheral blood NK cells on a pancreatic islet carcinoma cell line, and thus determine if NK cells can be further investigated as a treatment for neuroendocrine tumors.

Materials and Methods:
First, we prepared the effector and target cells. We cultured the pancreatic islet carcinoma cells from a QGP-1 cell line (Accegen Biotech ABC-TC0918). Next, we isolated NK cells from the peripheral blood mononuclear cells from a healthy donor. Then we used a calcein AM standard killing assay to measure cytotoxicity: the killing capacity of the NK cells. Our E:T cell ratios in the killing assay were 0:1, 1:1, 2:1, 5:1, and 10:1. The results were determined using flow cytometry.

Results:
The data from the first assay may be inaccurate because we had never used QGP-1 cells in the flow cytometer before. However, according to the first assay, the number of QGP-1 pancreatic carcinoma cells decreased. Successively greater numbers of cancerous cells remained in the wells with respectively smaller numbers of NK cells.

Conclusions:
The killing assay must be repeated for exact data. However, there seems to be some implication that the NK cells were effective against the neuroendocrine carcinoma cells. Through further experimentation, we will determine whether NK cells can be tested in mouse models against neuroendocrine tumors. Our hope is that a potential treatment for pancreatic neuroendocrine cancer can be found in NK cell therapy.

ABSTRACT #12

A Novel Fluorescent Dye Based Method for Detecting Autophagy

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Department of Genetics and Genome Sciences, Case Western Reserve University

Background:
Autophagy is a process in which a eukaryotic cell clears and recycles damaged organelles when necessary. Although a key survival-mechanism for the cell, when unregulated, autophagy can be bad as it could clear out healthy organelles that are necessary for cell survival. This can lead to many diseases. Autophagy is also a relevant part of cancer. Autophagy plays a two-sided role in cancer as it suppresses the growth of cancer cells, and yet cancer cells also take advantage of the recycled cytoplasmic materials as it uses the energy from the materials to survive under rough conditions. Current methods for detecting autophagy use fluorescent probes such as GFP-LC3 – a fusion of the fluorescent protein Green Fluorescent Protein (GFP) and the autophagosomal membrane associated microtubule-associated protein 1A/1B-light chain 3 (LC3). The expression of GFP-LC3 necessitates the use of transfection. These methods are all somewhat inefficient. Some require lots of time to perform transfections, with some cell lines being particularly resistant to transfection. GFP also tends to aggregate, leading to the observation of puncta even without autophagy. Many methods using amino groups change cell activity and levels of pH in the cells. None of the methods can be executed in all cellular states and environments (e.g., Blotting methods cannot be used to monitor autophagy in real time on live cells as it requires lysing all observed cells). Enter 6.1d: a novel red fluorescent dye with selectivity towards lysosomes. 6.1d has proven to be a promising detector of autophagy. Its low cytotoxicity and ability to maintain cellular pH levels allows for the live staining and imaging of cells. Additionally, 6.1d can be introduced into cells without transfection, merely requiring incubation with cells, which enables the method to be executed in significantly less time compared to existing methods.

Goals:
The goal of this research was to determine if the 6.1d compound could identify autophagy. If so, then 6.1d would serve as a powerful alternative to existing methods for the detection of autophagy with its short incubation times and low cytotoxicity.

Materials and Methods:
6.1d and GFP-LC3 were introduced to colon cancer cells of the line HCT-116. The cells were incubated with 6.1d for 30 minutes and looked at under imaging technology. Patterns of puncta were searched for in the images. We also co-stained the cells with GFP-LC3 and looked for co-localization of our imaging and the puncta locations. The cells used were incubated with the autophagy-inducing drug Rapamycin.

Results:
In our initial experiments, we found that in our sub-confluent cell cultures, there was co-localization of the puncta in the 6.1d imaging and the LC3 imaging, however most of our cultures were too confluent which initiated a difficulty in reading the images and finding the presence of autophagy. The few results we have been able to obtain proved our hypothesis that the 6.1d dye can act as an autophagy detector. The well in which co-localization was observed had been transfected with GFP-LC3 and incubated for 48 hours, starved for four hours in McCoy's 5A medium without Fetal Bovine Serum (FBS), and incubated with 6.1d for thirty minutes at 2 micromolar concentration.

Conclusions:
We can conclude from what we found so far that there was co-localization with 6.1d and GFP-LC3, showing that 6.1d works as an autophagy detector under certain conditions.

ABSTRACT #13

Effects of Processed and Red Meat on Blood Sugar Levels

Josh Bickerstaff, University School; Thomas LaFramboise, PhD, Department of Genetics and Genome Sciences, Case Western Reserve University

Background:
It is generally known that the intake of carbohydrates, such as breads, cookies, and other sweets increase blood sugar levels, especially in diabetics who are dependent on insulin. This is because insulin in the body is used to break down sugars that stem from carbohydrates that people eat. If you eat too many carbohydrates, it will lead to more sugars in your bodies, which will result in the insulin possibly being overwhelmed. This is what generally leads to high blood sugar levels. However, many scientists have found that the consumption of red and processed meats lead to increased blood sugar levels, even though the meat contains little to no carbohydrates. This is likely because of high levels of iron and amino acids in the meat that lead to insulin resistance. Resistance to insulin, whose function is to break down sugars in the body, will result in more sugar in the body, thus creating increased blood sugar levels.

Goal:
The goal of the research project is to see how and to what extent does red and processed meat increase blood sugar levels in humans.

Materials and methods:
63,257 adults between the ages of 45-74 had their red and processed meat intake monitored for 11 years. Also, another 357 adults between the ages of 40-70 had their red and processed meat intake monitored for a year.

Results:
In the 11 yearlong experiments, it was found that the highest quartile of red and processed meat intake had a 23 percent increase in risk of diabetes, which is a disease that stems from the body producing little to no insulin in order to break down sugars in the body. However, the lowest quartile of people who consumed red and processed meat only experienced a 15 percent increase in risk of diabetes. In the yearlong experiment it was found that 30 percent of the participants who ate red and processed meat regularly experience insulin resistance.

Conclusion:
The consumption of red and processed meat leads to an increase in blood sugar levels. The level of iron in red and processed meat causes oxidative stress, which leads to insulin resistance. The high levels of amino acids in the meat hinder the normal metabolism of blood sugar, which leads to insulin resistance as well.

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ABSTRACT #14

The Effect of Diet on Aviator Performance

Thomas Blossom, University School; Molly McCarthy; Ian Vannix; Cassandra Barone; Seth Fillioe, PhD, Michael Decker, PhD, Department of Physiology and Biophysics,
Case Western Reserve University

Background:
Aviators who are exposed to multiple long duration, high altitude flights ("sorties") often experience cognitive fatigue post-sortie. One of the underlying causes of this fatigue could be connected to diet. Recent studies show a relationship between specific diets and an inflammatory response in the human body. Inflammation is closely regulated by the body, to eliminate the initial cause of injury or irritation. In response to inflammation, various inflammatory biomarkers such as cytokines and chemokines can be secreted. The Decker Lab has been examining the physiological response of these biomarkers in relation to extreme aviation conditions.

Goal:
The goal of this study is to observe the effects of an aviator's diet on their cognitive performance and determine if there is a relationship between high-inflammatory diets and fatigue levels.

Methods:
Data from a previously executed study in the Decker Lab was analyzed. In that study, aviators (n = 22) were assessed over the course of a week (Baseline = Sunday, Midweek = Tuesday, Final = Thursday). The assessment included a 24-hour diet recall, a self-administered five-category multidimensional fatigue index (MFI) test and blood collection for subsequent serum biomarker analysis. Using the diet recall from this data, a pro-inflammatory score (2) was given for each day. Scores were compared against each participant's MFI and various biomarker data to assess for a relationship.

Results:
Aviators were previously separated into two groups, those whose physical MFI increased over the week and those whose did not. There were no statistically significant differences between the inflammatory scores of the two groups at any of the three time points. Aviators were separated into two new groups, those whose inflammatory scores increased throughout the week and those who did not. Biomarker concentrations at each time point were compared between the two groups. Ghrelin showed a statistically significant difference at the final time point, but not at baseline or midweek. The aviator group with decreased/unchanged inflammatory score showed a higher concentration of ghrelin at the final time point.

Conclusions:
There is no direct relationship between fatigue and dietary inflammation in this study. There is a relationship between inflammatory score and ghrelin. While there may be no direct relationship between aviator performance and dietary inflammation, other studies have shown that there is a relationship between diets high in protein and poor aviator performance. There are many proinflammatory forms of protein, which could explain this relationship. Some examples of proinflammatory proteins are burgers or processed meats.

ABSTRACT #15

Excess Dietary Iron and Intestinal Cancer

Emily Boron, Shaker Heights High School; James Swain, PhD, RDN, Department of Nutrition, Case Western Reserve University

Background:
Many research studies have shown links between diets and cancer development. Iron, like other minerals, is necessary for tissue growth and cellular homeostasis, but in excess can promote cancer cell development and growth. The purpose of this project is to combine data from a literature review with lab data to investigate and gain knowledge of possible links between diet and cancer. The data should show that as excess dietary iron increases, the incidence of cancer, particularly in the intestine, increases.

Goals:
The goal of this project is to gain knowledge through gathering information on the relationship between diet and cancer, and present it for the benefit of patients and the medical community.

Materials and Methods:
I conducted a literature review to study the relationship between excess dietary iron and cancer, using search engines such as Google and Pubmed. Common search phrases that I used were "excess dietary iron," "excess dietary minerals," and "iron and cancer." The number of results varied depending on the specificity of the search, but it could range from about 1000 to 100. I did not exclude studies using animals, thus utilizing both human and animal studies in the area of diet and cancer literary research. Lab data for review was derived via use of adenomatous polyposis coli mice, which are an animal model for human familial adenomatous polyposis, in turn used to study the effect of dietary iron on intestinal tumorigenesis. Mice were divided into three treatment groups, based on dietary iron: Normal, Moderately High, and Excessively High. After 2.5 months, mice were sacrificed and intestinal tissues were processed using immunohistochemistry (IHC), in which cell proliferation (ki67) and cell apoptosis (TUNEL) markers were evaluated in the tissues. The morphology of the intestines was also observed (microscopy), including the identification for an early formation of a tumor.

Results:
As excess dietary iron increases, so does development of cancer, particularly intestinal cancer. I plan to add more information to this section in my final report.

Conclusions:
Excess dietary iron increases the incidence and development of intestinal cancer. Providing new information related to the effect of iron, and other minerals on cancer development may improve cancer prevention and treatment approaches by increasing awareness of the widespread and relatively unknown issue of the effects of excess dietary minerals.

Emily Boron is a Martha Holden Jennings Scholar

ABSTRACT #16

Dietary Restrictions to Improve the Imbalance of Autism Spectrum Disorder (ASD) Microbiome

Luke Brandon, University School; Dr. Mahmoud Ghannoum, Center for Medical Mycology, and Integrated Microbiome Core, Department of Dermatology, Case Western Reserve University

Background:
The microbiome has 10-100 trillion symbiotic microbial cells in the human body. Most of the cells reside in the gut. Because of interpersonal deviations in the microbiome, it can be beneficial in personalized medicine; it is hard to determine what specific microbes make a healthy microbiome, so a "core" of microbes is looked to for a healthy microbiome. A healthy microbiome is that of any community absent of disease or health condition. Dysbiosis (also known as imbalance), which has been linked to autism, of the microbiome is a perturbation from balanced ecology which can prolong, worsen, or introduce problems to the host's health. High diversity of bacteria in the microbiome has been associated with health and stability. The stability is linked to higher redundancy which is from a more diverse set of microbes. Autism spectrum disorder (ASD) is a range of neurodevelopmental disorders. The neurodevelopmental disorders are specified by impairment in social behavior, communication and language, and restrictive and repetitive behaviors, as well as digestive symptoms. Estimated 1 in 45 children in the US have ASD; that is a significant increase over the past two decades. Standard of care therapy can be beneficial. To be effective behavioral therapy, it requires full-time engagement of a one-on-one therapist over many years. ASD children usually suffer more from GI symptoms compared to neurotypical people, mainly suffering from diarrhea and constipation. Like the intestinal barrier, ASD people have been found with impaired brain interiors. The interaction between the gut and brain (referred to as Gut-Brain Axis) is heavily inferred by the fact that the severity of the ASD correlates to the severity of the GI problems. Perturbances in the gut microbiome have been linked to many diseases, which can be explained by the importance of the microbiome's interactions with the brain. Behavioral therapies are needed with the majority of ASD research focused on the genetic cause of ASD. Atypical microbiome in ASD people, and disruption of the microbiome in ASD is related to GI problems. There is an imbalance of ASD's microbiome compared to neurotypical people. There is evidence that the microbiome affects immune and metabolic functions, gene expression, and brain and behavior development. Research into the balance of microbiomes is greatly needed as treatment.

Goals:
Find diet restrictions to help fix the imbalance of ASD microbiome for helping ASD people with their digestive problems.

Methods:
Literature review

Results:
To boost the diversity of the microbiome, protein-plant and animal-fish oil, low fat, date fruits, digestible and non-digestible carbohydrates, walnuts, probiotics, and polyphenols. These restrictions also limit bacteria that people with ASD have too much compared to neurotypical counterparts.

Conclusions:
Dietary therapies may be effective for treating ASD and require further research.

ABSTRACT #17

African American Screening Guidelines and Reasonings for a different set of Guidelines for African Americans

Anaria Britt, Hathaway Brown School; Rachel Gardenhire, Erika Trapl, PhD, Prevention Research Center for Healthy Neighborhoods, Department of Population and Quantitative Health Sciences, Case Western Reserve University

Background:
Prostate cancer (PCa) is the deadliest type of cancer for an American male to get and is especially deadly for African American men. The mortality rate of African American men compared to Caucasian males is almost twice as much. Many factors contribute to the deadliness of PCa including heritability, environmental and social factors. African Americans' environments also impact the severity of the prostate and their biological make-up all contribute to these antigens. PCa can be determined by the polygenic risk scores, a process in which the genetic variant that a person has, is assessed to determine the heritability risk of a disease. Certain genetic factors increase the probability of getting prostate cancer and these genetic aspects are found higher in African American men.

Goals:
The goal is to prove African Americans have different levels of risk than other races and have different levels of Serum Prostate specific antigens and PSAD which all contribute to the likelihood of prostate Cancer. To make changes to the overall guidelines for African American men and have a different screening for them so that prostate cancer can be more clearly identified and be approached in the appropriate manner.

Materials and Methods:
A literature review was performed using keywords such as African American Men, Prostate Cancer, PSA, and Polygenic Risk Scores to gain the information that is used throughout the paper. For all of our searches it was mandatory to use the words prostate cancer and African American but there was more freedom when adding additional words to the search. While searching, we looked for articles with the outcomes, PSA levels and the factors that contribute to Prostate Cancer in the comparison of Caucasians and African Americans. In other studies, there was the testing of the environmental factors that could possibly contribute to the likelihood of prostate cancer.

Results:
Serum prostate specific antigen levels were higher in African Americans than in any other race. For African Americans, the PSAD (PSA Density) was .078 whereas in whites and Hispanics the levels were .057 and .065. There were also multiple environmental factors that contributed to the likelihood of prostate cancer such as higher saturated fat foods.

Conclusion:
The USPSTF (United States Preventive Services Task Force) should change the guidelines for African Americans to have sooner and mandatory prostate screening along with new guidelines to catch it sooner.

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ABSTRACT #18

Nanoscale Protein Delivery Implementation and Obstacles

Janae Camargo, Andrews Osborne Academy; Kristyen A. Tomcik; Emma DiLavore; Ann Hanna-Mitchell; Department of Nutrition, Michael Kavran; Christopher Flask; Department of Biomedical Engineering, Madhu Gargesha, Bryan Scott; Mandeep Singh; John Tilton, MD, Department of Nutrition, Case Western Reserve University

Background:
Gene therapies are medical treatment strategies involving the introduction of RNA or DNA into a cell resulting in genetic modifications which may be used for beneficial purposes such as disease treatment. These methods, however, come with their fair share of obstacles. An approach to potentially overcoming these issues involves the use of the novel nanoscale protein delivery (nanoPOD) platform which involves the use of lentivirus-based nanoparticles that have been engineered to safely "infect" a host cell and transfer proteins and RNAs across biological membranes.

Goal:
The goal of this research is to determine if nanoPODSs can be used as an effective *in vivo* option for the delivery of therapeutic genetic cargo. More specifically, this research aims to prove that any protein or gene that does get delivered can, in fact, also be expressed in an organism after its injection. How can the lab look to solve the obstacles that face successful gene therapy?

Materials and Methods:
Human embryonic kidney 293 (HEK293T) cells were chemically transfected with DNA (3µg) containing a region which encodes for Cre (Creates Recombination) – an enzyme used to carry out site-specific (lox-P) recombination events along with a viral envelope protein. NanoPODs were harvested from the cell supernatant (60 µl) three days post-transfection via filtration (0.8 µM filter) and purification (500 kD Tangential Flow Filtration columns) methods and resuspended in 2 ml of filtered (0.1µM) phosphate buffered saline (PBS). *In vitro* activity was assessed by spinoculating the nanoPODs into HEK293T cells which had been chemically transfected with a DNA plasmid which expresses a green fluorescent protein (ZsGreen) in the presence of Cre. Effective nanoPOD variants were injected into ai14-Cre-TdTomato mice either intravenously, intraperitoneally, or directly into lungs via intrabronchial instillation. Mice were analyzed using fluorescent imaging and/or immunohistochemistry to determine cargo delivery efficiency. Additionally, human sera-derived NK cells (107 cells in PBS) were labeled with 625 nm semiconducting quantum dots (Qdots) and subsequently injected into NCR nu/nu nude mice in order to visualized cell trafficking patterns using whole body cryo-imaging methods (CryoViz).

Results:
***In vitro* analysis showed effective delivery of nanoPODs using VSV-G, H5N1, BaEVRLess, hCMV-BaEVRLess envelope proteins. At present concentrations, direct injection of the nanaPODs into the bloodstream was insufficient to detect using fluorescent imaging methods. Intrabronchial instillation, however, showed evidence of delivery in lung tissue. Qdot625-labeled NK cells and cryo-sectioning analysis clearly identified cell trafficking to a number of organs, most notably the liver, lungs, and bone marrow.**

Conclusion:
Testing different viral envelope proteins to achieve cell-free systemic delivery of nanoPODs has yielded a number of promising avenues for cargo delivery. The continued optimization of protocols for direct injection and transport of nanoPODs are issues team members are working to solve. Similarly, optimizing conditions for introduction of transgenes into cells has been aided by Qdot analysis and novel whole-body imaging techniques. These data analyses provide new information, which will continue to help guide future nanoparticle-based gene editing research, including the use of CRISPR Cas9 for nanoPOD development.

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ABSTRACT #19

The Efficacy of Using Deep Learning Algorithms to Assess Epicardial Fat in CT Calcium Score Exams

Neha Chellu, Beachwood High School; Justin Pieper, Shaker Heights High School; Aishwarya Krishnan; Bradley Wu; Tao Hu; Ammar Hoori; David Wilson, PhD,
Department of Biomedical Engineering, Case Western Reserve University

Background:
Cardiovascular diseases are known to have a myriad of causes and predictors. Over the past two decades, several studies have researched the association between the volume of epicardial fat (EF) to one's risk of contracting coronary atherosclerosis and/or ischemic heart disease. To try to assess these risks, many cardiovascular risk assessments have been developed based on the volume of this fat. The main problem is that identifying the EF is a time-consuming process, taking radiologists several hours to perform manually. In order to improve efficiency, researchers have proposed the use of Artificial Intelligence (AI) to automate the process. Specifically, through the use of a complex multi-layered neural network model that can self-learn certain tasks based on a set of training and testing data—otherwise known as a deep learning algorithm. This project focuses on determining whether or not deep learning algorithms can be used to reliably and efficiently segment EF deposits in CT Calcium Score scans of the heart.

Goals:
The goal of this project was to perform a pilot study that would test the hypothesis that a sufficiently developed deep learning algorithm could be used to automatically and accurately identify EF in CT Calcium Score Scans.

Materials and Methods:
A set of 10 chest CT studies of adult patients was obtained from University Hospitals. Four components were focused on during the CT segmentations: pericardial sac (the lining of tissue directly surrounding the heart), visceral fat (adipose tissue in the abdominal cavity), epicardial fat (visceral fat overlapping the pericardial sac), and pericardial fat (visceral fat outside the pericardial sac). Two independent observers (NC, JP) used *3D Slicer*, an open source imaging software, to manually segment, these four components in the same 10 CT scans. These same scans were inputted into a deep learning algorithm (DeepFat) to perform automated segmentation. Statistical analysis was performed in *Excel* to determine agreement in the volumetric measurements amongst the three sets of data, the inter-observer variability of the EF assessment between the two observers, and the accuracy of DeepFat to analyse EF.

Results:
Agreement between the two observers was reasonable as the t-tests yielded no statistically significant results during the comparison of EF volumes. The segmentations of DeepFat are still in progress but are predicted to be somewhat similar to those of each of the observers.

Conclusions:
As the inter-observer variability is minimal, if the comparisons of DeepFat's segmentations to those of observer-1 and observer-2 are also not statistically significant, DeepFat can then be applied to evaluate EF on a larger scale for population studies to determine the risk of future adverse cardiovascular events.

ABSTRACT #20

The Effects of Targeted Marketing on Tobacco use in Youth and Minority Populations

Maia Childress, Nathan Hale High School; Erika Trapl, PhD, Department of Population and Quantitative Health Sciences, Case Western Reserve University

Background:
Research has uncovered a widening gap in the use of cigarillo products by gender and sexual minorities and cisgender heterosexuals. This is mainly due to disproportionate targeting through advertisements and the unregulated sale of tobacco products generally. When asked about their cigarello use, over 16% of American Young adults reported that they use them regularly. Another factor used to target young sexual and gender minorities is flavors. Out of 523 18-29 year old college students, 40.9% of those non-whites, 75% reported that they regularly chose flavored cigarellos. This study also revealed that younger, female, and racial ethnic minorities were more likely to use flavored cigars. Within the disparity between SGM and cisgender heterosexual people, there is one between SGM men and SGM women. Bisexual and lesbian cisgender women are at least 1.5 times as likely to be using cigar products compared to cisgender gay males and gender minorities. In addition to this, SGM minorities are more likely to purchase flavored cigars as a result of strategic marketing.

Goals and Objectives:
The goal of this research is to understand the relationship between young SGM and tobacco use in order to create policies and regulation that will benefit the health and safety of SGM. A greater awareness and recognition of the disproportionate use of cigarellos tobacco use by SGM is crucial to decrease the use of these products thereby lessening the severity and amount of potential health risks caused by them.

Methods:
Various articles were used for this paper in order to establish the disproportionate use of cigarellos by SGM compared to their non-SGM counterparts. Proposals were used to further analyze the characteristics of SGM behavior and how to decrease the purchase of cigarellos.

Results:
Tobacco use in SGM is a serious problem. I have learned that there are also a multitude of factors contributing to it.

Conclusions:
Using this information is key to decreasing tobacco use in SGM. In the future, an actionable plan will be put in place with the newfound awareness of this topic.

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ABSTRACT #21

Can Kidney, Bladder and Lung Cancer deaths be linked to Smoking?

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Background:
Kidney, Bladder and Lung Cancer have many ways to form but one that they all have in common is smoking. Smoking is responsible for more than 480,000 deaths per year in the United States, including more than 41,000 deaths resulting from secondhand smoke exposure. This is about one in five deaths annually, or 1,300 deaths every day. It has already been discovered that 80% of those deaths are due to lung cancer caused by smoking, followed by 50-65% in bladder cancer deaths and 30% in kidney cancer deaths.

Goals:
My goal for this project is to use graphs and data from different counties in Ohio to show how smoking can cause kidney, bladder and lung cancers to become much worse and to show how many of the more outcomes are due to those people being non-smokers.

Materials and Methods:
Excel, tableau, google slides and scientific research sites to trace the number of incidents, the number of deaths, the number of deaths due to smoking and the number of successes due to not smoking.

Results:
My results will prove Smoking tobacco doubles the risk of developing these three cancers (and many more) and almost triples the risk of death. Even as exposure from second hand smoke can affect your chances of getting these cancers. People can develop these cancers without smoking but makes them more likely to have a better outcome. My research is important because it will help inform smokers. In the United States, cigarette smoking is linked to about 80% to 90% of cancer deaths overall.

Conclusion:
People should care about this research because it could affect the number of deaths due to kidney, lung and bladder cancer by showing how not smoking can prevent it. This research might remind someone who smokes to get tested regularly or maybe even help some people quit

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ABSTRACT #22

IL-33: Discovering the Calcium Dependent Mechanism of Release in Response to Allergens in Airway Epithelial Cells

Javan Cobb, University School; George Dubyak, Ph.D, Department of Physiology and Biophysics, Case Western Reserve University School of Medicine

Background:
Belonging to the IL-1 family of cytokines, IL-33 plays a key role in the immune system's response against allergens. More specifically, IL-33 provides defense against respiratory diseases such as asthma, one of the most frequently occurring respiratory diseases. As for most cytokines, IL-33 acts as a double-edged sword: when produced in excessive amounts it can result in both airway damage and dysfunction. While much is known about IL-33 and its properties, there are still aspects yet to be discovered such as the mechanism of its release, which was the focal point of the study. IL-33 is unique in the sense that it is localized in the nucleus, where it is then released into the cytosol and then out of the cell. In an attempt to discover and understand the means of IL-33 release, IL-33 release was activated in mouse airway epithelial cells by an Alternaria fungal extract in vitro. Both Ca^{2+} influx and LDH release assays were used in combination to determine whether the plasma membrane of the cell becomes permeable upon activation, or if cell lysis occurs thus allowing for IL-33 to exit the cell. An additional measurement of IL-33 release by ELISA led to the conclusion that cell lysis occurred in the airway epithelial cells.

Goals:
The primary objective of this study was to determine the mechanism of IL-33 release from mouse airway epithelial cells, whether it be through the formation of pores in the plasma membrane or plasma membrane lysis altogether.

Materials and Methods:
CMT-64 mouse airway epithelial cell cultures were used in vitro. Fluo-4 Ca^{2+} influx assay and PI influx assay of membrane permeability were performed together with analyses of Lactate Dehydrogenase (LDH) release as an index of cell lysis and IL-33 release by ELISA (enzyme-linked immunosorbent assay). Both fluo-4 and PI influx assays were completed in real time using a Cytation-5 imaging plate reader.

Results:
The activation of IL-33 release by Alternaria in mouse airway epithelial cells correlated with the rapid influx of Ca2+, as increased levels were seen in the readings of the Ca2+influx assay. Similarly, the results observed during the LDH release assay revealed that the Alternaria activated IL-33 release also induced the rapid release of LDH into the extracellular fluid. In conclusion, an additional measurement of IL-33 release by ELISA was conducted, thus leading to the conclusion that lysis of the plasma membrane had occurred.

Conclusions:
The results support the model that Alternaria induces rapid cell lysis by calcium sensitive enzymes which may include phospholipases and proteases.

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ABSTRACT #23

A systematic review of metastatic spinal melanoma

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Background:
Melanoma is a common cause of metastatic disease to the central nervous system. While spine metastasis from melanoma is rare, it presents a complex management issue. To date, no systematic review on metastatic spinal melanoma has been performed.

Goals:
Our aim was to present a comprehensive review of metastatic spinal melanoma and to identify trends in epidemiology, management, and outcomes.

Materials & Methods:
We performed a systematic review of PubMed for articles published from inception to July 2021 with the search term "metastatic spinal melanoma," including studies if they evaluated melanoma metastatic to the spine. Studies on primary spinal cord melanoma, review articles, and studies published in a language other than English were excluded. References of included articles were also reviewed to identify additional relevant studies. Given the use of publicly available, de-identified data, this study was exempt from institutional review board approval.

Results:
Overall, 359 non-duplicate articles were identified. After title/abstract and full-text review, 198 articles were excluded, resulting in inclusion of 161 studies. Review of included articles revealed that metastatic spinal melanoma is a rare tumor that can be confused for other spinal lesions (e.g. inflammation), therefore delaying diagnosis. Additionally, melanoma spinal metastases often present many years after resection and treatment of primary melanoma, further contributing to poor survival outcomes. While surgical or radio surgical resection with palliative care therapy have traditionally been first-line treatments, the recent advent of immunotherapy has contributed to decreased tumor burden and improved survival in patients.

Conclusions:
Patients diagnosed with metastatic spinal melanoma experience significant morbidity and mortality, but survival outcomes have improved in recent years. Future research efforts should be directed toward establishing optimal treatment guidelines for metastatic spinal melanoma.

ABSTRACT #24

Comparing Intracortical Microelectrode Tissue Staining Methods

Landon Dawson, Avon High School; George Hoeferlin; Hannah Olivares; Jeffrey Capadona, PhD, Department of Biomedical Engineering, Case Western Reserve University

Background:
Intracortical Microelectrodes (IMEs) are electrical devices that are implanted into the brain with the purpose of collecting and recording neurological signals. With the provided foundation from this technology, significant progress can be made to treating many nervous system conditions such as Huntington's, Parkinson's, and Spinal Cord Injury. However, the electrode suffers from three categories of failure: mechanical, material, and biological. The primary failure module ~~we focus on~~ is biological failure and how to mitigate, or even cease it. One of the ways we study this response and the electrodes is through immunohistochemistry. In this study, we compare manual hand staining, which has been used for some time, and automated machine staining, which saves significant amounts of time. This study can help progress research by allowing the staining process to take two hours, compared to the previous two days.

Goals:
Our goal of this project is to evaluate the hypothesis determining if there is a significant difference between manual hand staining and automated staining. We do this because automated staining provides the advantage of saving large amounts of time, which can advance research in this area.

Materials and Methods:
Tissue was collected from Sprague Dawley rats and sliced using a cryostat. The tissue was then stained by immunohistochemistry, which was performed using manual hand staining and automated staining. Specifically, we stained for neurons and astrocytes. Once stained, imaging of the tissue was done using an Axio Scan.Z1. Analysis over the images was performed using several MATLAB programs. After these steps were completed, ANOVA was used to determine a statistical difference between the methods.

Results:
Tissue will be scanned, imaged, and analyzed during the last week of my internship. Therefore, no results can be obtained and included in this manuscript at this point in time.

Conclusions:
No conclusions can be drawn at this point due to limited amounts of results and time. However, I plan to continue to attend the Capadona lab following the completion of this program throughout the following academic period to complete my research.

ABSTRACT #25

Identifying Target of Selective Cancer-Targeting Small Molecules

Manzili Denis, University School; Anna Zinsser; Matthew Pleshinger; Drew J. Adams, PhD, Department of Genetics and Genome Sciences, Case Western Reserve University

Cancer has affected millions of people around the world. Cancer can be treated by targeting the cancer cells. However, target identification is a massive barrier in drug development. Identifying the target allows us to understand how it is killing cancer cells and potential side effects of the compound. We have a compound titled SPOX that targets and kills cancer cells. SPOX causes the formation of oxidant species and changes the free fatty acid levels within the cell. SPOX also changes transcription levels inside the cell. Although we have information on the effects of SPOX in cancer cells, we do not know what it is specifically targeting. Therefore, we looked at different unbiased methods of target validation. There are multiple ways to identify targets, such as label-based approaches and label-free approaches. The label-based approach consists of using covalent interactions, keeping the compound bound to the target. Label-free approaches rely on having a mass amount of cells. The complexity of the compound makes it difficult to utilize the label-based approach. Forward genetic screening is a label-free approach that encourages natural selection within cells. In Forward genetic screening, a compound is introduced to groups of cells. The compound will irritate the cells, which will provoke the cells into mutating. We hypothesise that by using Forward genetic screening, we will be able to cause a shared mutation amongst the cancer cells. This shared mutation could be the phenotype that the compound is targeting. Therefore, If the shared mutation is found, then we will be able to understand how the SPOX kills cancer cells. If the target is not found, we will proceed to utilize a different method of target validation.

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ABSTRACT #26

How Electronic Cigarettes and other Tobacco Products affect your lungs.

Claire Dunn, Shaker Heights High School; Erika Trapl, PhD, Prevention Research Center for Healthy Neighborhoods, Department of Population and Quantitative Health Sciences, Case Western Reserve University

Background:
This research will focus on a very popular tobacco product, electronic cigarettes also known as "vapes" and other tobacco products specifically on how they affect your lungs. Tobacco use has been documented for over 8,000 years, since 5000 BC likely beginning in Central Mexico.
However, the popular tobacco product electronic cigarettes have been around since 1963 and became very popular around 2010. A misconception people have about electronic cigarettes is that they are a better option than other tobacco products, mainly cigarettes. However, they still damage your lungs. An e-cigarette is an electronic device that works by heating a liquid, which produces a vapor that the person then inhales. Why people think an e-cigarette is much better than a regular cigarette is because it does not contain tar however, it does contain other powerful chemicals that will damage the body. E-cigarettes produce a lot of different dangerous chemicals including acetaldehyde, acrolein, and formaldehyde. These toxic chemicals can cause lung disease.

Goals:
The goal of this project is to learn how tobacco can negatively affect your lungs and also to increase awareness to electronic cigarettes and inform the public that they are also bad for you and can negatively affect your lungs.

Methods:
Literature review of different articles focusing on tobacco, electronic cigarettes, and how both of those affect your lungs.

Results:
One chemical, called diacetyl, that's used in vapes, causes disease in the small airways of the lung, thickening the air sacs and causing inflammation. You may know of it as popcorn lung. Since electronic cigarettes haven't been in use for that long, it is not known if they cause lung cancer like cigarettes.

Conclusions:
In conclusion vapes and cigarettes are ~~very~~ bad for your lungs. Although vapes just became popular in 2010 but have been out for almost a half of century there isn't that much data and research as it is on cigarettes and other well-known tobacco products. But with what we know we should spread more awareness on how vapes and other tobacco products can damage your lungs so less people can stop using these products and we can save lives.

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ABSTRACT #27

The Biological Process of Transfection and Western Blotting

Thomas Dunn, Shaker Heights High School; Jessica Miley; Can Shi, PhD,
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Background:
Transfection is the process of the intentional introduction of nucleic acids (DNA/RNA) into eukaryotic cells. Transfection is a great aid in enabling the study and modulation of Gene regulation, and is also used as an alternative for viral infection. The main objective of transfection is to study the role of genes or gene products, by amplifying or inhibiting specific gene expression in cells. Transfection is a powerful analytical tool for looking at the function and regulation of genes or gene products, for the production of transgenic organisms, and as a method for gene therapy.

Goals:
To understand the process and methods of transfection.

Materials and Methods:
A literature review was performed due to absence in the lab. However, there are 2 main methods with transfection. Transient Transfection(>90%) and Stable transfection(<10%). Transient Transfection, the nucleic acids introduced into the cell are not permanently incorporated into the cellular genome. The effects of the nucleic acids within the cell typically last about 24-72 hours. This method is often used for pathway analysis and promoter or functional studies. Stable transfected cells are permanently integrated within the genome. These effects of the nucleic acids can be studied over longer periods of time. This method is reserved for research that needs it, such as gene therapy. There are many ways of getting the nucleic acids into the cell. Electroporation or microinjections, exposes cell membrane to high electricity to make cell membrane destabilize to allow nucleic acid to go through. Viral mediated transfection involves use of viral vectors to deliver nucleic acid. Particle based transfection via nanoparticles, cationic gold nanoparticles form complexes with negatively charged plasmid DNA. Immunoblotting or Western Blotting is a method used to identify proteins in a cell. Proteins are separated by molecular weight through gel electrophoresis. The first step in immunoblotting is Sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE). We boil the samples to denature back to their primary amino acids with a reducing agent to sever the disulfide bonds. The samples are loaded into lanes one by one on top of a resolving gel. An electric current is flowed through the canal, which causes the negatively charged particles to flow downward while the positively charged particles flow upward. This causes the proteins to separate by size. To accomplish a better migration through the gel, a resolving agent acrylamide is added. The amount added has to fit the needs of the protein. For smaller proteins a higher percentage of acrylamide is used and for bigger proteins a lower percentage is used. Once separated proteins are immobilized on a membrane. Once on the membrane the protein is layered onto blotting paper and compressed down. This is called a sandwich. An electric current is applied again to migrate the proteins onto the membrane. There are three types of ways you can immobilize proteins on a membrane.

Results:

Conclusions:
The main purpose of transfection is for studying the role of genes by introducing a nucleic acid to genetically modify the cell. Western blotting is used to detect specific proteins among other proteins. This method is highly effective among researchers to receive a strong indication of proteins

Supported in part by NIH, NCI, R25 CA221718

ABSTRACT #28

Photobiomodulation: Investigating the effect of light on the progression of Alzheimer's Disease using the *Drosophila* model

Adrik Dutta, Shaker Heights High School; Masashi Tabuchi, PhD, Department of Neurosciences, Case Western Reserve University

Background:
Alzheimer's Disease (AD) is a currently incurable condition that affects over 44 million people worldwide. It is caused by the buildup of amyloid beta (Aβ) plaques as well as neurofibrillary tangles of tau proteins in the brain. Recently, researchers have looked to environmental factors such as light as a prospective therapy for the progression of AD. This phenomenon, called photobiomodulation, will be used to test its efficacy on the *Drosophila* model of AD.

Goals:
There will be two main goals of this experiment. The first is to analyze the effects of exposure to different wavelengths of light, on the progression of AD in *Drosophila.* The second is to assess the effects of a disrupted circadian rhythm on AD progression, via a group exposed to no light. I hypothesize that red and blue light will slow the progression of Alzheimer's, while the group with no light will make the progression more severe.

Materials and Methods:
To conduct this experiment, I will be using four cardboard boxes with a light bulb attached in three of them. This will create environments with red and blue lights, a control with white light, and a group with no light to mimic a disruption of the circadian rhythm. The bulbs will be connected by extension cords to a timer that switches power in a 12 hour light and dark cycle. Each group will have 10 *Drosophila* genetically modified to have AD, and they will be exposed to light for 10 days. After exposure, I will perform electrophysiology on the brain of each group to detect the effects of light on synaptic transmission in the *Drosophila*. The resultant data will be analyzed using Axon PClamp 11 and Matlab softwares in the Tabuchi Lab.

Results:
My research is ongoing and definitive results are not yet available. However, based on existing literature on transcranial photobiomodulation as well as data from the Tabuchi lab using AD *Drosophila*, I expect the flies exposed to red and blue light to both have a higher synaptic transmission compared to the control flies. Conversely, I expect the flies that were exposed to no light will have a lower synaptic transmission compared to control flies.

Conclusion:
As Alzheimer's Disease reduces synaptic transmission of the neurons, these results could provide a new treatment for AD patients that is cheaper and non-invasive. Additionally, the negative effects of the no light group will help propose lifestyle changes to individuals with AD to maintain a healthy circadian rhythm.

Adrik Dutta is a Martha Holden Jennings Scholar

ABSTRACT #29

What are the differences between signet-ring & colorectal cancer

Le'Aona Dysart, Cleveland School of Science and Medicine; Debra Mikkola; Sanford Markowitz, MD, PhD, Stephen Fink, PhD, Case Comprehensive Cancer Center, Case Western Reserve University

Background:
Colorectal cancer is the second leading cause of cancer-related death in the United States, with an estimated 53,000 deaths each year. The median survival rate of colorectal cancer at 5 years is 64%. Colorectal cancer can occur in both men and women, and the most common form of colorectal cancer presents as an adenocarcinoma (95% of cases). Colorectal cancer most commonly occurs in patients over the age of 50, and treatments such as surgery, chemotherapy, and molecular targeting are used to help treat patients with the common form of colorectal cancer. Signet-ring colorectal cancer (SR-CRC) is a rare form of colorectal cancer and only accounts for 1% of all colorectal cancer cases. SR-CRC is a very aggressive cancer, and patients with this disease have a very poor prognosis. Also, SR-CRC can affect patients at a much earlier age, with some cases occurring in teenage years. Very little is known about how SR-CRC develops or how it is different from regular colorectal cancer. Because of these facts, it is imperative to find out how signet-ring is different on a genetic level to help explain why it is so aggressive and to help in discovering new therapies for this type of colorectal cancer.

Goals:
The purpose of our study is to see if there is a difference in the frequency of mutations in the key genes important for colorectal cancer development, specifically comparing regular colorectal adenocarcinomas and rare signet-ring colorectal cancer.

Material and Methods:
A literature review was performed to learn about what is cancer, the hallmarks of cancer, how colorectal cancer develops, and the different types of colorectal cancer. A PubMed database search was performed to look for papers describing mutations in SR-CRC. These papers were analyzed for mutational differences between SR-CRC and regular colorectal cancer. Polymerase chain reaction (PCR) amplification and sequencing was performed to determine if mutational differences found in the literature were detected in a SR-CRC cell line (V451) compared to regular colorectal cancer cell lines (FET, DLD-1, and SW480).

Results:
The PubMed search resulted in 3 papers describing mutational differences between SR-CRC and regular colorectal cancer. Through the literature review, it was learned that 4 genes were prominent in colorectal cancer development but had different mutation frequencies in SR-CRC and colon cancer. These genes include APC BRAFF, KRAS, and PIK3CA. The Mutational frequency of these genes are being tested to learn whether they are different between SR-CRC and regular colorectal cancer cell lines by PCR. These genes are being sequenced to determine the mutations in those regions. Results are forthcoming.

Conclusions:
From researching various literature reviews, I determined different mutational frequencies in key colorectal cancer genes between signet-ring and regular colon cancer. I hypothesize that my sequencing will show a difference in SR-CRC and regular colon cancer when the results come back.

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ABSTRACT #30

Resiliency in African Americans and the Impact of Potentially Traumatic Events

Chloe Echols, Hathaway Brown; Peter Hovmand, PhD, Center for Community Health Integration, Case Western Reserve University

Background:
Resilience is a trait that every human has the capacity to enact after having faced or coming into contact with a potentially traumatic event (PTE). Many definitions have been formulated about PTE over the years but the current definition stands as being able to have "healthy functioning after a highly adverse event." Research has looked at the different factors that might enhance or bring about resilience for an individual or factors that are not acceptable in the normal world but still produce resilience, since there is not one single way to be resilient. An example of this can be someone with an inflated ego or people with a self-enhancement bias. Studies have also been conducted around resilience and recovery and, concluded that these are separate. They can be measured by experience and observation, not logic. More research has been done to include minorities analyzing the psychological effects of racism and discrimination. Studies have shown that the people who have experienced these "stressors" usually undergo injurious effects on their mental and physical health, and noted discrimination was strongly related to depression, anxiety, psychological distress, and psychiatric disorders. More data is needed about resilience and the possible variation in coping skills between cultures and different types of PTE (chronic, long lasting, severe, etc.).

Goal:
The goal of the literature review was to first gain an understanding of the innate human capability of resilience, the different types of resilience, and the statistics of resilience after PTEs from the specific community of this study. The goal of this study was to test the hypothesis that the greater frequency of the PTE, the longer resilience will take to occur or emergent resilience (resilience that emerges with time) will take place not minimal impact resilience (which is resilience that occurs shortly after the PTE), and add to the current knowledge of resilience in POC.

Materials & Methods:
A literature review was conducted on human capability for resilience, "race related stressors", definitions of resilience, emergent resilience, minimal impact resilience and the psychological effects of racism on African Americans. Additionally, a causal loop diagram and interface were made to test the hypothesis previously mentioned.

Results:
Resilience, effects of racism, and coping skills for PTE were learned. Results from the causal loop diagram and interface are pending, but the predicted outcome is that it will match the hypothesis since levels of anxiety, depression, and other disorders are linked to racism and discrimination.

Conclusion:
Resiliency is more likely than not to be shown after facing a PTE. There is ample proof to suggest that discrimination and racism have negative effects and are included in the occurrences that are known as PTEs. While resilience after these events is shown, individuals who have experienced these PTEs will most likely report mental and physical illness. It is important that this field of study continue to grow, possible treatments for health issues, strategies for coping, understanding of mental health need to be expanded or created.

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ABSTRACT #31

Comparison of MRI CT and Ultrasound for assessing cartilage grafts

Ahmed Elsharkawy, St. Edward High School; Larissa De Souza; Akua Sarfo, MD, PhD; Bryan Carroll, MD, PhD, Case Western Reserve University

Background:
Mohs surgery is a technique used to treat skin malignancies that has been increasing in use over the years. This specialized surgical technique allows for conservation of normal tissue while excising the whole cancer. The defect that results from Mohs and the removal of affected tissues/skin cancers requires reconstruction. Some examples of techniques used in reconstruction include simplex or complex closure with sutures and grafted tissues or flaps. Incorporating a cartilage graft does not pose the risk of rejection or failure that synthetic biomaterials or cadaveric grafts do. These grafts must be able to be viewed by an imaging modality and this report will compare and contrast the utility of CT, MRI, and ultrasound for the purpose of assessing cartilage grafts. Magnetic Resonance Imaging (MRI) uses strong magnets and computers to produce images of the body organs being scanned. An ideal MRI study of cartilage should evaluate thickness, volume, integrity, provide details about cartilage and underlying bone morphology, and assess cartilage biochemistry and physiology including collagen and proteoglycan matrices. MRI has become more popular due to its excellent tissue contrast. A Computed Tomography (CT) scan uses computers and rotating x-rays to create cross-sectional images of the body. CT provides some soft tissue contrast. CT can identify regions of different cartilage, with results similar to MRI. However, fine details of cartilage are not easily visualized with standard soft tissue CT imaging. Ultrasounds use high-frequency sound waves to produce images of structures within the body. Ultrasound has been accurate in assessing cartilage volume and provides a noninvasive, low-risk option. It does not expose patients to radiation, does not require sedation, and it is relatively quick and inexpensive.

Goals:
In this study we performed a literature review to assess the above 3 imaging modalities - MRI, CT, and ultrasound and their efficacy in the evaluation of cartilage for the purpose of designing cartilage grafts.

Materials and Methods:
Pubmed from 1995-present, with the keywords “Cartilage Graft, CT, MRI, Ultrasound, Reconstruction, ear”, and excluded articles regarding animals. We searched articles for information regarding the imaging of the cartilage grafts and the observations made in the article about the cartilage grafts.

Results:
MR imaging provides a high soft-tissue contrast and combined with manual segmentation of ear cartilage proved to be accurate. It was precise enough to detect patient-specific variation in ear cartilage and volume. It has also been shown that biochemical MR approaches are able to provide a specific measure of the composition of cartilage. A combination of morphological and biochemical MRI may represent a desirable multimodal approach to diagnosis as well as for routine clinical follow-up after cartilage repair procedures. Compositional MR imaging provides the opportunity to measure the biochemical and microstructural time-dependent processes of maturation occurring within the repair tissue. Another study showed that T1 MRI images provided the best assessment of graft viability. However, it was difficult to compare the MRI images over time. Studies showed that CT examinations for preoperative evaluation of rib cartilage could be a useful method for planning microtia reconstruction.

ABSTRACT #31 CONTINUED

It has also been shown that Cone-beam CT is a useful tool for determining the position of ossicular reconstruction prostheses in situ and has potential for intraoperative assessment, to check positioning after the prosthesis has been covered with a cartilage graft and tympanomeatal flap. It has also been proven that ultrasound can accurately determine dimensions of cartilage. All longitudinal and transversal harvested cartilage lengths were within 0.4cm of the ultrasonographic length.

Conclusions:

~~W~~e found evidence for each imaging modality, MRI, CT and Ultrasound, to be useful and accurate, however, most of the evidence points towards the conclusion that MRI is the most accurate modality. ~~However,~~ if more evidence can be found that could point towards a relationship of non-inferiority it could be much safer to use a different imaging modality such as Ultrasound due to its quick and cheap nature. It also does not expose patients to radiation, unlike CT.

ABSTRACT #32

Evaluating the effects of exercise on muscle metabolism and insulin sensitivity

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Background:
Type 2 Diabetes (T2D) patients have low insulin sensitivity due to impaired insulin signaling and high accumulation of intra-myocellular triglycerides. Exercise on the other hand improves insulin sensitivity in T2D patients and affects energy metabolism in skeletal muscle. However, in some T2D patients exercise has been shown to not promote overall improvement in insulin sensitivity and glucose homeostasis. Over the last few years several studies also have reported abnormal mitochondrial function in skeletal muscle of T2D patients. Some studies using ^{31}P-magnetic resonance spectroscopy (^{31}P-MRS), in vivo technique that can monitor and measure dynamic changes in energy metabolism in skeletal muscle, have shown abnormal mitochondrial function present in T2D patients. Here in this study, we assess mitochondrial function in vivo using ^{31}P-MRS on preclinical model of T2D before and after exercise training.

Goals and Objectives:
At the end of the study, we want to know if exercise training improves mitochondrial function in T2D rats which then also improves their glucose metabolism. In addition, we would also want to know if no improvement in mitochondrial function may result in no improvement in glucose metabolism.

Methods:
In this study Zucker fatty obese (ZFO) rats, a preclinical model of T2D will undergo 10 weeks of exercise training using treadmill. Before the training, we will quantify the Zucker fatty obese (ZFO) rats' glucose metabolism using oral glucose tolerance test (OGTT). Next, we will quantify and characterize ZFO rat's skeletal muscle's mitochondrial oxidative capacity as well as creatine kinase (CK) rate constant in vivo using ^{31}P-MRS. The ZFO rats will then go through 10 weeks of exercise training using treadmill. After 10 weeks of exercise training, we will perform OGTT to measure trained ZFO rat's glucose metabolism as well as its mitochondrial oxidative capacity and CK rate constant. We will also perform in vitro analysis of isolated mitochondria in ZFO rats in the skeletal muscle.

Results:
These experiments are in progress.

Conclusions:
Results will determine if exercise training improves skeletal muscle mitochondrial function in ZFO rats.

ABSTRACT #33

BG34-200 Engagement with Integrin CD11b for Modulating Tumor-Associated Myeloid Cells in Pancreatic Cancer

Kaitlyn Ernst, Laurel School; Mei Zhang, PhD, Department of Biomedical Engineering, Case Western Reserve University

Background:
Cancer immunotherapies such as checkpoint inhibitors and CAR-T therapies are becoming a therapeutic option for cancer patients with advanced and metastatic diseases. However, clinical success has been limited as tumor cells exploit multiple mechanisms in the tumor microenvironment (TME) to create an immunosuppressive environment, escaping immune destruction. Recent studies have shown that the immunosuppressive myeloid cells in TME is the major mechanism of cancer resistance to immunotherapy; myeloid cell marker, integrin CD11b, represents a new and innovative target to potentially modulate myeloid cell functions for enhancing immunotherapy. The CD11b integrin can mediate a variety of myeloid cell functions, such as adhesion, migration, differentiation, and proliferation in response to binding to a broad diversity of ligands. In our study, we investigate whether the recently developed BG34 biomolecule can interact directly with the CD11b integrin to potentially drive myeloid cell differentiation and M1 activation.

Goals:
The objectives of the project are to understand the engagement of myeloid cell marker (integrin CD11b) with in-house developed ligands (BG34 molecules) through characterizing binding site[s] and associated signaling pathways. Results of the study will lead to the development of a modulatory agent for eliminating immunosuppressive myeloid cells.

Methods and Materials:
To pursue this, we applied overlapping peptide microarray technology to characterize the binding sequence of CD11b to BG34 molecules with different molecular weights. Specifically, we designed experiments to 1) determine the impact of Mw on binding and binding affinity, 2) characterize both sequence and conformational structures, and 3) investigate sequence and binding affinity via data analysis.

Results:
Not yet determined and research still in progress

Conclusion:
This project serves as the first step for understanding the engagement between myeloid cell marker CD11b with its potential differential ligand, BG34 molecules. This lays the foundation for following studies to characterize the signaling pathways essential for modulating immunosuppression. A successful completion of this study will lead to an exciting opportunity for the development of BG34-based immunotherapy for cancer patients who failed to respond to standard of care chemotherapy, radiation therapy, and immunotherapy.

ABSTRACT #34

The Abundance of PML in Estrogen Receptor Alpha Breast Cancer

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Department of Biochemistry, Case Western Reserve University

Background:
Estrogen Receptor Alpha-positive Breast Cancer (ERα BC) accounts for seventy percent of all breast cancer patients. The proliferation of ERα-positive BC cells is induced by the female hormone estrogen. Estrogen binds to a type of nuclear receptor, estrogen receptors, in the cytoplasm or nucleus of the cell, functioning as a transcription factor. Promyelocytic Leukemia Protein, PML, is an acknowledged tumor suppressor that plays a role in transcription, DNA damage repair, cell proliferation, and apoptosis. Recently, studies suggest that PML promotes tumor growth. This experiment focuses on the effect of the drugs tamoxifen and fulvestrant on the abundance of the promyelocytic leukemia protein in ERα BC cells. Tamoxifen is a widely used selective estrogen receptor modulator (SERM) that binds to estrogen receptors, inhibiting the binding of estrogen and ER-mediated transcription activation. Fulvestrant is a selective estrogen receptor degrader (SERD) that induces ERα protein degradation.

Goal:
The goal of this experiment is to measure the abundance of the PML protein in ERα BC cells treated with tamoxifen or fulvestrant. In measuring the abundance of PML in the BC cells, we are able to link the effectiveness of the drugs in affecting PML protein levels and identify possible mechanisms of treatment for ERα BC patients.

Materials & Methods:
Cell culture
The estrogen receptor-positive breast cancer cell line MCF7 was cultured in DMEM with 10% Fetal bovine serum (FBS). All the cells were maintained in 37℃ incubator with 5% CO2.

Western blot
Cells were split into 3 6cm plates and cultured in the presence of 1μM Tamoxifen or 1μM Fulvestrant or DMSO for two days. Cells were scraped off the plates and lysed with cell lysis buffer. Protein concentration was determined by a BCA assay. Samples were loaded in a 10% SDS-PAGE gel, and protein was transferred to the NVDF membrane and probed with PML, ERα, and β-actin monoclonal antibodies. Signals were developed with chemiluminescence, imaged using ChemiDoc.

Proliferation assay
1,500 cells were counted and seeded into a 96-well plate after centrifugation. The cells were cultured in the presence of 1μM Tamoxifen or 1μM Fulvestrant or DMSO. A CCK8 Kit was used for the proliferation assay. On day 0, day 3, day 5, 10 μl CCK8 was added to the wells. The absorbance values at OD450 nm were measured.

Results:
Experiments in Progress

Conclusion:

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ABSTRACT #35

In what ways does CDK5 inhibit immune evasion of tumor cells?

Adora S. Ezepue, Campus International High School; Muta Abiff; Alex Huang MD, PhD, Department of Pediatrics, Case Western Reserve University

Background:
Cyclin-dependent kinase 5 (Cdk5) is a non-stereotypical Cdk protein, specifically an enzyme, that is encoded by the Cdk5 gene. Cdk5 contributes to apoptosis, myogenesis, angiogenesis, vesicular transport, and senescence in nonneuronal cells, including tumors, which makes Cdk5 a potential therapeutic target in cancers. To evade immune surveillance, tumors adopt peripheral tissue tolerance mechanisms including expression of programmed cell death-ligand 1 (PD-L1), inhibition of which results in potent anti-tumor responses. Although assessment of PD-L1 expression on tumors can predict the success of immune checkpoint blockade, it's expression in tumor development is a dynamic process as over the course tumor is subjected to various immunepressures. Cdk5 is a vastly expressed multifunctional serine/threonine kinase. It's dysregulation has been implicated in development of various diseases including cancer. Its importance in various cancer development is ~~still~~ being studied. Recent publications show it's importance in pediatric cancers such as medulloblastoma (MB) and rhabdomyosarcomas (RMS) as well as other solid cancers. Our research has shown a role of Cdk5 in PDL1 upregulation in murine MB.

Goals:
We aim to study how *in vitro* treatment of murine MB cell lines with Cdk5 inhibition affects PD-L1 upregulation on cells upon Interferon gamma (IFNɣ) stimulation.

Methods:
To understand Cdk5-specific functions, we disrupted Cdk5 in wildtype murine MB cells (MM1 WT) by short hairpin– mediated RNA interference (MM1 shCdk5). The "sh" refers to the method in which the CDK5 gene expression was knocked down, which was with short hairpin RNA (shRNA). It's a synthetic RNA molecule that binds to the CDK5 mRNA and prevents it from being translated into protein. We plated MM1 WT and MM1 shCDK5 cells in RPMI cell media. Once the cell plates were confluent, we treated one MM1 shCDK5 plate and one MM1 WT plate with 10 µMol -/+ IFNg, the others were left untreated (to be used as controls). After 24 hours the cells were harvested. We prepared and transferred the harvested samples into a 96 well plate to measure protein concentrations in preparation for Flow Analysis and Western Blots.

Results:
We are completely prepped to do Western Blots and Flow Analysis on our samples. However, due to time restraints we have not yet conducted said procedures. We do not have any new data. In the next week we should be completing our first round of experiments and imaging.

Conclusion:
To be determined following acquisition of results

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ABSTRACT #36

The Impact of VCAM-1 on Tumor Associated Macrophages

Jenny Fan, Revere High School; Emma Pronovost, Tulane University; Sung-Hee Choi, PhD; Alex Huang, MD, PhD, Department of Pediatrics, Case Western Reserve University

Background:
Osteosarcoma is the most common form of childhood bone cancer. Osteosarcoma tumor cells release a protein called vascular cell adhesion molecule-1 (VCAM-1), which helps to regulate leukocyte migration in the body. There are two particular types of leukocytes that are critically involved in tumor development: M1 and M2 macrophages, collectively referred to as tumor-associated macrophages (TAMs). M1 macrophages increase inflammation while M2 macrophages create anti-inflammatory cytokines. M2 polarization thus promotes tissue synthesis and tumor development. To clarify, most TAMs are thus M2-polarized cells. M2 macrophages notably secrete the protein arginase 1 (Arg1), whose expression thus may be measured to determine the phenotype of TAMs. It has previously been suggested that VCAM-1 prompts M2 polarization in macrophages, so treatments for osteosarcoma may benefit from targeting VCAM-1.

Goals:
The goals of this project were to determine the mechanism behind the phenotypic changes in macrophages in response to exposure to VCAM-1 and to test the hypothesis that VCAM-1 promotes M2 polarization in macrophages.

Materials and Methods:
K7M2 is a highly metastatic, osteosarcoma murine cell line derived from pulmonary tumors. An ELISA was conducted to determine the levels of VCAM-1 present in the supernatant of purchased K7M2 cells. Next, macrophages were derived from the bone marrow of mice, harvested from the femur and tibia. After the macrophages were grown for twelve days, the K7M2 supernatant was added to the samples for variable durations of time--six hours, twelve hours, and twenty-four hours. One sample acted as a control and had no supernatant added. The RNA of the cells was then isolated and used to build cDNA. A real-time polymerase chain reaction (RT-PCR) used this genetic material to illustrate the relative amounts of gene expression for seven genes, including GADPH as a control, Arg1, CCL22, CCL12, IL-10, TGFβ, and Mrc-1. Using Microsoft Excel, relative amounts of induction were charted in a bar graph.

Results:
In the macrophages, levels of Arg1 rapidly increased and peaked at twelve hours of treatment before decreasing slightly in the twenty-four hour treatment. Levels of CCL22 were greatest at six hours and decreased rapidly in the twelve and twenty-four hour wells. CCL12 amounts significantly increased after six hours and remained relatively stable in the twelve and twenty-hour time increments. IL-10 amounts increased gradually over time while quantities of TGFβ remained roughly the same as the control cells' levels of TGFβ. Mrc-1 only increased slightly after twenty-four hours of treatment.

Conclusions:
The results appear to be consistent with the hypothesis that VCAM-1 promotes M2 polarization in macrophages. Potential therapies for osteosarcoma that target VCAM-1 can be developed and put through clinical trials.

ABSTRACT #37

An evaluation of the efficacy of Bax inhibiting small compounds to prevent iBax cell death

Abem Fetene, University School; Shigemi Matsuyama, PhD, Department of Ophthalmology, Case Western Reserve University

Trauma via chronic or acute injury as well as light-induced stress can result in retinal ganglion cell death and photoreceptor cell death, which can lead to blindness. Bax, a pro-apoptotic protein, holds an important role in this process. Bax changes conformation in response to stress and later translocates to the mitochondria, prompting cytochrome c induced cell apoptosis. To counteract the initiation of Bax-induced blindness, the PI and his collaborators synthesized Bax Inhibiting Small Compounds (BISCs) to prevent the eventual release of cytochrome c from the mitochondria. In preliminary tests, the most effective BISCs were (BISC)-5 and (BISC)-7. These compounds became structural blueprints for future BISC derivatives, BISC-A (BISC-5 analog) and BISC-B (BISC-7 analog). BISC-A, BISC-B, and BISC-C, an analogous derivative of BISC-A, proved to be efficient at preventing Bax-induced cell death. In order to test the efficacy of BISC, iBax cells (induced Bax cells) were placed into a medium where Doxycycline, a Bax inducer, would catalyze the apoptotic process. Afterwards, the BISCs (A, B, C) were administered at various concentrations. 24 hours after the administration of BISC, the cells were placed into a 96-well assay where dead cells were imaged and later analyzed using the EVOS M7000 imaging system. Subsequently, the IC50 values were calculated using datasets from a related caspase luminescence experiment. From this, it was found that BISC-A was the most efficient of the tested BISCs.

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ABSTRACT #38

Degradation of mutant P53 in HPV- in Head and Neck Cancer

Dennae Foster Jr., Ginn Academy; Quintin Pan, PhD, Department of Otolaryngology, Case Western Reserve University

Background:
Head and Neck cancer can be caused by multiple factors, including the excessive consumption of alcohol and tobacco, which would be HPV-negative, and high-risk Human Papilloma Virus infection, which is HPV-positive. In HPV-negative head and neck cancer, the P53 gene is often mutated. Mutant P53 is assumed to be the cancer driver gene and in this case; and researchers are currently trying to find a way to counteract its expression in cancer cells.

Goals:
To degrade the mutant protein in HPV – HNSCC

Materials and Methods:
FaDu, an HPV-negative cancer cell line was infected with HPV. The expression of mutant P53 protein was analyzed by western. The proliferation of the infected cells was also monitored for 4 days.

Results:
The FaDu infected with HPV showed degradation of mutant P53protein compared to the non-infected cells. Moreover, they displayed a slower growth curve compared to control cells.

Conclusions:
The HPV infection in this HPV negative cell line induced degradation of mutant P53 which was concentrated with a deceleration of cell proliferation.

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ABSTRACT #39

Determining the pathways for transmembrane water and CO_2 flux via AQP5

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Background:

13 human aquaporins (AQPs) have been identified and cloned. Named for their ability to conduct H_2O, each AQP displays different transmembrane permeabilities for glycerol, urea, and other small solutes and also for gases including CO_2, O_2 and NH_3. Functional AQPs are complexes of four copies of the same AQP protein, with each monomer within the tetramer consisting of six transmembrane spanning alpha helices, arranged around a water-conducting monomeric pore (MP). At the center of each MP is the aromatic/arginine (ar/R) constriction selectivity filter and two asparagine-proline-alanine (NPA) motifs that for most AQPs allows the passage of H_2O over ions and other solutes. The monomers within each tetramer assemble to create a central pore (CP) which is lined by hydrophobic amino acid residues. We hypothesize that the hydrophobicity of the CP makes it a favorable pathway to conduct gas. CO_2 and O_2 exchange occurs in the lung alveoli that are lined by type I and type II pneumocytes. AQP5 is localized in human and rat type I pneumocyte apical membranes. In mouse, both type I and II pneumocytes apically express AQP5. It has been hypothesized that gas exchange is AQP5's primary physiological function in these cells, while other AQPs govern H_2O flux.

Goals:

Using an osmotic swelling, and a Neutral Buoyancy Assay (NBA), we will determine the relative contribution of the MP and CP to transmembrane H_2O and CO_2 flux via AQP5.

Materials and Methods:

We inject stage V-VI *Xenopus laevis* oocytes with H_2O (control) or 12.5 ng of cRNA transcribed *in vitro* from linearized pGH19 plasmids that contain the open reading frames for human AQP5, or the AQP5-T41F or AQP5-R188E mutants. The osmotic water permeability (P_f) is determined in a volumetric swelling assay. Following a 30 min equilibration in ND96 solution (195 mOsm), we transfer the oocytes into a hypotonic ND96 variant set to 105 mOsm, creating a +90 mOsm gradient between the inside and the outside of the oocyte. We acquire digital images at 1 s intervals for a total time of 60 s and compute P_f from the time course of the projection area of the oocyte. We obtain the channel-dependent P_f values (P_f*), by subtracting mean P_f values of day-matched H_2O injected control oocytes from the P_f values of individual AQP-expressing oocytes. Originally developed to measure N_2 efflux from *Xenopus* oocytes, we modified the NBA for this investigation to measure CO_2 influxes. We inject a precise volume of N_2 gas (number of gas molecules = n_{Gas}) into an oocyte, which we transfer to a saline-containing tube. The saline in the tube is pre-equilibrated with 100% CO_2/95 mM HCO_3^-/pH 6.66. We then increase the pressure (PNB) in the air phase above the air-water interface so that it is sufficient to collapse the injected bubble enough to make the oocyte neutrally buoyant, 5 cm depth below the meniscus. Throughout the experiment, a camera/computer combination detects any depth change by the oocyte multiple times a second as gas enters or exits the cell, and increases or decreases PNB to maintain the oocyte neutral buoyancy at 5 cm depth. Calibration exercises allow us to compute the time course of Δn_{Gas}, and thus transmembrane gas flux from the PNB record.

ABSTRACT #39 CONTINUED

Results:

Volumetric swelling assays determine that AQP5 oocytes have significantly greater P_f* than control oocytes. P_f* for AQP5-T41F oocytes, which is hypothesized completely block of the extracellular entrance to the AQP5 CP, is not significantly different from AQP5 oocytes, while P_f* from AQP5-R188E oocytes in which we switch the positively charged arginine of the ar/R selectivity filter, immediately adjacent to the second NPA motif, for a negatively charged glutamate, was comparable with control oocytes. In the NBA, immediately after time = 0, n_{Gas} rapidly increases as CO_2 rushes into the cell, and peaks at <200 s. N_2 exit then dominates and nGas decreases. Compared to control oocytes, AQP5 oocytes have a significantly greater maximal rate of nGas increase (i.e., CO_2 influx) and the peak Δn_{Gas} is larger and more delayed. Furthermore, when we express the AQP5-T41F mutant, peak Δn_{Gas} is not significantly different from control oocytes. However, the AQP5-R188E mutant exhibits a peak Δn_{Gas} that is intermediate between AQP5 and control oocytes. Thus, the AQP5-T41F mutant has greater selectivity for H_2O over CO_2 vs. wild-type AQP5, and the AQP5-R188E mutant has a greater selectivity for CO_2 over H_2O vs. wild-type AQP5.

Conclusions:

AQP5 is both a H_2O and CO_2 channel. Experiments on the AQP5-T41F and AQP5-R188E mutants determine that the CP is the major route for CO_2 through AQP5. The MP exclusively gates H_2O fluxes. We also demonstrate that it is possible to create an almost pure CO_2 channel by blocking water flux via the AQP5 MP. This result is of potential significance in creating "designer gas channels" that are highly selective for single gases like CO_2, O_2, or N_2.

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ABSTRACT #40

A pathway enrichment analysis of genes that modify tobacco-smoking risk for multiple sclerosis

Benjamin Frostino, Padua Franciscan High School; Farren Briggs, PhD, Department of Population and Quantitative Health Sciences, Case Western Reserve University

Background:
Multiple sclerosis (MS) is a neuroimmunological disorder that causes the immune system to rewire itself and attack myelin sheath coverings, an essential protection of neuronal axons, which results in a variety of neurological symptoms and disabilities. Genetic variation and environmental exposure both contribute to MS risk, including tobacco smoking (TS) - which increases risk for MS by 50%. While not all smokers will develop MS, the biological pathways through which TS amplifies MS risk are not known. Despite a declining prevalence of TS, 34 million American adults are active cigarette smokers, therefore it continues to be important to uncover the mechanisms that contribute to MS risk in smokers.

Goals:
To determine if there is an enrichment of genes associated with specific biological pathways amongst genes that modify TS risk for MS. Understanding the underlying biological mechanisms are essential to uncovering the complexity of the disease and its progression as a whole, and may provide insights for developing new drug targets.

Materials and Methods:
Enrichment analyses were conducted for a list of genes that were previously shown to modify the effect of TS risk for MS in a genome-wide gene-environment (GxE) investigation (interaction $p < 0.001$). Using PANTHER Classification System, statistical overrepresentation tests were run for PANTHER Pathways and Reactome Pathways using all *Homo sapiens* genes as the reference gene list. Fisher's exact tests were used to determine significant pathway enrichment, allowing for the comparison of the proportion of genes that overlap across gene sets versus what would be expected by chance alone.

Results:
There were 359 GxE genes (interaction $p < 0.001$) that were previously shown to modify TS risk for MS. Pathway enrichment of these genes using the PANTHER database suggested that there was an overrepresentation of genes involved in Axon guidance mediated by netrin (fold enrichment=8.69, p=0.00044), Nicotinic Acetylcholine Receptor signaling pathway (fold enrichment=4.17, p=0.002), and Cadherin signaling pathway (fold enrichment=3.05, p=0.006). Pathway enrichment of the Reactome database showed significant overrepresentation in the biological mechanisms of the Neuronal System (fold enrichment=2.96, p=0.000042) and axon guidance (fold enrichment=2.52, p=0.00011). These findings implicate prominent roles for cell-cell communication and axon growth.

Conclusions:
Enrichment analyses of genes that modify TS risk for MS emphasizes a prominent role of biological mechanisms involved in neural development (axon guidance and cadherin signaling), and neuromuscular and neuronal transmission (nicotinic acetylcholine receptor signaling). We can hypothesize that variation in the architecture of the nervous system impacts how TS may cause MS in a subset of smokers. These results may also inform how TS accelerates MS progression, leading to our conclusion that smoking cessation is an important tool for decreasing MS risk.

Benny Frostino is a Sam Miller Scholar

ABSTRACT #41

Flavored Tobacco Product Use Amongst the Younger Population

My'Desire George-Wiggins, Shaw High School; Erika Trapl, PhD, Department of Population and Quantitative Health Sciences, Case Western Reserve University

Background:
Flavors are added to tobacco products to improve the taste by reducing the bitter tastes. Flavored tobacco products are disproportionately preferred by adolescents and young adults. Flavored tobacco products promote youth smoking initiation and help young occasional smokers to become daily smokers by reducing or masking the natural harshness and taste of tobacco smoke and increasing the social acceptability of the toxic tobacco product. Flavored tobacco products are tremendously harsh to the bodies of the people who use them. These products are harder to quit and more addictive than regular tobacco products. A majority of adolescents and young adults are exposed to cigarillo advertising in magazines and storefronts and on social media. Many teenagers and young adults are appealing to these products because of the flavors, the advertising, and the overpowering flavors that they recognize.

Goals:
The goal of this project was to evaluate the use of flavored tobacco amongst teenagers and young adults.

Materials and Methods:
I conducted a literature review to examine the difference between flavored tobacco products and regular/unflavored tobacco products, the difference in advertising, the reasoning for the use of tobacco products, the difficulty of quitting these products, gender roles, and the numbers if young adults and teenagers who use them. I evaluated articles that studied the population of youth and young adults using these products. I have studied the statistic in the U.S. of flavored tobacco users from 2019-2021.

Results:
Teenagers and young adults perceive flavored tobacco products as more appealing because of the better tastes than non-flavored tobacco products. In 2020, among high school students who currently use any type of flavored e-cigarette, the most commonly used flavor types were: › Fruit (73.1%), › Mint (55.8%), › Menthol (37.0%), and › Candy, desserts, or other sweets (36.4%). Flavored tobacco product use is higher in younger adults than in older adults. Nearly three-quarters, 72.7% of young adult current tobacco users report flavored tobacco use, compared to just 28.6% of adults over 65.9 > Among young adult non-cigarette tobacco users, 83.5% report that they use a flavored product. Hookah users reported the most flavored product use, with nearly 86% followed closely by e-cigarette users with 85.2%.

Conclusions:
Advertisements and placement are responsible for the surge in young adults and teenagers using flavored tobacco products. Future research will include how to prevent the use of these tremendously harmful products by finding healthier alternatives. Future research will also result in finding ways to support the communities affected by the preying of very big tobacco companies on younger audiences and minorities.

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ABSTRACT #42

Role of RNA binding proteins dysregulation in cancer development and progressions

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Background:
RNA binding proteins (RBPs) serve as regulators for the expression of specific genes. RBPs are engaged in the control of RNA at multiple levels including mRNA stability control, mRNA localization, translation, and splicing. All those mechanisms are critical for maintaining essential cellular processes like cell metabolism, differentiation, intracellular transport, cell proliferation. Therefore, dysfunction of RBPs were found to be associated with many diseases including cancer. hnRNPK is an example of RBPs which exhibit a wide spectrum RNA control. The last two decades of research have revealed that hnRNPK is able to regulate the expression of target genes involved in transcription, translation, and splicing. hnRNPK is usually classified as an oncogene because it is overexpressed in most of the solid tumors like melanoma, breast cancer, prostate, esophageal, head and neck, colorectal and GI cancer. Altered hnRNPK regulation usually correlates with advance tumor stage. Mechanistically hnRNPK upregulation results in enhanced cell migration and proliferation. One of the characteristic hnRNPK features in cancer is its mis-localization. At physiological conditions, hnRNPK is mainly restricted to the nucleus. Some solid cancers like colorectal, prostate or head and neck cancer showed hnRNPK cytoplasmic accumulation. The consequences of hnRNPK cytoplasmic localization are not yet fully understood. This work aims to address how cytoplasmic hnRNPK contributes to cancer development and progression.

Goals:
The long-term goal of the project is to determine how cytoplasmic accumulation of hnRNPK affects processes typically dysregulated in cancer related to cell survival and proliferation. The aim of my project is to generate an hnRNPK expression vector with an NLS to provide an essential investigative molecular tool.

Materials and Methods:
Site directed mutagenesis will be utilized to modify hnRNPK sequence on two plasmid vectors encoding hnRNPK – pBabe and MigR1. Deletion of the N-terminal NLS will be pursued by PCR reaction with specifically designed primers to replicate plasmid DNA with the desired mutation. Newly amplified vectors will be delivered to E.Coli bacteria by heat-shock transformation. Next, several E.Coli clones will be selected to purify mutated plasmids. Restriction analysis along with Sanger sequencing will be applied to identify clones with correct sequence. Finally, positive clones will be transfected into HEK293T cells in order to verify expression and localization of hnRNPK by Western-Blot.

Results:
I anticipate successful mutagenesis, which will allow for overexpression and cytoplasmic accumulation of hnRNPK in mammalian cells. Some fraction of overexpressed DNLS-hnRNPK is expected to be still localized in nucleus since hnRNPK has second non-canonical nuclear import sequence- KNS.

Conclusions:
Site directed mutagenesis is a potent genetic engineering tool that allows for various modifications of studied protein or DNA sequences. My work will let me continue the exploration and testing of abnormal hnRNPK properties in cancer.

Supported in part by NIH, NCI, R25 CA221718

ABSTRACT #43
Proximity Labeling to Identify Protein Interactions Involving the Nonsense-mediated mRNA decay proteins UPF2 and UPF3

Nalin Gupta, Solon High School; Sarah Nock; DaJaun Whiteside; Kristian Baker, PhD, Department of Genetics and Genome Sciences, Case Western Reserve University

Background:
The transcription of DNA to mRNA is a critical first step in the process of gene expression and in the production of cellular proteins. Throughout gene expression, mRNA is continually monitored to ensure transcripts can faithfully express functional polypeptides. Nonsense-mediated mRNA decay (NMD) is an essential quality control process that identifies aberrant transcripts containing premature stop codons and rapidly degrades them to prevent accumulation of potentially harmful, shortened proteins. The core NMD machinery involves three proteins: UPF1, UPF2, and UPF3; deletion of any of these proteins from the cell prevents NMD from occurring. UPF1, UPF2 and UPF3 interact with each other and are believed to function as a trimeric complex. The function of UPF1 during NMD has been well studied, however, the roles of UPF2 and UPF3 in this process are unclear. It remains to be determined whether UPF2 and UPF3 function only within the trimeric complex or have additional, independent functions in mediating NMD.

Goals:
To evaluate whether UPF2 and UPF3 may function outside of its complex with UPF1, protein interaction partners of UPF1, UPF2 and UPF3 will be identified using a Proximity Labeling approach. Proximity Labeling will allow us to compare interactive protein partners of all three NMD proteins and determine whether they likely work together as a complex, or have additional function and/or activity during their role in NMD.

Materials and Methods:
PCR amplification of DNA; agarose gel electrophoresis; gel extraction; Gibson cloning; DNA precipitation; bacterial cell transformation; yeast cell transformation; restriction digestion; cell culturing; protein lysate preparation; SDS-PAGE; Western blotting.

Results:
Plasmids expressing UPF2 or UPF3 fused to the bacterial biotin ligase (BirA; also known as TurboID) and the HA epitope tag were constructed using PCR amplification and Gibson cloning. PCR amplification and restriction digestion were used as diagnostic tools to confirm correct construction of the desired plasmids. Sanger DNA sequencing is underway to confirm the sequence of the plasmids and ensure that the desired fusion proteins will be expressed. Yeast cells were transformed with either the UPF2:BirA:HA or UPF3:BirA:HA plasmid. Cells were then grown in media containing biotin and harvested for analysis. Protein lysates from these cells were separated by SDS-PAGE electrophoresis and the interacting proteins of UPF2 and UPF3 - that are biotinylated due to their proximity to the UPF proteins - will be detected by Western Blotting using an antibody directed against biotin (i.e. HRP-conjugated streptavidin) and compared to UPF1 protein partners. Once completed, these data will reveal interacting partners of all three NMD proteins and inform as to their function inside the trimeric complex or out.

Conclusion:
Construction of UPF2:BirA:HA and UPF3:BirA:HA have been preliminarily confirmed and will provide important information regarding what proteins each of these NMD factors interact within cells. Comparing these protein 'fingerprints' to that of UPF1, will provide novel insight into the function of UPF2 and UPF3 in NMD.
Nalin Gupta is a Sam Miller Scholar

ABSTRACT #44

Association between Pediatric Brain Cancer and Learning, Sleep Quality, and Myelination: A Systematic Review

Hannah Holt, Charles F. Brush High School; Sarah Markt, PhD, Department of Population and Quantitative Health Sciences, Case Western Reserve University

Background:
Brain cancer is a growth of abnormal cells in various regions of the brain. In the United States, the incidence of brain cancer from 2013-2017 was 23.8 per 100,000 in adults and 6.1 per 100,000 in children (aged 0-19 years). The tumor itself, including location and size, and treatment, can contribute significant neurological damage to patients.

Goals:
The objective of this study was to investigate the hypothesis that pediatric brain cancer, and specifically treatment for it, negatively influences learning and sleep quality. We also aimed to understand the pathways through which treatment impacts neurocognitive damage and learning.

Materials and Methods:
We used the CDC US Cancer Statistics (USCS) to first describe the epidemiology of brain cancer in children (aged 0-19 years). Then, to conduct our systematic review, we searched PubMed and Google Scholar using the following terms: “Brain cancer,” “children,” “cognition,” “sleep,” “learning,” and “myelination”. Over 1,200 articles met those search criteria. We then further refined our search ~~using~~ the advanced search option and included the terms: “pediatric,” “brain tumor,” “malignant,” and omitted the terms: “adults” and “geriatric.”

Results:
In 2018, the age-adjusted rate of malignant brain tumors among children was 2.9/100,000, and benign brain tumors was 2.7/100,000. In the US, brain cancer is the third most commonly diagnosed cancer. The age-adjusted incidence rates are slightly higher among white patients (3.2/100,000), compared to Black (2.3/100,000), Asian/Pacific Islander (2.3/100,000), American Indian/Alaska Native (1.8/100,000) and Hispanic (2.3/100,000). The most common type of malignant brain tumor in children is pilocytic astrocytoma (0.8/100,000) followed by glioma (0.5/100,000). Following review of titles and abstracts, we included 13 articles in the final systematic review. The majority of them found that tumor location/size could contribute to neurological deficits such as decline in executive function. Furthermore, seven studies found that radiotherapy can damage healthy tissue and disrupt neurological processes that help children learn, like metacognition. However, new treatment advancements, like Proton Beam Therapy (PBT), treat tumors with better precision, and may reduce some cognitive damage. One study found a potential mechanism for the association between brain cancer and cognition ~~is~~ through myelination, as brain cancer cells themselves can hijack the process of myelination allowing proliferation of cancerous cells.

Conclusion:
Brain cancer severity and treatment both significantly influence neurocognitive development. With the help of PBT and effective academic recovery programs for brain cancer patients, the negative effects of treatment on pediatric brain cancer may be diminished.

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ABSTRACT #45

Blood Vessel Extraction from Retinal Images

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Background:
Retinal blood vessels are an imminent part in the identification and reception of different retinal illnesses like arteriosclerosis, hypertension, diabetic retinopathy, and glaucoma. Consequently, retinal vasculature extraction is significant in terms of helping experts reach the conclusion and treatment of precise diseases. These extraction methods include Green Channel Extraction, Gaussian Filtering, CLAHE, Gaussian Matched Filtering, Decontour/Masking. In this paper, a means of creating a well thought out methodology is created to extricate retinal blood vessel networks to help identify the best method of extraction so these different retinal illnesses do not interfere with the day-to-day life of the patients.

Goals:
The goal of this project is to figure out what is the best extraction method that would help the most patients as well as finding out how we can better overcome these struggles by figuring out ways to prevent different retinal diseases.

Materials and Methods:
A literature review in the PubMed Central database was conducted to obtain information about different retinal extraction methods. These articles investigated the efficacy of such methods, as well as analyzed the results of the procedure and the effect it had on the patients. Additionally, use of Python and different algorithms were used in order to get a better picture of certain retinal images as well as seeing how those images changed as we used different extraction methods.

Results:
With the use of Python and a full literature review in the PubMed Central database, we were able to figure out that Gaussian matched filtering allowed us to be able to filter out different types of blood vessels better. When light passes through the fundus retina, due to the different reflection coefficients of the retinal epidermal tissue and the retinal blood vessels, the blood vessels in the retinal image show a darker brightness characteristic. And by analyzing the cross-sectional information of retinal blood vessels, it can be known that the gray distribution of retinal blood vessels can be simulated with a Gaussian matched filter function, that is, the shape and direction of the Gaussian matched filter function are used to approximate the retinal image blood vessels.

Conclusion:
Gaining a better understanding of retinal diseases and the environment surrounding the different extraction methods are perhaps critical to finding meaningful treatments for patients that develop these rare retinal diseases. Although Gaussian matched filtering is critical for the health of the patients, there is much work to be done ~~yet~~ with the clinical potential.

ABSTRACT #46

Tumor-Associated Macrophages: Contributing to Therapy Resistance in Breast Cancer

Ahmad Islambouli, Cleveland School of Science and Medicine; John Letterio, MD, Department of Pediatrics, Case Western Reserve University

Background:
Macrophages are a type of cell that carry out many immunological and host defense functions in the body. Tissue macrophages are derived from a common myeloid progenitor and are part of the innate immune system, meaning that their functions are programmed within them. These cells work by first detecting a harmful substance, then actively undergo phagocytosis and destroy the threat, such as bacteria and other harmful pathogens. Among the functions of the macrophage, the role it plays in host defense is most important. However, despite being necessary for survival, these phagocytes can also negatively affect the response of cancer treatment. Upon being impacted by treatment, cancer cells begin to release substances that bind to receptors on the macrophage, in turn, causing the macrophage to release substances that activate signaling pathways in the cancer cell, activating gene transcriptional programs that confer resistance to the treatment. Tumor-associated macrophages (TAMs) are found in abundance in many cancers, and evidence suggests that TAMs are associated with tumor progression and poor prognosis.

Goals:
There are two major goals of this study; the first is to identify concrete examples of how macrophages interfere with response to treatment in breast cancer. Second, to identify examples of how targeting or therapeutically eliminating macrophages may improve treatment.

Materials and Methods:
Various studies have demonstrated that macrophages employ many different mechanisms, such as cytokine and chemokine secretion, that provide breast cancer tumors therapy resistance. Through histological examination, dense areas within the tumor have been found to contain substances highly associated with macrophages, showing that macrophages do provide some form of relative therapy resistance to breast cancer tumors. PubMed.ncbi.gov, published original articles and reviews dating within the past six years were used to help formulate results.

Results:
Through various methods of research on multiple forms of breast cancer and treatments, macrophages have been shown to play a major role in breast cancer tumor progression. TAMs (tumor-associated macrophages) interfere with many mechanisms that mediate the response to cancer therapy, and in some cases, directly enhance the maintenance of the tumor cell itself. These observations suggest that inhibition of TAMs will overcome therapy resistance and ultimately improve treatment effectiveness.

Conclusion:
Through a review of the published literature, we were able to identify evidence that macrophages employ many mechanisms to enhance breast cancer tumor progression. These studies imply that efforts to identify ways to inhibit macrophage activity will create opportunities to advance new therapies to overcome resistance and these efforts will lead to an overall better patient prognosis.

Ahmad Islambouli is a Mort and Iris November Scholar

ABSTRACT #47

CYTOKERATIN PROFILE OF HUMAN ORAL MUCOSA

Ta'nea Jackson, Shaw High School; Santosh Ghosh; Aaron Weinberg, DMD, PhD, Department of Biological Sciences, School of Dental Medicine, Case Western Reserve University

Background:
Normal oral mucosa consists of a highly proliferating layer of epithelial cells covered by multiple layers of stratified squamous epithelium. Differentiation is the process by which progenitor cells, from the basal layer, acquire functional capabilities; i.e., undergo distinct changes as they differentiate from the basal layer to the spinous, granular, and cornified layers.

Goals:
Our goal was to analyze cytokeratin's expression of normal human oral mucosa as cells undergo normal differentiation.

Methods:
In the present study we analyzed cytokeratines expression data generated from three different layers of oral tissues. Zones 1 (stratum basale), Zones 2 (intermediate) and Zones 3 (differentiated). Data sources: *Affymetrix Clariom S* Human expression microarray data generated from the RNAs of three different zones (1, 2 and 3). These three zones were originally isolated from oral tissues biopsied from the cheeks of three healthy subjects, by subjecting them to Laser Capture Microdissection (LCM).

Results:
Variations in cytokeratin profile were observed among different layers of oral mucosa.

Conclusions:
Higher expression of Keratins 1,2 3,10,13, 23 and 76 and lower expression of keratin 5 were observed in differentiated layer (Zone 3) compared to basal layer (Zone 1).

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ABSTRACT #48

Comparing the Predicted Secondary and 3D Structures of Betacoronavirus Stem-Loop 1s

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Background:
With over 190 million cases and four million deaths to date, the coronavirus disease 2019 (COVID-19) pandemic has been unprecedented. The virus responsible is severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), one of several coronaviruses in the *Betacoronavirus* (beta-CoV) genus which infect humans. Beta-CoV RNA genomes contain 5' untranslated regions (UTR), which regulate viral RNA synthesis and replication. Located in beta-CoV 5' UTRs are structural motifs called stem-loops, which have an increased probability to be sites for interactions between molecules. In particular, stem-loop 1 (SL1) interacts with the 3' UTR to produce sub genomic mRNAs. Investigating the secondary and 3D structures of beta-CoV SL1s allows for comparisons of their structures between beta-CoVs. This may prove helpful in developing or selecting a drug to prevent infections caused by several coronaviruses.

Goals:
The objectives of this project are to compare the stem-loop 1 (SL1) predicted secondary and 3D structures in 10 beta-CoVs to obtain insight into their similarities and differences, as well as investigate SL1's evolutionary conservation across the beta-CoVs.

Materials and Methods:
Nucleotide sequences of beta-CoV SL1s were obtained from the NCBI nucleotide database. Simulated secondary and 3D structures of beta-CoV SL1s were obtained from RNA structure and RNA Composer respectively. SL1 3D structures were visualized using PyMOL. The multiple sequence alignment (MSA) of beta-CoV 5' UTRs was performed using Clustal Omega.

Results:
All beta-CoV SL1s studied had similar sizes. In SL1 secondary structures, similarities were most frequent among beta-CoVs of the same lineage, in both loops and helices. In tertiary structures, several SL1 structures have at least one apical loop nucleotide oriented towards the outside. Furthermore, each SL1 has at least one groove on its surface, with some variation. Similar to secondary structures, common RNA surface structures are most frequent among viruses from the same lineage. The MSA demonstrated that SARS-CoV-2 had similarities not just with SARS-CoV, but also several viruses in beta-CoV lineage A.

Conclusions:
SL1 has commonalities among beta-CoVs and could be targeted for inhibition to prevent coronavirus replication. Furthermore, studies suggest that RNA binding proteins (RBPs) are hijacked by SARS-CoV-2 during infection, with some being able to bind to SL1. Drugs such as Nilotinib, Sorafenib, and Deguelin have been shown to bind to RBPs and block their function, precluding viral replication. Further investigation of the effects of these drugs is suggested to better understand their effect on the function of SL1 and ultimately their effect on inhibiting coronavirus infections.

ABSTRACT #49

Identifying Targeted Therapies for Treating TGF β-Resistant Esophageal Adenocarcinoma

Anushree Jakate, Solon High School; Andrew Blum, MD, PhD, Case Comprehensive Cancer Center Case Western Reserve University

Background:
Esophageal cancer (EC) is an increasingly common malignancy, with over 19,000 diagnoses estimated this year in the US. Esophageal adenocarcinoma (EAC), a subset of Esophageal cancer, contributes the most to these statistics, representing approximately 80% of all EC diagnoses. Diagnosis of EAC has skyrocketed by up to 400% from 1975 to 2015 yet despite the increasing incidence, EAC is a highly mortal malignancy with only 1 in 5 patients surviving 5 years past diagnosis. One reason for the high mortality associated with this disease is that standard chemotherapy and radiotherapy are generally ineffective, and there are no effective targeted treatments for EAC.

Goals:
The goal of this project is to evaluate the results of a large-scale drug screen in order to link common genomic alterations with novel molecular dependencies in EAC. Results of this effort may inform future therapeutic development in this disease.

Materials and Methods:
Our lab undertook a screen of 3000 bioactive compounds for their effects on cell growth of 6 cell lines: one squamous line (EPC2), one non-dysplastic Barrett's esophagus line (CPA), and 4 EAC cell lines (EsoAD1, FLO1, OE19, Eso26). Cell viability was measured in response to drug treatment, relative to vehicle controls. Candidate dependencies were evaluated through comparing 1) non-malignant and malignant cell models, 2) SMAD4-WT vs. SMAD4 mutant cell models, and 3) ERBB2 amplified vs. non-amplified cell line models.

Results:
Through the drug screen, our lab identified 40 candidates for further analysis. Notably, as anticipated, ERBB2 amplified lines were found to have increased sensitivity to EGFR/ERBB2 inhibitors compared to non-amplified lines, giving confidence in our experimental results. Interestingly, we additionally found that cell lines with ERBB2 amplification show increased response to drugs that generate reactive oxygen species, compared to cell lines without ERBB2 amplification. Also, cell lines with deleterious SMAD4 mutations show increased sensitivity to CHK1 inhibitors compared cell lines without SMAD4 mutations.

Conclusions:
Our analysis linked drug screen hits to the underlying biology of the tumor, as exemplified by the increased sensitivity to EGFR/ERBB2 inhibitors of ERBB2 amplified lines compared to non-amplified lines. This gives weight that the additional identified dependencies may be related to the underlying tumor biology. Additional studies are needed to validate these findings in preclinical models in anticipation of therapeutic translation.

ABSTRACT #50

Investigating Immunotherapy Treatment Methods for Metastatic Melanoma

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Background:
Melanoma is an aggressive form of cancer characterized by the malignant growth in melanocytes. If detected in the early stages, melanoma can be removed through surgical excision with high survival rates. However, survival rates diminish when melanoma metastasizes. Although melanoma is not the most common dermatological malignancy, it can have a high mortality rate if not treated aggressively. Immunotherapy is an effective treatment for metastatic and unrestrictable melanoma and increases survival rates.

Goals:
Analyze various immunotherapy treatment options for metastatic melanoma, focusing on effectiveness, the mechanisms of action, adverse reactions, indications, and contraindications.

Materials and Methods:
Literature review in the PubMed Central database to obtain information about immunotherapy options to treat metastatic melanoma. The studies described different factors that may have had an impact on treatment response, including melanoma staging and immunosuppression status. Additionally, I looked for adverse reactions amongst the participants recorded throughout the studies.

Results:
Two of the most common drugs used to treat metastatic melanoma are nivolumab and pembrolizumab. Both drugs inhibit the program cell death protein 1 (PD-1), activating the immune system to target and eliminate the cancer cells. Another drug is ipilimumab, which inhibits the cytotoxic T-lymphocyte–associated antigen 4 (CTLA-4). CTLA-4 is a protein which prevents T-cells from killing malignant cells. Thus, like nivolumab and pembrolizumab, ipilimumab helps stimulate the immune system to fight cancer cells. A combination of ipilimumab and nivolumab is recommended for certain patients with stage IV metastatic cancer. Dermatologic toxicity is the most common immune-related adverse event (irAE) associated with checkpoint inhibitors. Other common irAE associated with nivolumab and pembrolizumab are eczema, vitiligo, and pruritus. Additionally, about half of all patients treated with ipilimumab will experience rash and/or pruritus.

Conclusions:
Early detection of melanoma is often treated with surgical excision with high survival rates. When the cancer metastasises, treatment is more difficult. Immunotherapy offers patients with metastatic or unresectable melanoma a chance of increased survival. Treatment must be balanced with adverse reactions and response to therapy.

ABSTRACT #51

Triple Negative Breast Cancer in African American Women

Davionna Johnson, Euclid High School; Jennifer Cullen, PhD, Department of Population and Quantitative Health Sciences, Case Western Reserve University

Background:
Triple negative breast cancer, also known as (TNBC), has been described by scientists since the 1980's, but has likely always been present. It is a breast cancer subtype that lacks three important receptors, including: (i) estrogen receptor (ER), (ii) human epidermal growth receptor 2 (HER-2) and (iii) progesterone receptor (PR). Since TNBC is missing those 3 receptors, and most current treatments for breast cancer are targeting those 3 receptors, this makes treating and curing TNBC very difficult. In this study, we examine the rates of TNBC in African American women, which are known to be twice as high as for women of other races in the U.S. This study examines the possible causes of this important disparity in cancer.

Goals:
To examine the rates of TNBC in African American (AA) women and possible reasons for why AA women are more likely to develop TNBC than women of other race groups.

Materials and Methods:
The National Library of Medicine's search engine for research articles, named PubMed, was used to find articles on the topic of TNBC in African American women. The search terms used for this topic included: (i) "Triple negative breast cancer and race" and (ii) "Triple negative breast cancer and African American women". When those exact terms were searched, 472 articles were found for the first search and 265 articles were found for the second search. Among these articles, we examined the topics that were addressed, including treatment and causes of TNBC. Next, this study used Google search engine to find U.S. maps of the national rates of TNBC for African American women in different areas of the U.S.

Results:
The papers found on PubMed showed that African American women have a higher percentage of TNBC than any other race. Also, TNBC is more likely to be found in the later stages in young African American women making it harder for treatments to be completed safely. There are also increasing rates of triple negative breast cancer in African American women in the Southeastern United States. But it is proven that Southeastern AA women had a lower prevalence of TNBC than those U.S. born and Western born AA women. A lot of the papers that were found were published in the early 2000's.

Conclusions:
There has been a lot of research on this topic and a lot of other searches are similar but haven't been able to pinpoint a reason why AA women are more likely to get TNBC. Although this work was able to show that triple negative breast cancer is one of the worst types of cancers and that it's more so targeted at African American women than White women or Hispanic women. Something that is causing this difference is because AA women are always diagnosed at a more advanced stage. Knowing this information can help scientists increase their knowledge on the topic providing information that will help prevent it until a treatment for TNBC is found otherwise people will die. To continue this work my next steps would be to examine a few women from every race and see what is different and what may be the reason why African American women are two times more likely to get triple negative breast cancer than women from other races.

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ABSTRACT #52

EPHRINB2 in Esophageal Adenocarcinoma

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Case Comprehensive Cancer Center, Case Western Reserve University

Background:
Esophageal adenocarcinoma (EAC) is a highly aggressive cancer and has a short selection of treatment options. This disease has been related to a complex esophageal metaplasia disorder called Barrett's Esophagus (BE). Ephrin receptor B2 (EphrinB2) tyrosine kinase has been found to be overactive during the beginning of EAC development. Studies have shown that EphrinB2 is a regulator of c-MYC, which is part of a family of proteins that regulate a cell's function to reproduce and die. Single-cell RNA studies showed increased EphrinB2 and MYC activity with BE.

Goals:
The goal of this study was to see what role EphrinB2 and MYC played in promoting EAC.

Materials & Methods:
To test for the different amounts of proteins we had a negative control, the stuffer, a control that had the normal protein, the wild type, and the mutant, which is constitutively active. We started by culturing cells that we obtained from a nitrogen tank that kept cells preserved for our use. We then prepared 6 samples, 2 for a stuffer, two for a wild type, and two for F613D. They were placed in Petri dishes with media and Fetal Bovine Serum. We placed them in a stable incubator that was kept at 37° C to keep the conditions similar to that inside a human. After two days we then counted the cells. We then used a TrypLE Express which got the cells, that were stuck to the Petri dishes, off of the sides and allowed us to be able to transfer them into tubes to then centrifuge the cells to separate them from the media before we put in a lysate and buffer to get rid of everything in the cell besides the proteins. We then centrifuged the new sample, which separated the proteins from the debris of the cell; the debris is heavier so it falls to the bottom compared to the protein, which hangs around in the lysate solution. We then extracted the protein and transferred it into a different tube. Then we added some buffer and heated up the proteins to keep them from destroying but allow them to denature and become straight, instead of coiled, so that the western blot reading will be easier. We then added a dye to the proteins so that we could see them in the western blot. We then added the 6 samples into 12 different wells in the western blot so that we could test for 5 different proteins in the end. We then transferred the readings from the western blot onto a membrane. We cut two membranes we had into 5 pieces to test for 5 different proteins. Those membranes were then placed in a container with a buffer, TBST, and some antibodies to allow for the proteins to be isolated when the second antibody was added. After the second antibody was added, the proteins were isolated in the different membranes. We then took the membranes to a chemiluminescence machine and examined the 5 different proteins: MYC, v5, ephrinb2, py, p62, and actin. We then took the images from the machine to test later.

Results:
We found similar levels of actin in the western blot which means that we put the same amounts of protein in the wells of the western blot. We found an increased level of MYC and p62 proteins in the "stuffer" sample, less in the wild type sample, the F613D. We found similar levels of the v5 and py proteins in all the samples. There were increasing amounts of EphrinB2, where the stuffer had the lowest and the F613D had the highest.

Conclusions:
More trials are needed to obtain conclusive results

ABSTRACT #53

Sighs: A Biomarker Inflammation in the Circuitry of Respiratory Control

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Background:
Your breath starts from areas in your brainstem. For inhalation, output of these areas coordinates muscles in the airway to reduce airway resistance and in the chest wall to expand the thoracic cavity. We can measure the magnitude and timing of inhalation using a technique called plethysmography. In this study, we injected (lipopolysaccharide, LPS) in rats intra-abdominally and recorded their breathing pattern both before and after injection. Specifically, we measured the frequency of sighs in the breathing pattern. Sighs are large breaths, described as a breath upon a breath and a pause in the pattern following a sigh. Sighs evoke a sense of emotional relief but also prevent atelectasis, which is the collapse of alveoli and thus maintains oxygenation during illness. In this research, we conditioned rats with intra-abdominal (referred to intraperitoneal, *i.p.*) injections of LPS once a day for 3 days, to test that the hypothesis that sighs will progressively increase across the days.

Goals:
The goal of this research was to analyze sighs in the breathing rat's breathing records before and after LPS injections to determine if the expected increase in sigh frequency occurred progressively.

Materials and Methods:
To measure sighs, we placed un-anesthetized rats in plethysmography chambers. The rats were unrestrained and breathed freely. We recorded their breathing for me to analyze later. The protocol required four days of recording. On the first day, rats were placed in the plethysmography chamber, for a baseline recording using the Spike2 software. On the second through fourth day, rats were injected with either LPS (24 mg/kg bw, n=8) or phosphate-buffered saline (PBS 0.3 ml, n=3) *i.p.* The rats were placed in the plethysmograph for recording. I counted the number of sighs that occurred during these sessions compared for significance.

Results:
Based on our preliminary analysis, after receiving LPS *ip*, the frequency of sighing (fS) increased in the rat. Instantaneous sigh frequency plotted against recording time on four consecutive days. Baseline recording: The rat was placed in the plethysmography chamber without additional handling. Average sigh frequency was 0.33 Sighs/min and the coefficient of variation was 0.18. Day 1 Recording: Sigh frequency (fS) increased after the first LPS injection (24mg/kg, *i.p.*). An increase in fS was evident at the start of the recording but it increased markedly starting at ~2h into the recording. Days 2 & 3 Recordings: Compared to Day 1, the fS decreased and a time-dependent response was absent The CV of fS remained high in the recordings after LPS.

Conclusions:
We conclude that the sickness behavior induced by LPS includes increased sighing. The latency to increased sighing sickness was biphasic. The short-latency response was a modest increase in fR but included paired sighs defined as an intersigh-interval (>1/3 of the mean), which underlies the high coefficient of variation for fS. The short-latency response could be due to evoked reflexes including evoked 'sickness behavior'. In contrast, the long-latency response is consistent with the time required for expression of pro-inflammatory cytokine and chemokines in the brainstem. Thus, the secondary and sustained increase in sighing may be related to direct brainstem inflammation.

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ABSTRACT #54

Immunohistochemistry Staining of Colorectal Cancer Tissue to Confirm the Liver Microenvironment's Paracrine Activation of the HER3-Akt Pathway

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Background:
Colorectal cancer (CRC), with an estimated 150,000 cases and 53,000 patient deaths per year in the United States, is the US' second-leading cause of cancer-related deaths. Patients with early-stage CRC have 5-year survival rates between 90% and 72% (localized and regional CRC, respectively). However, the 5-year survival rate of patients with metastatic colorectal cancer (mCRC) in distant organs, such as the liver, is a drastically lower 14%. Moreover, ~50% of all CRC patients develop metastases, ~80% of which are in the liver, making it the most common site for such metastases. In other research groups' preclinical studies on glioblastoma, hepatocellular carcinoma, and other cancers, generic endothelial cells (ECs) – specifically, human umbilical vein ECs (HUVECs) – were found to secrete paracrine factors that activate the NF-κB (nuclear factor-kappa B) pathway, the EMT (epithelial-mesenchymal transition), and other pathways that promote cancer cells' proliferation and metastasis. Our laboratory, however, has focused specifically on primary liver ECs. Our findings suggest that liver EC-secreted factors activate HER3 (human epidermal growth factor receptor 3) and one of its downstream targets, Akt (protein kinase B), thus promoting cancer cells' proliferation and chemoresistance. This work has identified HER3 as a key mediator of liver EC-induced CRC cell survival, and suggests potential in treating mCRC metastases in the liver with HER3-targeted therapy.

Goals:
Our overarching goal is to design more effective clinical therapies and improve patient outcomes with respect to both primary CRC and mCRC in the liver. The specific focus of this immunohistochemistry (IHC) staining work is to determine whether the HER3-Akt pathway is activated in mCRC tumors in the liver, and, additionally, to validate HER3 phosphorylation as a potential predictive marker for positive patient responses to HER3-targeted therapy.

Materials and Methods:
Using sections from xenografted CRC tumors previously exposed to liver CM, we will stain for both the total and phosphorylated amounts of HER3 and Akt, as phosphorylation is indicative of proteins' activation. We will also stain for Ki-67, an established cell proliferation marker, to determine the number and location of the proliferative cells in the tumors. Lastly, time and resources permitting, we will stain for and compare these proteins' expression and phosphorylation in tissue samples from both primary CRC and mCRC tumors in the liver. The characteristic steps of the staining protocol are as follows. First, a paraffin-embedded tissue sample is washed with xylene and ethanol to remove the paraffin and rehydrate the tissue. Additional antigens are unmasked by boiling the tissue in a citrate-based antigen retrieval solution. Then, the tissue is blocked from undesired protein binding, before the chosen primary and secondary antibodies are bound to their antigen targets. The tissue is chromogenically stained before it is examined and analyzed under bright-field illumination.

Results:
Unfortunately, we have not been able to stain our CRC tissue yet due to delays within the University Hospitals core histology facility. However, we expect to be able to retrieve, stain, and analyze our tissue samples within the next couple of weeks, and the final abstract and manuscript will include the subsequent findings. Specifically, the results section will include the average proportions of the cells with HER3, Akt, and Ki-67 expressed, as well as the average proportions of the cells with phosphorylated HER3 and Akt. We will also include representative images of each tissue sample type and antigen stain.

ABSTRACT #54 CONTINUED

Conclusions:

We have not been able to stain our own experimental tissue yet, but based on our previous work and assays, we expect that HER3 and Akt will be phosphorylated at higher levels in CRC cells conditioned with liver CM than with CRC CM. Thus, the conclusion section will likely resemble the following:
The high expression of HER3, Akt, and Ki-67, and particularly, the high levels of phosphorylated HER3 and Akt in the CRC tissue exposed to liver EC CM corroborate that the HER3-Akt pathway is activated by liver ECs' paracrine secretions. Thus, HER3-targeted therapies may potentially be used to treat patients with CRC liver metastases that are unresponsive to chemotherapy.

ABSTRACT #55

P7C3-A20 Treatment Protects Against Neurodegeneration and Neurobehavioral Deficits After Whole-Brain Radiation Therapy

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Background:
In patients with cancer, whole-brain radiation therapy (WBRT) is applied as a treatment for brain metastases or as prophylaxis against developing brain metastases. While WBRT significantly improves acute symptoms associated with cerebral metastases in more than 80% of cases, it is also associated with an increased risk of chronic neurocognitive decline and diminished quality of life. Indeed, 50-90% of patients experience a significant decline in neurocognitive function one year after WBRT. The aminopropyl carbazole P7C3-A20 is a neuroprotective agent that promotes survival of both mature neurons and newborn neurons in the brain. By promoting the survival of young newborn hippocampal neurons in the postnatal brain, P7C3 compounds increase the net magnitude of neurogenesis. To date, P7C3 compounds have shown significant cognitive protection in pre-clinical models of age-related cognitive decline, stress-induced depression, traumatic brain injury, stroke, Parkinson's disease, and Alzheimer's disease. Preliminary results have shown a protective effect that is associated with preservation of the blood-brain barrier. Degradation of the blood-brain barrier is associated with harmful neuroinflammation in the brain, which contributes to neurodegeneration. We hypothesize that P7C3-A20 treatment will also reduce neuroinflammation in the brain after WBRT.

Goals:
The goal of this project is to evaluate and characterize in a preclinical model of WBRT if P7C3-A20 treatment can protect against WBRT-induced brain damage, cognitive decline, and depression-like behavior. Specifically, we investigated the question of whether P7C3-A20-mediated protection of the blood-brain barrier after WBRT is also associated with reduced neuroinflammation.

Materials and Methods:
A literature review (PubMed) was conducted and immunohistochemistry for Iba1 was completed in the brains of young (3-month-old) wild type C57/Bl6J mice that had been treated with daily P7C3-A20 (20 mg/kg, intraperitoneal), or vehicle, for one month. We used immunostaining with an antibody to Iba1 on paraformaldehyde-fixed 40 micron thick coronal brain sections. Images of stained brain tissue were scanned, and positive signal in the hippocampus and cortex was quantified in an automated and unbiased manner, blind to the treatment group. GraphPad Prism was used to analyze the data and determine statistical significance.

Results:
Treatment of mice with P7C3-A20 after WBRT attenuates cognitive deficits, reduces neurodegeneration, protects endothelial cells, and lowers neuroinflammation after WBRT.

Conclusions:
Our results suggest that pre-treatment with P7C3-compounds before WBRT might provide therapeutic benefits for patients by reducing normal tissue damage and preventing cognitive decline. We have also observed that aging-related increases in neuroinflammation are decreased by P7C3-A20 treatment, which could additionally help protect the aging brain even in the absence of WBRT treatment.

ABSTRACT #56

PTPmu Fluorescent Imaging Agents for the Detection and Treatment of Glioblastoma

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Background:
Glioblastoma (GBM), a form of high-grade glioma, has a very low survival rate even after surgical resection and is hard to completely treat due to invasive tumors. The current standard of care consists of surgery, radiation and chemotherapy. However, it is difficult for surgeons to visualize the tumor margins and surgically remove the highly dispersive tumor cells that infiltrate the rest of the brain due to their migratory nature and microscopic size. Complete tumor resection correlates with increased survival rates in adult GBM patients.

Goals:
Better imaging technology that can detect infiltrative, highly dispersive tumor cells responsible for recurrent tumors need to be developed. The transmembrane cell adhesion molecule protein tyrosine phosphatase mu (PTPmu) is expressed in normal glial cells and is cleaved in GBM. Coupling a peptide agent, SBK2, that targets the unique PTPmu fragments specific to dispersed GBM cells with fluorescent dyes could prove as a viable imaging technique for the detection and visualization of GBM during surgery.

Materials and Methods:
Using 3D cryo-imaging of mouse xenograft brain tumor models, we looked to see if the peptide agent SBK2 coupled to the fluorescent dye Cyanine 5 (Cy5) could effectively label rat CNS-1 or human LN-229 GBM tumors and invasive tumor cells that migrate away from the primary tumor mass. We also tested SBK2 coupled to the fluorescent dye indocyanine green (ICG).

Results:
SBK2-Cy5 successfully labeled the migrated tumor cells up to 4mm away from the main tumor based upon cryo-imaging. We also recently analyzed SBK2 conjugated to the near-infrared (NIR) dye indocyanine green (ICG). SBK2-ICG was able to label heterotopic flank tumors and orthotopic intracranial brain tumors.

Conclusions:
The SBK2-Cy5 agent may facilitate the development of targeted therapeutics and open up possibilities for new fluorescent dyes to be used with SBK2, such as the only FDA-approved dye ICG. SBK2 conjugated to both Cy5 and ICG are able to specifically detect invasive GBM tumors. These fluorescent agents will allow better surgical resection of tumors.

ABSTRACT #57

Cloning Truncations Mutants of CHMP5 to Investigate Thymocyte Selection

Andrew Loney, Shaker Heights High School; Katharine Umphred-Wilson; Stanley Adoro, PhD, Department of Pathology, Case Western Reserve University

Background:
The immune system is a network of different cells and proteins that work together to help the body fight off pathogens. This works by coordinating innate and adaptive immune responses. The innate response is the immediate, non-specific first line of defense, driven by immune cells such as neutrophils and macrophages. The adaptive response takes days to weeks to become established because it is pathogen-specific, and driven by T and B-cells. T-cells clear infected host cells and provide help to B-cells. Unlike the rest of the immune cells which mature in the bone marrow, T-cells are educated in the thymus and are selected to ensure proper signaling and to prevent autoimmunity. It has recently been discovered that the Endosomal Sorting Complex Required for Transport (ESCRT) protein, CHMP5, is required for positive selection of thymocytes and successful T-cell development. CHMP5 regulates this process by acting as an "adaptor" to prevent the ubiquitination and degradation of pro-survival proteins downstream of the T-cell receptor, independent of the ESCRT pathway. Previous studies have suggested that proteins associated with the ESCRT pathway interact with the C-terminus of CHMP5, while proteins that are stabilized by CHMP5 may interact with the N-terminus. To further study this phenomenon, I used DNA cloning to generate truncated mutants of CHMP5 in a lenti-viral plasmid to transduce T-cells and study the interactions of CHMP5 and its effect on T-cell survival.

Goal:
Clone truncated mutants into a lenti-viral vector to transduce T-cells and confirm their expression for downstream applications.

Materials and Methods:
Plasmids are small circular pieces of DNA that replicate independently from the host's chromosomal DNA and are manipulated by a process called "cloning" in the laboratory. First, truncated and FLAG-tagged forms of CHMP5 were inserted into a vector plasmid for lenti-viral generation through restriction enzyme digest and ligation. It was then transformed into bacteria, to amplify copies of the plasmid. After confirmation by restriction digest to ensure the presence of the inserted gene, lenti-viral particles were produced by transfection of HEK293T cells and used to transduce a T-cell leukemia cell line. Successful transduction of the plasmid was validated by GFP expression using flow cytometry and FLAG-tag expression by western blot.

Results:
I confirmed the presence of the truncated mutant inserts of CHMP5 in the donor plasmids and isolated them through restriction enzyme digest and gel electrophoresis. After ligation into the pHAGE vector, the clones were transfected into HEK293T cells to create virus. Further results are pending on how the truncated mutants of CHMP5 affect its interactions and T-cell survival.

Conclusions:
I predict that mutants with the C-terminus deleted will only affect CHMP5 binding to the ESCRT pathway and therefore will still promote T-cell survival. However, the N-terminal deleted mutants will not be able to bind to pro-survival proteins such as BCL-2, and will not be able to rescue CHMP5 knockout thymocytes. This will also help us investigate which proteins are regulated by the "adaptor" protein function of CHMP5 versus the ESCRT function of CHMP5 in thymocytes.

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ABSTRACT #58

The role of a cytoskeletal protein (CP) in hair cell mechanotransduction

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Department of Otolaryngology, Case Western Reserve University

Background:
Hair cells are sensory cells that control senses such as hearing. Over the years, much progress has been made in working out the molecular basis of hair cell function using vertebrate animal models. Due to the transparency of the inner ear and tools utilized, zebrafish have become an increasingly popular model organism for the study of the function of the auditory system. Research indicates that Tmcs are necessary proteins in hair cell mechanotransduction. HCP is a member of a family of calcium and integrin binding proteins, and it interacts with TMC proteins. CPs are broadly expressed intracellular adaptors that link a variety of membrane protein complexes. We hypothesize that the CP in hair cells links TMC to the actin cytoskeleton.

Goals:
The goal is to test the hypothesis that the CP in hair cells link TMCs to the actin cytoskeleton in zebrafish.

Methods:
CRISPR/Cas9, a technology that allows altering sections of a DNA sequence will be utilized to knock-out CP.

Results:
We have performed genomic analysis of the CP region in zebrafish and have initiated CRISPR/Cas9.

Conclusions:
Using CRISPR, we are testing the hypothesis that the CP in hair cells IV analink TMCs to the actin cytoskeleton in zebrafish.

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ABSTRACT #59

Cellular Adaptation to Osmotic Stress

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Background:
Hypertonic stress response plays an important role in the development of dry eye syndrome, a pathological condition where human corneal cells are chronically exposed to the hypertonic tear film. This exposure is key to the pathophysiology of this disease and thus it is important to understand how corneal cells survive and adapt to hypertonic stress at the molecular level. To this end, our laboratory performed ribosome foot printing and RNA-seq of human corneal cells exposed to mild hypertonic stress (500 mOsm) for 1 h (acute stress) and 6 h (osmoadaptation). This work revealed that factors involved in pre-mRNA splicing were among the most differentially expressed genes. Specifically, CLK1 and MBNL2 were highly induced both at the level of mRNA and translation at 6 h. Upregulation of factors involved in the regulation of the splicing suggests that the cell may use post-transcriptional control mechanisms to diversify protein output that can play important role in the osmoadaptation..

Goals:
To better understand the mechanisms behind cellular adaptation to hypertonic stress. Specifically, the goal of this experiment is to examine the presence and abundance of proteins involved in alternative splicing in human corneal cell cultures after varying amounts of osmotic stress. These proteins include CLK1 and MBNL2.

Materials and Methods:
Human corneal cell cultures were exposed to a 500 mOsm salt solution for 30 min, 1 h, 3 h, 6 h, 9 h, and the proteins were examined by performing Western Blot.

Results:
Based on previous experiments, it is expected that at 1 h the protein levels will not change. At 6 h, protein levels are expected to be elevated. While treatment for 30 min and 3 hrs has not yet been done, the abundance of proteins is expected to follow a similar pattern. At 9 hrs, the protein levels could continue to increase from 6hrs, level off, or even decrease. Previous results have shown that the cells shrivel up during acute stress, but return to their normal shape during longer treatments.

Conclusions:
The return of the cells to their normal shape after gradual stress indicates that the cells were able to adapt to the osmotic stress. The expected Western Blot results would confirm the role of CLK1 and MBNL2 in the cellular adaptation process. Since all these proteins are primarily involved in splicing, this indicates that alternative splicing is indeed a crucial part of cellular adaptation.

ABSTRACT #60

Glial Cells in the Nervous System

Shay McDermott, Shaker Heights High School; Paul Tesar, PhD, Department of Genetics and Genome Sciences, Case Western Reserve University

Glial cells are the supporting cells of the neural system. Glia are thought of like glue that holds the neurons together. Glial cells are a part of the enteric nervous system and the central system. The molecular differences between glia of the enteric nervous system and the central nervous system are unknown. However, knowing these potential similarities and differences may inform our understanding of glia in both systems. Previously we used single nuclei RNA-sequencing to identify differences in gene expression between glia in the brain and the gut. Here, I employed quantitative PCR on glial cDNA from the enteric and central nervous system to measure the abundance of transcripts found to be enriched in gut glia or brain glia. I identified differences in gene expression between enteric glia and central nervous system cells. These differences may yield insights into the functions of each of these cell types.

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ABSTRACT #61

The effectiveness of Apigenin as a potential histone deacetylase inhibitor

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Background:
Cancer is a leading cause of death worldwide and accounts for approximately 2 million new cases and more than 600,000 deaths in the United States. Chemoprevention is a modality that uses naturally occurring dietary agents or chemical compounds to intervene in early stages of cancer. Apigenin is a bioactive compound commonly found in various fruits and vegetables including parsley, chamomile, celery, vine-spinach, artichokes, and oregano as some of the richest sources. Apigenin exhibits anticancer properties through altering the activity of several enzymes and proteins that have relevance to cancer. Maspin is a secreted protein encoded by a class II tumor suppressor gene and its role is well established in cell migration. Maspin exerts endogenous inhibitory effect on class I histone deacetylases (HDACs). Class I HDAC levels are increased in prostate cancer and their aberrant expression correlates with decreased tumor suppressor activity, drug resistance, and poor prognosis. Apigenin has shown to inhibit class I HDAC activity and whether this decrease has an effect on maspin levels is not been elucidated. Here we evaluate the effect of apigenin treatment on maspin expression affecting migration of prostate cancer cells.

Goals:
The goal of this study was to test the effectiveness of apigenin on increasing maspin expression in prostate cancer cells.

Materials and Methods:
Human prostate cancer LNCaP and DU145 cells, which possess high class I HDAC activity and low maspin expression were treated with 5-20 μM apigenin and 25 nM trichostatin A, a known HDAC inhibitor for 24 h. The cells were subjected to migration assay and lysates were prepared for Western blotting. In addition, a commercial ELISA assay kit determined HDAC enzyme activity.

Results:
Apigenin caused the inhibition of cell migration in LNCaP and DU145 cells. Treatment of cells with apigenin (5–20 μM) resulted in dose- and time- dependent inhibition of class I HDACs activity (HDAC 1, 2, 3 and 8) but not the expression levels. Exposure of LNCaP and DU145 cells with 5-20 μM of apigenin resulted in dose-dependent increase in maspin expression and p53 activation through acetylation at the Lys305 residue. Discontinuation of treatment with apigenin resulted in the loss of maspin, p53 acetylation and migration of these cells.

Conclusions:
Our findings provide insight into the mechanisms whereby apigenin alter p53-mediated maspin regulation by inhibiting class I HDACs. These studies further demonstrate the potential beneficial effects of apigenin that may lead to the development of novel, safe and effective preventive and/or therapeutic strategies in the management of prostate cancer.

ABSTRACT #62

Quantitative MRI Assessments of Kidney Disease Progression in Patients with Autosomal Recessive Polycystic Kidney Disease (ARPKD)

Arul Mehta, Saint Ignatius High School; Elise Keshock; Jacob Perino; Katherine MacRae Dell; Chris Flask, PhD, Department of Radiology, Case Western Reserve University

Background:
Autosomal Recessive Polycystic Kidney Disease (ARPKD) is an important cause of morbidity and mortality in children with chronic kidney disease (CKD). Novel therapies have shown efficacy in ARPKD animal models, but clinical trials in ARPKD patients have not been possible due to the lack of sensitive measures of kidney disease progression. Non-invasive Magnetic Resonance Imaging (MRI) techniques, including novel MR Fingerprinting (MRF), show promise in addressing this unmet need. We previously identified MRF-based T1 and T2 mapping as potential biomarkers of ARPKD kidney disease in animal models and initial human studies. In the current study, we evaluated the relationship between these MRF-based imaging parameters with clinical assessments of renal function in ARPKD subjects.

Goals:
To compare novel quantitative MRI assessments with established clinical measures of kidney disease progression in subjects with ARPKD.

Method:
ARPKD subjects were scanned on a Siemens 3T MRI scanner utilizing novel MRF technology to simultaneously generate kidney T1 and T2 maps in 15 secs/imaging slice with no sedation or injectable contrast agent. These two MRI metrics were compared with conventional clinical assessments of estimated glomerular filtration rate (eGFR) as a measure of kidney function.

Results:
Seven subjects with ARPKD (2M/5F, age range = 06-22; eGFR range = 52-109 ml/min/1.73m^2) were scanned. Mean kidney T2 values demonstrated a significant negative correlation with eGFR (R^2=-0.59, p=0.043). Mean kidney T1 also showed a strong negative correlation (R^2=-0.51) and did not yet reach significance (p=0.07). Mean T1 and T2 values for the right and left kidneys did demonstrate a significant correlation (T1: R^2=0.99, T2: R^2=0.74).

Conclusions, further questions:
This is the first study to establish a relationship between MRI-derived imaging biomarkers (T1, T2) and kidney function (eGFR) in ARPKD subjects. Despite the small cohort, data clearly demonstrate that mean T1 and T2 both increase with declining eGFR. These important findings suggest that MRF-based T1 and T2 mapping may provide a safe, non-invasive, quantitative, and reproducible measure of kidney disease severity to support future clinical trials to identify subjects at high risk for disease progression and monitor response to treatment.

Arul Mehta is a Sam Miller Scholar

ABSTRACT #63

Inflammatory Bowel Disease: Crohn's Disease and Ulcerative Colitis

Kyimani Miller, Beachwood High School; Mihn Lam, Ph.D; Fabio Cominelli, MD, PhD, Department of Medicine

Background:
Inflammatory bowel disease (IBD) is a chronic relapsing/remitting inflammatory maladies of the Gastrointestinal tract (GI) that includes two clinical entities: Crohn's disease and ulcerative colitis. These two subtypes of IBD have been studied together because they share common features such as similar symptoms, structural damage and therapies as well as pathogenesis. Both Crohn's disease and ulcerative colitis are associated with multiple pathogenic factors including environmental changes, an array of susceptibility gene variants and more. Despite decades of research focusing on the environmental, genetic, and defective immune responses toward intestinal microbes, a full understanding of IBD pathogenesis is still unknown. Currently, available biologics and other therapeutic paradigms for IBD are not curative, but often have adverse side effects. In addition, half of the individuals suffering from IBD experience at least one episode of extraintestinal manifestation (EIM), which include musculoskeletal, integumentary, ophthalmic, hepatobiliary, pancreatic, renal, cardiovascular, pulmonary, and neuropsychological. As in IBD, the pathogenesis of EIM is unknown; however, understanding the link between IBD and EIMs using mouse IBD models will potentially unravel the underlying mechanisms of IBD itself, which may lead to novel therapies that target different pathways and positively transform the current therapeutic landscape of IBD.

Goals:
Due to the lack of understanding of EIMs in IBD, we reviewed the current literature on the mechanism(s) or connection between extraintestinal manifestations in patients with IBD.

Methods and Materials:
A comprehensive search was performed in PubMed (Jan 1990- Jan 2021) using specific terms, such as extraintestinal manifestations, inflammatory bowel disease, Crohn's disease, ulcerative colitis, joints, skin, eyes and hepatobiliary tracts, cardiovascular diseases, gut-brain axis, and oral-gut axis.

Results:
It is believed that the diseased gastrointestinal mucosa can trigger immune responses in extraintestinal sites due to similar epitopes in genetically susceptible individuals. Alternative, it is believed that IBD biologics themselves can be a cause of EIMs.

Conclusions:
The evidence to connect between IBD and EIMs is compelling and has puzzled investigators for years. However, the current mechanism(s) explaining this intrigue relationship remains elusive and requires further elucidation. Mouse models of IBD may be key in this understudied investigation.

Supported in part by NIH, NCI, R25 CA221718

ABSTRACT #64

The Effects of Inhibitors of Uracil DNA Glycosylase on Cancer Cell Growth

Janailyn Morris, Cleveland School of Science and Medicine; Stanton Gerson, MD; Yan Yan, Case Comprehensive Cancer Center, Case Western Reserve University

Background:
Base excision repair (BER) is a process that aids in correcting DNA damage by removing damaged bases. Uracil DNA glycosylase (UNG) is a BER enzyme that removes uracil that maybe present in DNA. Targeted cancer therapy is drugs or other substances that prevent the growth and spread of cancer by targeting specific molecules. Previously the lab has characterized UNG as a potential target for cancer therapy since depletion of UNG by shRNA caused the loss of cell viability in multiple cancer cell lines. Four cancer cell lines, A549, MCF-7, MDA-MB-231, and DLD1 that show differential dependency on UNG for survival were selected for this study. A few drugs are known to inhibit UNG; ATA, MS275, and SAHA. ATA was identified by the lab that inhibits UNG by directly binding and destabilizing the UNG protein invitro. SAHA and MS275 are HDACi that have been shown to mediate proteasomal degradation of hyperacetylated UNG2 in B- and T-lymphoma cell lines. These drugs will serve as tools to validate the effect of the dependency on UNG for survival in the four cancer cell lines.

Goals:
The objective is to utilize ATA, MS275, and SAHA which display different mechanisms of UNG inhibitory activity, and test their cytotoxicity inA549, MCF-7, MDA-MB-231, and DLD1 cancer cell lines. Also, to examine whether the cytotoxicity of these drugs correlated with the effect of loss of viability observed in shUNG depleted cancer cells.

Methods and Materials:
Human cancer cell lines MCF7, A549, DLD-1, and MDA-MB-231were all grown and maintained in standard cell culture. To ascertain the cell viability of particular drugs on cancer cells; the cells were seeded into 96-well cell culture plates. The succeeding day, ATA, MS275, and SAHA with a concentration of 2 fold dilutions, were added to the cells in the 96-well plate. Each drug remained on the cells for 72 hrs. After 72 hrs., only the media was extracted from the wells. MTT assay was added to each well to test cell viability and toxicity. The absorbance for each 96-wellplate was then tested which shows the effectiveness of that drug.

Results:
For ATA treatment, the drug sensitivity pattern was correlated with the cell survival by shUNG at lower doses but did not display differential cytotoxicity between cell lines at a higher dosage. For SAHA and MS275, the cytotoxicity of four cell lines did not correlate with the cell survival by shUNG.

Conclusion:
We tested the cytotoxicity of ATA, SAHA, MS275 with previously described UNG inhibitory activity in four cancer cell lines, A549, MCF7, MDA-MB-231, and DLD1. The cytotoxicity pattern did not correlate with the effect of shUNG on cell survival. This could be due to the non-specific effect of ATA, SAHA, and MS275 on human cancer cell lines and their activity on UNG need to be validated.

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ABSTRACT #65

An Understanding of Protein Aggregation

Jaida Motley, John F. Kennedy High School; Helen Miranda, PhD, Department of Genetics and Genome Sciences, Case Western Reserve University

Background:
Protein aggregation is the process by which misfolded proteins adopt a conformation that cause its polymerization into aggregates and organized fibrils. Protein aggregation can be intimately related to protein stability and folding. Protein aggregation is higher, yet ignored and people work around it but when experimenting protein folding it is probably not noticed. The effect will be lethal in patients who suffer from other diseases with protein aggregation like amyloidosis, prion diseases even other protein deposition disorders.

Goals:
To evaluate the hypothesis that protein aggregation is responsible for the pathological features associated with muscular atrophy diseases.

Materials & Methods:
I looked over different literatures to first learn about protein aggregation and tried to get a good understanding of it. While reading I learned that protein aggregation is a phenomenon intrinsically disordered proteins or mis-folded aggregate or intra- or extracellularly. I learned what causes protein aggregation Problems occur during translation or transcription. While transcription DNA is copied into mRNA and start forming a strand of pre-mRNA it undergoes RNA to form mRNA. While translation, ribosomes and tRNA it help translate the mRNA sequence into amino acid sequence.

Results:
Protein conglomeration has high fixation while Protein accumulation is regularly seen as an undesirable connection between protein monomers. However a developing field of exploration is committed to understanding the instruments of this marvel, which can be valuable, practical or undesirable. In situations where a family background of SMA exists or manifestations reminiscent of the sickness introduce themselves, hereditary testing can assist with affirming the conclusion by taking a gander at hereditary material to decide whether the SMN1 quality is absent. The conformational change may advance the infection either by gain of a poisonous movement or by the absence of natural capacity of the locally collapsed protein. As various atomic instruments are associated with the development of the different types of protein totals.

Conclusions:
The understanding of protein aggregation might be summarized as follows. It's the amino sequence that ultimately decides the propensity of aggregation modulated environmental conditions. The aggregates will mostly be formed for the interaction of partially folded intermediate that are containing significant native structure.

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ABSTRACT #66

Developing an Autoencoder to Improve the Efficiency of QSAR Modeling

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Background:
Computational techniques have been widely used to predict interactions between unrelated drugs but less so between drugs and implants. However, unintended interactions could lead to unhealthy drug buildup, polymer implant failure, and accumulation of contaminants. Quantitative structure activity relationship (QSAR) models, a type of machine learning model, can predict interactions between molecules. These models use descriptor inputs, which are physical or chemical characteristics of molecules and polymers that can be evaluated numerically. Open-source software can be used to calculate descriptors, but this often results in thousands of inputs, some of which are excessive or insignificant. Thus, autoencoders, a type of machine learning algorithm used to compress data, can be developed to simplify the descriptor input dataset and improve efficiency of models. Autoencoders can also back-calculate the original data from the compressed data.

Goals:
The goal of this project is to build and train an autoencoder that effectively compresses and simplifies a descriptor input dataset with minimal reconstruction loss between the decompressed and original versions of the descriptors. It is expected that this will simplify future machine learning models and increase their accuracy.

Materials and Methods:
The molecules used are from the FDA Orange Book of Approved Drug Products. A custom Python script was generated to download structural data files (SDFs) for the drugs from PubChem. Using PaDEL-Descriptor, the descriptors for the drugs were calculated. The autoencoder contained an encoding portion to compress the data and a decoder portion to reconstruct the input. In the training process, the descriptor inputs were set as the outputs; however, a layer in the middle contained the condensed information. After each epoch, the model was trained based on mean squared error of the reconstructed features.

Results:
The autoencoder was trained and ran successfully. The algorithm yielded sufficiently accurate reconstructed features when compared to the original descriptor inputs.

Conclusions:
The autoencoder successfully developed in this research can be applied to other machine learning models to reduce the complexity of inputs and make more effective models for implant development, drug, and polymer screening, and patient treatment.

ABSTRACT #67

An Evaluation of the Role of Tumor-Associated Macrophages and CD59 Membrane Proteins in the Advancement of Pancreatic Cancer

Tina Nguyen, Mayfield High School; Neelima Singh, MD, Department of Pediatrics; John Letterio, MD, Department of Pediatrics, Case Western Reserve University School of Medicine

Background:
Macrophages regulate a plethora of essential functions throughout the body, including tissue homeostasis. Numerous macrophage lineages can coexist and perform specialized functions despite having different origins. Macrophages are also associated with the development and progression of chronic ailments. An example is tumor-associated macrophages (TAMs), which promote malignant activity in pancreatic cancer by upregulating an inhibitory protein called CD59, which protects cancer cells from complement-dependent cytotoxicity (CDC). Higher infiltration of TAMs and higher levels of CD59 expression are associated with lower patient survival rates.

Goals:
The goal of this particular literature review is to analyze the role that TAMs and CD59 played in cancer cell survival and determine how eliminating these factors could affect cancer growth.

Materials and Methods:
A literature review was performed to determine the relationship between TAMs, CD59, CDC, and pancreatic cancer. Scientific articles were accessed using the PubMed database, and numerous articles had also been obtained from networks outside of the archive. Articles that discussed the role that TAMs and CD59 played in protecting cancer cells from CDC were analyzed to determine how such factors could affect disease development. Figures composed based on research data were also assessed to evaluate how varying levels of CD59 protein expression could impact pancreatic cancer cell survival.

Results:
Published studies demonstrated that cancer cells co-cultured with TAMs in vitro had better survival compared to cells that weren't co-cultured with TAMs. Macrophages that were co-cultured with cancerous cells had greater levels of IL-6 secretion. Experiments in which IL-6 expression was inhibited decreased CD59 expression and also reduced the protection that CD59 provided for cancer cells against CDC. Similarly, these studies show that suppression of the levels of the IL-6 activated STAT3 protein in cancer cells using AG490 also resulted in a decrease of CD59 in co-cultured cells. Additional studies demonstrated that inhibition of CD59 expression led to the suppression of cancer metastasis, enhancement of CDC, and reduction in cancer cell survival.

Conclusions:
TAMs are known to contribute to disease progression in pancreatic cancer. Published data shows that cancer cells are protected from CDC through increased levels of CD59 expression and that IL-6 helped to regulate this process. Thus, the evidence suggests that strategies designed to therapeutically target TAMs, CD59, and IL-6 with multi specific antibodies may be a promising approach for the immunotherapy of cancer. However, there is no universal or effective treatment for pancreatic cancer and further therapeutic combinations must be investigated to improve treatment efficacy.

ABSTRACT #68
Vitamin E and the Effects of Oxidative Stress on Fertility

Andrea Okocha, Bedford High School; Danny Manor, PhD, Department of Nutrition, CWRU

Background:
Although oxidative metabolism is an efficient source of energy in most 'higher' animals, oxygen is also a significant challenge since it can produce harmful free radicals. Free radicals are molecules that contain oxygen and have an unshared electron, which are highly energetic and react rapidly with oxygen to form reactive oxygen species (ROS). Free radicals are beneficial to the body but when unchecked, they can attack DNA, lipids, and protein, causing a number of diseases to develop due to an imbalance between antioxidants and free radicals, or oxidative stress. Antioxidants are the body's natural defense system against the negative effects of free radicals and are split into two groups: enzymes that detoxify free radicals and dietary antioxidants like Vitamins C and E. Vitamin E is a fat-soluble antioxidant found in many plants. Vitamin E as an antioxidant is used to prevent many oxidation-related diseases and disorders including coronary heart disease, cognitive decline, and some neurodegenerative disorders. A deficiency in Vitamin E would increase the risk of developing oxidation-related illnesses. One was found to be an increase in infertility and incomplete pregnancies that were initially found in rats. In rodents, Vitamin E deficiency was also shown to cause 'fetal resorption': severe female infertility characterized by the inability to carry a pregnancy to term. Although much less is known regarding fertility in humans, there is ample evidence correlating oxidative stress in the reproductive system and fertility disorders, such as low birth weight, higher risk of preterm birth, and an overall increase in unexplained miscarriages. There has even been a strong correlation found between low levels of Vitamin E before and during pregnancy and an increased risk of preeclampsia, a pregnancy disorder that can be caused by oxidative stress and may result in maternal and neonatal mortality. The inability to conceive after a year, or subfertility, is cited to be experienced by 40-50% of couples, and over 20% of pregnancies end in miscarriage. These observations raise the possibility that treatment with Vitamin E may provide an effective approach for treating infertility in women. Unfortunately, Vitamin E levels are scarcely tested for, and most American diets are lacking in the suggested intake levels of Vitamin E.

Goals:
Though it has already been established through various studies and trials that a lack of Vitamin E can result in a decrease in fertility and incomplete pregnancies due to increased oxidative stress in the reproductive system, the goal of this paper is to evaluate whether a supplement of Vitamin E can increase fertility rates and complete pregnancies. I hypothesize that the widespread subclinical deficiency in Vitamin E could account for a number of cases of subfertility and miscarriages in the country.

Materials and Methods:
A literature review of previously published scientific papers and studies that analyze the relationship between Vitamin E, oxidative stress in the reproductive system, and fertility.

Results:
Results of the literature review will be expounded on throughout the paper and will be stated once the analysis concludes.

Conclusion:
Given the high prevalence of infertility and the wealth of data in animals and the established effects of oxidative stress on fertility, we may conclude that Vitamin E can be used to offset and treat the damaging effects of free radicals in the reproductive system. However, there has been little to no evidence to support the hypothesis that Vitamin E can be taken as a supplement to improve fertility. In such a case, it is possible that instituting the practice of testing for Vitamin E levels in fertility clinics will provide an important first step towards improving fertility rates in our population.

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ABSTRACT #69

Determination of Prostate Specific Membrane Antigen (PSMA) Expression in Prostate Cancer Cells

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Background:
Prostate cancer is the most prevalent cancer among men, about one in nine men will be diagnosed with it in their lifetime, and it is the second leading cause of cancer deaths in men. Among the biomarkers for prostate cancer, Prostate-specific membrane antigen (PSMA) is especially attractive for imaging and therapy due to its abundant expression in prostate cancer. Different prostate cancer cell lines express PSMA to varying degrees. Understanding which cell line expresses PSMA most abundantly, allows us to determine the most suitable cell line to study.

Goals:
To test various prostate cancer cell lines and find the cell line with the most PSMA expression.

Materials and Methods:
Prostate cancer cell line PC3, PC3pip, PC3flu, LNCaP, C4-2 and CWR22 will be used. Cell lysates will be collected and western blot with these cell lysates will be performed to determine PSMA expression in these cell lines.

Results:
According to literature, PSMA expression should be found in PC3pip, LNCaP, C4-2 and CWR22 cells, but not in PC3 and PC3flu cells.

Conclusions:
PC3pip, LNCaP, C4-2 and CWR22 cells express different levels of PSMA. They can be used for in vitro and in vivo experiments for PSMA targeted image and therapy studies. PC3 and PC3flu cell can be used as negative controls.

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ABSTRACT #70

Using Quantitative PCR and Western Blot to Explore FXII Expression In Glioma Cells

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Background:
Glioblastoma (GBM) is the most common primary malignant brain tumor in adults, responsible for 48% of all brain tumors. Despite all treatment options, the survival rate of GBM is very low, approximately 12-15 months and only 40% of patients survive one year. Without therapeutic intervention, this tumor can kill in the first six months or less. GBM is a grade IV glioma, the highest-grade glioma, often times progressing from lower grade gliomas. GBMs can travel to other parts of the brain through connection fibers; however, it is rare for GBM to metastasis from the brain. There is evidence that FXII and FXIIa can cause neutrophil functions in cancer. Neutrophils are white blood cells that promote cancer cell survival which can lead to metastasize and contribute to macrophage polarization, which then induces T-cell differentiation in vivo. T cell differentiation can be bad in this situation because this suppresses anti-tumor immunity ultimately facilitating cancer maintenance. Although FXII has been reported to play a role in immune dysfunction, no work has described its expression in glioma stem cells.

Goals:
To learn quantitative real time PCR (qPCR) and western blotting techniques in order to explore the expression of factor XII in glioma cell lines.

Materials and Methods:
I used qPCR and western blotting techniques to determine FXII expression in glioma cell lysates. qPCR is a way of finding out how much mRNA is in a sample in real time by using a nonspecific dye and sequence specific DNA probes containing fluorescent reporter oligonucleoutides to detect PCR products in a sample. Western blotting is a widely used technique used to detect specific proteins in a sample of tissue, homogenate or extract.

Results:
qPCR showed factor XII expression in glioma cell lines at the mRNA level and western blotting showed FXII expression in glioma cells at the protein level.

Conclusions:
Glioma stem cells were found to have factor XII, which turns out, is a part of the process of coagulation, which was originally thought to only be caused by blood platelets.

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ABSTRACT #71

The Role of the MIZ1 gene in Triple-Negative Breast Cancer in Cell Proliferation and 3D-growth

Angel Ononogbo, Orange High School; Perrone Joseph; William P. Schiemann, PhD,
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Background:
Triple-negative Breast cancer (TNBC) is an aggressive type of breast cancer composed of a diversified group of tumors that exhibits resistance to chemotherapy. The Schiemann lab discovered that the aberrant activation of the MIZ1 gene is associated with increased mortality rates, especially in African American women. Through Inflo, a data science program that analyzes differences in gene expressions, our lab concluded that the irregular activation of the MIZ1 gene in TNBC is apparent in African American (AA) women but not in their European American (EA) counterparts. These findings suggest that MIZ1 signaling may underlie the aggressive nature and disparate mortality observed in AA TNBCs.

Goals:
To determine the role of the MIZ1 gene in cell proliferation and 3D growth in TNBCs.

Materials and Methods:
We used three different TNBC cell lines: HCC70, MDA-MB-436, and MDA-MB-468. The HCC70 and MDA-MB-468 are African American cells, and the MDA-MB-436 is the European American cell. All the cell lines were engineered to lack the MIZ1 gene to observe cell proliferation. Using the three cell lines, we arranged each one into two categories; one with a controlled gene with the MIZ1, which is called shScram, and the other without the MIZ1, which is the shMIZ. We conducted four different assays to look at cell growth: a regular cell culture/proliferation assay to observe tumor cell growth; a mammosphere assay and a limited dilution assay (LDA) to observe stem cells; 3D culturex to observe stem cell proliferation as a 3-dimensional structure; a Western Blot analysis to monitor the extent of the knockdown of MIZ1 in these TNBC cell lines.

Results:
In the 2D Proliferation assay, the HCC70 shScram cell grew more rapidly as days elapsed. However, the HCC70 shMIZ1 cell grew in a slower and linear process. Lastly, the 468 shScram and shMIZ1 cells didn't show a significant difference in growth as days passed. The Western blot verified that the MIZ1 gene in the shMIZ1 cells for HCC70, 436, 468 cell lines were not present, and the gene in the shScram cells for all the three cell lines was present.

Conclusions:
Results support our hypothesis that MIZ1 plays a prominent role in cell proliferation and division. Using our three cell lines provided apparent data that revealed cells with the MIZ1 gene grew more rapidly, and those without grew slower. Although this topic is still in the early stages, these findings may prove helpful as a biomarker in predicting recurrence of Triple-negative breast cancer in African American and European American women.

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ABSTRACT #72

African American male screening results will show greater risk for prostate cancer at a younger age

Kwabena Owusu, Solon High School; Erika Trapl, PhD, Department of Population and Quantitative Health Sciences, Prevention Research Center for Healthy Neighborhoods, Case Western Reserve University

Background:
African American men have at least a 50% greater risk of developing prostate cancer compared to European American men, and are more than twice as likely to die from it. African American men are diagnosed with prostate cancer at a younger age and at a higher stage than European American men. The prostate-specific antigen (PSA) test is the most commonly used screening method for prostate cancer. However, the PSA test is associated with overtreatment and over diagnosis of patients. Genomic data is also being used to screen for prostate cancer. Polygenic risk scores for prostate cancer can be made with genomic data. The vast majority of studies with polygenic risk scores have been conducted with Caucasian men, and thus little information has been collected with African American men.

Goals:
The goal of this literature study was to explain how results from screening tests could show greater risk in African American men at younger ages. Another objective was to investigate the biological and social factors that would account for greater risk, incidence, and mortality in prostate cancer in African American men.

Materials and Methods:
I reviewed scientific literature about PSA testing, its issues, and differences in the results of African American and Caucasian men; biological differences that could account for differences in screening results and aggressiveness; and social factors associated with African Americans such as socioeconomic status, diet, and obesity.

Results:
Lower socioeconomic status has been associated with increased incidence and mortality from prostate cancer. Obesity may or may not increase the incidence of prostate cancer, but it can be associated with increased mortality rates. Differences in genomics can also make prostate cancer more aggressive in African American men. These factors can play a role in the diagnosis of high-grade prostate cancer at younger ages in African American men.

Conclusions:
African American men are at tremendous risk for incidence and mortality. Separate guidelines should be made for African Americans by the U.S. Preventive Services Task Force (USPSTF). More work also must be done investigating polygenic risk scores with African American men, as there is a large gap in research.

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ABSTRACT #73

Lung Airway Segmentation: An Automated Algorithm Approach

Haridu Peiris, Twinsburg High School; Cristian Barrera; Mehdi Alilou; Anant Madabhushi, PhD, Center for Computational Imaging and Personalized Diagnostics, Department of Biomedical Engineering, Case Western Reserve University

Background:
The bronchial tubes, or lung airways, are essential to the respiratory system, allowing for the passage and flow of air down the trachea and to the alveoli. Accurate visualization of these airways is essential in the detection of lethal and/or prevalent diseases, as detecting variants in shape (such as narrowed airways leading to bronchitis and chronic obstructive pulmonary disease COPD)) and obstructions (tumors from lung cancer) can help us diagnose and quantify diseases. However, manual segmentation of the airways from CT scans can sometimes take over 7 hours, and even then can be inaccurate due to interference from other tissue types. Therefore, an automated process for airway segmentation was proposed, using a combination of region growing and morphological processing in Python.

Goals:
The objective of this project is to create an efficient and accurate method to segment the lung airways that is not as time consuming as the conventional method of manual segmentation. The purpose of the algorithm itself is to segment the airways so the final product ends as one connected airway.

Materials and Methods:
A public dataset of 3D thoracic CT scans (with limited slice counts of 64 slices per scan rather than the conventional 400) was used to develop and test this algorithm. The original voxel size (value of 3-dimensional space) of the images was also normalized from .7mm x .7mm x 5mm to 1x1x1. The algorithm itself begins with detection of the trachea using Hough Transform, detection of the main airway using 3D region growing, and finally detection of the small airways with morphological processing.

Results:
The algorithm successfully segmented the airways for two sample cases. In the first case, the final product was missing a large portion of the right airways. In addition, it was registered as 74 components rather than one connected unit. Furthermore, for the second case, the airways were visualized as 49 components, which was a slightly higher performance, but still not optimal

Conclusions:
Though the many components of the airways registered were not ideal, the main airways that were detected through region growing were visualized as one airway. The small airways also had some adjacent parenchyma (lung connective tissue) that were detected as airways. The standardization and the thresholding method due to the limitations of the dataset likely caused the inaccuracies. In addition, the algorithm will need to be modified for use on other datasets, as it is currently tuned to the parameters of the limited dataset used. The ideal next step is to modify the algorithm to be more universal to other lung CT datasets, or to rewrite it to allow for it to be scored quantitatively (using ground truth segmentation or dice score efficiency).

Haridu Peiris is a Martha Holden Jennings Scholar

ABSTRACT #74

The effect of temperature on acoustic stability and movement of nanobubble ultrasound contrast agents

Eric Pieper, Shaker Heights High School; Michaela Cooley; Agata A. Exner, PhD, Department of Radiology; Biomedical Engineering, Case Western Reserve University

Background:

Microbubbles (MBs) and nanobubbles (NBs) are bubbles with a lipid or protein shell. They are used for applications including drug delivery and ultrasound imaging. The stability of MBs and NBs has been studied extensively *in vitro*, typically using phosphate buffered saline (PBS) at room temperature. However, these conditions do not translate to *in vivo* conditions. To overcome this limitation, we have employed human whole blood (WB) and varying temperatures ranging from room to hyperthermic temperatures in order to analyze the stability of NB contrast agents under continuous contrast-enhanced ultrasound imaging. We have also analyzed the movement of NBs in the aforementioned conditions to improve understanding of how NBs interact with their environment and whether this interaction affects ultrasound signals.

Goals:

Our goal is to observe the effect of temperature on the stability and movement of NBs in PBS compared to human WB.

Materials and Methods:

Lipid shell stabilized C_3F_8 NBs were formulated through agitation and isolation based on differential centrifugation. Here, we analyzed the effects of temperature (23, 30, 35, 37, and 39°C) on the stability of signal enhancement of NBs (~4.07 x 10^9 NBs/mL) in PBS and human WB. A pourable silicone rubber phantom (Ecoflex™) with a 14 mL inlet (5.4 cm x 1.6 cm x 1.7 cm) was created for the PBS experiments (13.86 ml of PBS and 0.14 ml of NBs). To conserve blood, the inlet for WB experiments was 5 mL (5.4 cm x 1.6 cm x 0.7 cm), and the ratio of WB:NBs was 100:1 (4.95 ml of WB and 0.05 ml of NBs). For both PBS and WB experiments, the phantom was placed in a water bath over a hot plate to maintain temperature. The temperature probe remained inside the phantom for the duration of the experiment. A clinical ultrasound scanner was used for all experiments under continuous contrast-enhanced ultrasound imaging for 500 s. The focus was centered in the middle of the depth of the phantom for PBS and WB phantoms. The transducer was in direct contact with the WB or PBS solution. NBs were injected into the temperature-controlled solution at room temperature to mimic *in vivo* injections and were triturated with a pipette and then stirred with a glass stir rod. US signal enhancement was measured by taking an area of interest within the inlet and subtracting the background. All trials were repeated 3 times. The autocorrelation coefficient, which assesses the randomness of NB movement over time, was determined using MATLAB, and decorrelation time was defined at 0.5.

Results:

In general, PBS enhancement curves reached lower peak values than WB curves. Further, the PBS curves always had lower initial values than WB curves. For all temperatures in both PBS and WB, except room temperature (23°C), the initial enhancement increased and reached a peak value. However, for PBS at room temperature, there was minimal change in signal enhancement over time. At 30, 35, 37, and 39°C, PBS and WB enhancement curves all rose to a peak and then decreased. There was a downward trend in decorrelation time with WB groups as temperature increased. However, there was no obvious trend seen with PBS. The PBS decorrelation time (e.g. 1.3 ± 0.6 s at 23°C) was significantly faster than WB decorrelation time (e.g. 25.7 ± 20.2 s at 23°C) at all temperatures. Additional data analysis is ongoing.

ABSTRACT #74 CONTINUED

Conclusions:

There are distinct differences in decorrelation time and signal enhancement curve trends between PBS and WB. NBs in WB tend to have a brighter initial and peak signal enhancement than NBs in PBS and their decorrelation time is longer. As temperature increases, decorrelation time in WB tends to decrease, but it stays the same at all temperatures in PBS. This study shows that temperature may play an important role in the stability and movement of NBs *in vitro*, especially in the presence of WB.

Eric Pieper is a Martha Holden Jennings Scholar

ABSTRACT #75

Assessment of CT Calcium Score Images Using Deep Learning

Justin Pieper, Shaker Heights High School; Neha Chellu, Beachwood High School; Bradley Wu; Aishwarya Krishnan; Tao Hu; Ammar Hoori; David Wilson, PhD,
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Background:
Coronary artery disease (CAD) is a major cause of death across all demographics. Two predictors of CAD are pericardial fat (PF) and epicardial fat (EF) deposition. EF has also been shown to mechanistically lead to CAD. CAD often leads to coronary atherosclerosis (CA), which can lead to myocardial infarction. Early detection of EF can alert both the physician and patient, enabling protective intervention. Using 3D imaging, EF depositions can be visualized and analyzed to determine an individual's risk of CAD development and myocardial infarction. However, this 3D imaging is time intensive. We propose using deep learning networks for automated segmentation of EF deposits. Deep learning is a form of programming that utilizes artificial neural networks reflecting the human brain. Deep learning is able to incorporate existing information and formulate a new output based on that information. This can be applied to medical imaging to improve efficiency and allow physicians to better assess a patient's risk for CAD.

Goals:
The goal of the project is to determine the accuracy of a deep learning program in comparison with the manual assessment of EF in patients. We hypothesize that the deep learning program will accurately represent epicardial fat deposition in patients.

Materials and Methods:
The program 3D Slicer 4.11.20210226 was used to segment EF deposition of 10 patients. Two expert readers each independently segmented the EF deposition for each patient. A deep learning program was then used to generate results for the same 10 patients. The results of the two readers and the program were compared with each other. We then determined the dice score of the results. Lastly, a Student's T-Test was conducted to compare the closeness of the results.

Results:
We evaluated the variability of volumes among the segmentations between the 2 expert readers. We did this using dice scores, a two-tailed paired t-test, and r^2 values. The dice score evaluated the similarity between the segmentations, and the t-test concluded whether there was a significant difference in how the pericardium, EF, and PF were segmented. The pericardium, EF, and PF had average dice scores of 0.88901229538, 0.67241716914, and 0.560823343. The t-test concluded that there was no significant difference in segmentation between both readers. Finally, we found the r^2 values of the segmentations. The pericardium, EF, and PF had r^2 values of 0.9799037323, 0.9849341702, and 0.9651823731. The results from 2 patients and the deep learning program are still in process.

Conclusions:
We conclude that there was no significant difference between both expert readers. Generally, the pericardium was segmented much more similarly compared to the EF and PF. However, there was no significant difference in the way the two expert readers segmented the three segmentations. The two readers also had a r^2 value indicating a strong correlation between the two. Comparison of deep learning to the expert readers is currently in progress.

Justin Pieper is a Martha Holden Jennings Scholar

ABSTRACT #76

CITED2 limits LPS-induced pro-inflammatory macrophage activation

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Background:
Macrophages are the principal component of the innate immune system. They play a critical role in eliminating foreign agents, tissue repair, and preventing excessive inflammatory response to subtle environmental changes. Macrophages recognize foreign agents by utilizing pattern recognition receptors, including Toll-like receptors (TLRs). The TLRs relay extracellular cues inside the cytoplasm and nucleus utilizing adapter proteins and transcriptional factors (NFκB, STAT1, and IRFs) for robust pro-inflammatory macrophage activation. However, uncontrolled macrophage inflammatory response leads to many chronic and acute inflammatory disease conditions. Thus, probing the cell-intrinsic negative regulatory mechanisms will help us to better understand the pro- and anti-inflammatory signaling dynamics in disease pathogenesis.

Goals:
The goal of this project is to understand the role of Cbp/p300 interacting transactivator with Glu/Asp rich carboxy-terminal domain 2 (CITED2), a cell-intrinsic negative regulator of inflammation, on pro-inflammatory signaling in macrophages.

Materials and Methods:
Western blotting was performed to determine the CITED2 protein expression in bone marrow-derived macrophages (BMDMs) from *Lyz2*$^{cre/cre}$ and *Cited2*$^{fl/fl}$*:Lyz2*$^{cre/cre}$ mice. Real-time quantitative PCR was performed to determine the expression of *Irf1, Irf2, Irf9*, and IRF1 target genes in BMDMs after exposure with lipopolysaccharides (LPS).

Results:
Western blot analyses confirmed a substantial reduction in CITED2 protein levels in *Cited2*$^{fl/fl}$*:Lyz2*$^{cre/cre}$ mice BMDMs. LPS challenge robustly elevated *Irf1* mRNA expression in CITED2 deficient BMDMs. In addition, CITED2 deficiency also modestly elevated *Irf2* and *Irf9* expression following the LPS challenge. However, CITED2 deficiency did not significantly alter LPS-induced *Stat3* expression in macrophages. LPS stimulation also robustly induced IRF1 target gene expression (*Batf2, Ccl8, Isg15, Ifi47, Slamf8, Irg1, Mmp13, Dnase1l3, Kynu, Gbp3, Gbp2*, and *Gbp5*) in *Lyz2*$^{cre/cre}$ mice BMDMs.

Conclusions:
Our results provide evidence that CITED2 deficiency augments IRF1 target gene expression in macrophages following LPS challenge.

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ABSTRACT #77

Chromosome Therapy for Large Chromosomal Aberrations

Trinity Pruitt, Cleveland School of Science and Medicine; Anthony Wynshaw-Boris, MD, PhD, Department of Genetics and Genome Sciences, Case Western Reserve University

Background:
There are several potential treatment options for genetic diseases caused by single-gene disorders. Chromosomal abnormalities can result from large deletions or duplications as well as irregular structures, which are major causes of birth defects and intellectual disability. Currently, there are no therapeutic options for correcting these disorders. Chromosome therapy is a potential therapeutic method for fixing large chromosomal abnormalities by removing/silencing, replacing, or reprogramming the aberrant chromosomes. During the research, it was discovered that the ring chromosome is deleted and replaced with a normal chromosome when reprogramming ring chromosomes. From this, we are now testing the idea that forcing the formation of a ring chromosome then reprogramming the ring chromosome can be used for correcting abnormalities.

Goals:
Our project aims to force an aberrant chromosome to form a ring chromosome, followed by reprogramming to correct the abnormality. If successful, such ring chromosome rescue may be applied in the future as a treatment for chromosomal abnormalities, which we have termed chromosome therapy.

Materials and Methods:
To initiate ring chromosome formation we first insert a cassette into each of the arms of a chromosome that has a deletion. Once these are inserted, the cassette from one arm of the chromosome will make the cell yellow, and the cassette on the other arm of the chromosome will make the cell cyan. The cell will also be G418 resistance and puromycin resistant. To verify the cassettes are in the correct spots we will use PCR. Once the correct insertion of both cassettes has been confirmed, the cells will be transfected with CRE, which will force the chromosome into a ring. The cell will also become tdTomato positive, and lose its yellow and cyan expression. Finally, karyotype analysis will show that there is a ring chromosome.

Results:
TBD

Conclusions:
The successful application of chromosome therapy via ring chromosome rescue in cells in culture will provide a potential means to alleviate large chromosome aberrations in a cell in vitro. Determining how this works may lead to its application during development as a treatment for a large chromosomal aberration in vivo, which may lead to a reduction in the number of birth defects and miscarriages since it is estimated that 50% of miscarriages are from chromosomal aberrations.

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ABSTRACT #78

Prostate Cancer Screening and Screening Guidelines Incorporating Biological and Sociological Factors Affecting African American Men with Prostate Cancer

Martina Richter, Shaker Heights High School; David Busch, PhD, Department of History; Rachel Gardenhire; Erika Trapl, PhD, Prevention Research Center for Healthy Neighborhoods, Department of Population and Quantitative Health Sciences, Case Western Reserve University

Background:
The highest incidence and mortality of prostate cancer in the U.S is among African American men. However, the majority of screening for prostate cancer has been done on European American men, meaning that the sociological and biological differences that affect African American prostate cancer are not represented in screening guidelines provided by the US Preventive Services Task Force. Screenings for prostate cancer include polygenic risk scores (PRS), which are evaluations of the genetic variants in an individual's genome to assess susceptibility for prostate cancer. Another screening method measures the levels of prostate specific antigen in the prostate.

Goals:
The goal of this literature review is to evaluate the biological and sociological factors that cause disparities in prostate cancer in African American men so that this information can be incorporated into screening and screening guidelines to accurately predict prostate cancer risk and lead to treatment. Specifically, the USPSTF could set new guidelines based on data from a more diverse population of men. They could also reduce the age at which men should start screening for prostate cancer, as well as recommend prostate specific antigen (PSA) level testing in combination with a polygenic risk score and genetic counseling.

Materials and Methods:
PubMed used to conduct this literature review; keywords led me to clinical trials and literature reviews about recent studies and information regarding prostate cancer and how preventive measures can improve public health. I also reviewed the Cleveland African American Prostate Cancer Project's (CAAPP) letter of intent as an example of a prostate cancer screening project. I interviewed three researchers working on the CAAPP in order to learn more about screening methods for prostate cancer and how the project was going to cater to the needs of African American men. (by potentially) lessening disparities for African American men by taking into account biological and sociological factors.

Results:
There are over and under expressions of certain genes and receptors in African American men that are attributed to more aggressive prostate cancer. These biological factors can show differences in prostate cancer in African Americans compared to other races/ethnicities as well as causes for a higher aggressivity in African American prostate cancer. Environmental factors that contribute to poorer health can make men more susceptible to prostate cancer. Many social determinants of health affect African American men more than other racial/ethnic groups.

Conclusions:
African American men would benefit from new guidelines from the USPSTF that take into consideration the biological and sociological factors in prostate cancer that make it more prevalent and aggressive. Such guidelines could include the importance of screening at a younger age for African American men as well as recommend the use of a PRS with a PSA level test in order to avoid overtreatment and misdiagnosis of prostate cancer that could result from the use of only a PSA test.

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ABSTRACT #79

The Effect & Possible Solutions of Wearable Devices on Gynecological Cancer

Tai Roberts, Andrews Osborne Academy; Stefanie Avril, MD, Case Comprehensive Cancer Center, Case Western Reserve University

Background:
Cancer begins when cells mutate or grow rapidly out of control. The cells often form a lump or mass known as a tumor. These tumors, if cancerous, can invade nearby regions of the body. The cancer can be categorized based on the area of the body or the group of organs it has overcome. An example is cancer of the endometrium. This is the most common gynecologic malignancy in developed countries and the second most common in developing countries, behind cervical cancer. Endometrial cancer forms in the tissues of the endometrium, which is the lining of the uterus. Additionally, endometrial cancer is also referred to as uterine cancer. Other cancers can form in the uterus, like uterine sarcoma which starts in the muscle walls of the uterus, but are an uncommon cancer in comparison to endometrial cancer. Typically detected at an early stage, the symptoms of endometrial cancer are frequently diagnosed upon abnormal vaginal bleeding after menopause, pelvic pain, or bleeding between periods. Cancer of the endometrium is just one of many examples related to gynecological cancer. The cause of endometrial cancer is yet to be discovered and like many other gynecological cancers, detection is delayed relatively late in order to slow down or stop the spreading of the particular gynecological cancer. Furthermore, since the cause is unknown, the use of wearable devices in the medical industry is increasing. Wearable devices can help detect vital signs, physical activity, and major variables that play a role in cancer formation, like gynecological cancer.

Goals:
The purpose of this project is to take existing ideas of wearable devices or construct innovative ideas to detect types of gynecological cancer at the earliest stage possible or signs that cancer may be impending through abnormal body functions.

Materials and Methods:
Focused on doing research about potential various solutions or treatments for gynecological cancer. Additionally, discussing any significant articles about further information discovered to improve the prevention of gynecological cancer and its effects on the body, long-term and short-term. Essentially, finding ways or shortcuts of detecting uterine cancer before the effects of the cancer take over the particular region of the body compromised by tumors, or the entire body as a whole, through usage of wearable devices.

Results:
Hence working virtually, the results gathered from the scientific articles about wearable devices for infectious diseases, like Covid-19 or others works well. When wearable devices are in the picture, if contagious the spread of the disease can be slowed or hopefully halted. Additionally, wearable devices can potentially catch the beginning of the disease's stage before it infects regions of the body. As a result of this information, wearable devices have been used to detect atrial fibrillation.

Conclusions:
The idea of wearable devices contributes to the medical industry heavily. As the world progresses, along with the science and technology fields prospering, gynecological cancer detection will hopefully increase at primarily early cancer stages. Nonetheless, further research and testing is needed to be done and recorded in order to begin to use wearable devices for the identification of gynecological cancer. Essentially, wearable devices for gynecological cancer have the utmost potential for detection, but more experiments and analyses are required for the medical field to become fully dependent upon wearable devices.

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ABSTRACT #80

Identification of P7C3-S321 Associated Neuroprotective Pathways in a Rodent Model of Alzheimer's Disease

Sophia Rose, Shaker Heights High School; Kalyani Chaubey, PhD; Andrew A. Pieper, MD, PhD, Harrington Discovery Institute, Department of Psychiatry, Case Western Reserve University

Background:
Alzheimer's disease (AD) is a leading worldwide cause of morbidity and mortality, which currently has few treatment options. The Pieper laboratory has previously demonstrated that treatment of a rat model of AD (TgF344AD) with the neuroprotective compound P7C3-S321 safely and effectively protected the animals from developing depression-like and cognitive behavioral deficits reminiscent of AD. Importantly, protection with P7C3-S321 was attained without intervening in tau or amyloid pathology, which have historically been targeted for putative therapeutic effect. Thus, this study provided evidence that pathways mediated by P7C3-S321, independent of traditional AD targets, may help treat patients suffering from AD. However, the downstream neuronal signaling and metabolic pathways associated with the neuroprotective efficacy of P7C3 compounds are unknown. Identifying these mechanisms will broaden our knowledge of the processes that control neuronal vitality and point to new therapeutic targets in the field of AD and neurodegeneration.

Goals:
The goals of this project are to (1) identify the major cellular signaling pathways and functional classes that are altered during AD, and (2) identify the effects of P7C3-S321treatment on those pathways.

Materials and Methods:
For this study, 9-month-old WT and AD animals were treated with P7C3-S321 and vehicle for 6 months. At 15 months of age, their brain hippocampus was collected and label-free proteomics was performed. To determine disease-specific changes, WT + vehicle vs AD + vehicle group was compared. The effect of P7C3-S321 was determined by comparing the changes in AD + vehicle vs AD + P7C3-S321. Proteins that were either up or down regulated ≥1.5 fold with adjusted p-value < 0.05 were selected as a significant candidate for subsequent functional analysis.

Results:
We identified 999 proteins that were significantly up-regulated and 188 proteins that were significantly down-regulated during AD through label-free proteomics analysis. Of those changes, the P7C3-S321 treatment restored 988 upregulated proteins and 5 down-regulated proteins to normal levels. These P7C3-S321-normalized proteins were found in various pathways related principally to metabolism, gap junctions, synaptic vesicle cycling, and phagosome physiology. The top molecular mechanisms implicated belong to protein, ATP, GTP, NAD^+-binding, cytoskeletal structure, and cell-cell adhesion functions.

Conclusions:
This study highlights proteomic changes during AD and the effects of neuroprotective P7C3-S321 treatment on those pathways. Specifically, our results implicate protein, ATP, GTP, NAD^+-binding, cytoskeletal structure, and cell-cell adhesion functions as possible points for therapeutic intervention in AD.

ABSTRACT #81

Melanoma: Pathophysiology, Risk Factors and Treatments

**Yaritzy Santizo, Cleveland School of Science and Medicine; Diya Ramanathan;
Dr. Joseph Kamel; Sonal Shah, MD, Department of Dermatology, Case Western Reserve University School of Medicine**

Background:
Melanoma is a type of skin cancer. Although it is much less common than other types of skin cancers, it is the most serious. It is the most serious because if it is not caught in its early stages it has the ability to spread rapidly to other organs. Melanoma develops when pigment-producing cells called melanocytes mutate and begin to divide uncontrollably. Melanoma more commonly develops in areas where the skin is exposed to the sun. A few common areas include the face, back, arms, and neck. It can also develop in other parts of the body such as the eyes and mouth but these sites are much less common.

Goals:
Researched of various articles on different types of skin cancers. To narrow the scope of research, I selected melanoma as my topic of interest and decided to explore questions such As, "Who gets affected by melanoma?", "How is melanoma treated?", and "What are the different stages of melanoma?"

Materials and Methods:
To answer these questions, I used scholarly articles and research papers, summarizing my findings.

Results:
Melanoma develops when melanocytes mutate and begin to divide out of control. It tends to affect individuals who are older in age. Risk factors such as increased UV exposure, fair skin, and having a weakened immune system can place individuals at a higher risk for developing melanoma. I also learned that you should do a skin self-exam once a month. In doing so, individuals can notice any changes in existing moles and detect melanoma early. There are also symptoms that can be warning signs of melanoma and should be kept in mind. Symptoms may include a skin sore that fails to heal, a sore that changes in sensation and changes in the surface of a mole.

Conclusions:
Melanoma can be a serious type of skin cancer if it is not detected in its early stages. It can develop anywhere in the body but it commonly forms in areas where the skin is exposed to the sun. Anyone can develop melanoma but people with fair skin, light colored hair, and light colored eyes are at higher risk. You can detect melanoma early by doing skin self-exams. Things you can do to help prevent melanoma are reducing the amount of UV light exposure.

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ABSTRACT #82

The Impact of Prescription Drugs on Cancer Risk

Joseph Scott, Cleveland School of Science and Medicine; Fredrick Schumacher, PhD, Department of Population and Quantitative Health Sciences, Case Western Reserve University

Although variation exists, as individuals age the probability of developing a chronic disease increases rapidly. For example, 47% of individuals over the age of 55 have on average, two or more chronic medical conditions, whereas individuals under the age of 55 have an average of XX medical conditions. These comorbidities include conditions such as type 2 diabetes, hypertension, hypercholesterolemia, and heart disease, among many others. The majority of these health problems must be treated with prescription drugs or they will continue to progress. One example of health problems that a lot of men face is prostate cancer. There are drugs that aren't typically used to treat prostate cancer, but have an effect on it. One example of this is metformin therapy. Metformin is a drug mainly used to treat type 2 diabetes. Even though its primary use is to treat type 2 diabetes, it has been shown to reduce the incidence of prostate cancer. Metformin is an oral biguanide that has demonstrated anti-neoplastic effects in several additional types of tumors, including prostate cancer. Metformin reduces cancer risk by activating the AMPK pathway and suppressing the expression of genes involved in mitosis. Metformin has advantages in prostate cancer treatment. Some medications can reduce a person's risk of cancer, while others may increase it. For example, a recent meta analysis identified 8/14 drugs had a tentative signal in a Cox regression analysis and 6/8 increased cancer risk. Oxazepam has been linked to liver cancer. Nifedipine has been linked to esophageal and liver cancer. There are other possible confounders such as race, ethnicity, cigarette smoking, and body mass index. In conclusion, the best way to be healthy is to practice a healthy lifestyle instead of taking prescription drugs, because they may increase your risk for cancer.

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ABSTRACT #83

Tissue Macrophages Promote the Progression and Therapy Resistance in Breast Cancer

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Macrophages or (TAMS) Tumor Associated Macrophages are the key components for breast cancer microenvironment. Breast Cancer is one of the leading cancers in the world and mostly in women, but men can get it too. This means 90 percent are alive 5 years after they have been diagnosed with breast cancer. Breast cancer forms when cells start to grow out of control from different parts of the breast. However, most breast cancers begin in the duct that carries milk to the nipple, some start in the glands and others start in other tissue in the breast. While we look closer into the primary functions of TAMS and macrophages, we will see how TAMS and Macrophages play. TAMS are the most inflammatory cells, which orchestrate different stages of breast cancer development. TAMs participate in the angiogenesis, invasion, metastasis, and chemoresistance in breast cancer. There have been clinical studies that indicate the association between the high influx TAMS in tumors with poor prognosis in ovarian, cervical and breast cancer. Therefore, TAMS can either enhance or antagonize the antitumor efficacy of cytotoxic agents and antibodies cancer cells targeting depending on the treatment.

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ABSTRACT #84

CITED2 attenuates IRF1 signaling in macrophages

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Background:
Monocyte-derived macrophages are distributed across mammalian tissues and play an essential role in priming immune response. The macrophage-mediated inflammation is an explicitly robust process that is controlled at the molecular level to prevent unwanted tissue damage and deleterious effects on the host. The uncontrolled macrophage inflammatory response leads to many chronic and acute inflammatory disease conditions such as arthritis, atherosclerosis, lupus, inflammatory bowel diseases, and sepsis. There exist many cell-intrinsic negative regulators, which play a crucial role in restraining the intensity of inflammation to prevent uncontrolled inflammation by calibrating inflammatory gene expression in myeloid cells. Thus, a better understanding of cell-intrinsic negative regulatory mechanisms will provide a better understanding of pro- and anti-inflammatory signaling dynamics that are operative in chronic/acute inflammatory diseases.

Goals:
The goal of this project is to determine the role of Cbp/p300 interacting transactivator with Glu/Asp rich carboxy-terminal domain 2 (CITED2) in the regulation of interferon-gamma (IFNɣ)-induced IRF1 signaling in macrophages.

Materials and Methods:
Western blotting was performed to determine the CITED2 protein expression in bone marrow-derived macrophages (BMDMs) from *Lyz2*$^{cre/cre}$ and *Cited2*$^{fl/fl}$*:Lyz2*$^{cre/cre}$ mice. Real-time quantitative PCR was performed to determine the expression of *Irf1, Irf2*, *Irf9*, and IRF1 target genes in BMDMs after exposure with interferon-gamma (IFNɣ).

Results:
Western blot analyses confirmed the complete absence of CITED2 protein expression in *Cited2*$^{fl/fl}$*:Lyz2*$^{cre/cre}$ mice BMDMs. IFNɣ challenge elevated *Irf1* mRNA expression in CITED2 deficient BMDMs. Surprisingly, CITED2 deficiency did not significantly affect IFNɣ-induced *Irf2, Irf9, Stat1,* and *Stat3* expression in macrophages. In addition, IFNɣ challenge significantly elevated expression of *Isg15, Cmpk2, Irg1, Ccl5, Ptgs2, Dnase1l3, Ddit3, Il12rb2, Tmem140, Pfkfb3, F3*, and *B2m* expression in CITED2 deficient macrophages.

Conclusions:
Our results provide evidence that CITED2 attenuates IFNɣ-induced IRF1 and its target gene expression in macrophages.

ABSTRACT #85

Environmental Risk Factors of Lung Cancer in Ohio

Sidney Sheppert, Stow Munroe Falls High School; Cheryl Thompson, PhD, Department of Nutrition, Case Western Reserve University

Background:
Lung cancer has a tremendous effect worldwide. Lung cancer mortality rates can be drastically decreased if more people are educated on what may increase their risk of receiving the disease. Pollutants in the environment have been shown to be associated with an increased risk of lung cancer. The pollutants we are exposed to on a daily basis without knowing impacts everyone, but at different levels depending on where you live.

Goals:
The goal of the project was to see if levels of the ten different air pollutants are associated with cancer risk, mortality, lung cancer risk and lung cancer mortality in Ohio.

Materials and Methods:
We obtained overall and lung cancer incidence and mortality in each of the 88 counties from the State of Ohio website. We averaged readings of the following pollutants: carbon dioxide, carbon monoxide, methane, nitrous oxide, NOx, organic compound, PE(Cond), PE(Filt), PM10, PM2.5, sulfur dioxide, and VOC from emissions data publicly available on the Ohio EPA's website. We calculated the correlation coefficient and p-value of the correlation of each of the air pollutants with incidence and mortality by county.

Results:
I found that the pollutants: PE(Cond), PE(Filt), PM10 had a significant correlation with an increased lung cancer mortality rate in the counties in Ohio($R=.25$, $R=26$, and $R= .26$, respectively, $p<0.05$). The pollutant organic compound also shows an increased risk of overall cancer mortality ($R=.24$, $p<0.05$). None of the pollutants was statistically significantly associated with lung or overall cancer incidence.

Conclusions:
Lung cancer risk and mortality can be decreased worldwide if policies can help reduce environmental risk factors of the disease. Here we showed further data supporting the effect of air pollution on lung cancer. My research project is important because the findings can help inform policy on environmental pollutants reducing the burden of lung cancer.

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ABSTRACT #86

Organization and Quality Control of Large-Scale Prostate Medical Imaging Datasets for Machine Learning Research

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Department of Biomedical Engineering, Case Western Reserve University

Background:
Hospital MRI data consists of several sequences: T2 weighted (T2W) images, diffusion-weighted imaging (DWI), and apparent diffusion coefficient (ADC) maps derived from DWI. From this, T2W images and ADC maps must be standardized and registered, respectively. Organization and quality control (QC) of this data are critical pre-processing steps in artificial intelligence research of medical images that maintain a level of quality among images in a directory. Without QC, machine learning and deep learning pipelines fail to produce accurate and reproducible results, hindering their ability to generalize well across data from multiple institutions. Recently, researchers have developed a new, generalizable QC method called MRQy that uses machine learning pipelines to identify certain metadata values corresponding to components of an image's quality and adjust those values to primarily reduce three entities negatively affecting the image's quality: (1) sound and noise artifacts, (2) site- and scanner-specific variations, and (3) the Batch Effect.

Goals:
The goal of this study was (a) to create an organized pre-processed database of large-scale prostate MRI studies, and (b) to perform QC using software tools (e.g, MRQy) and identify the most useful set of images among a directory of prostate MRI scans belonging to approximately 580 patients.

Materials and Methods:
Using a directory of approximately 630 images belonging to 580 patients, a Python script was used to convert each patient's DICOM ADC and T2W images to NIFTI and was modified to accept patients' folders with different numbers of subdirectories. A script was generated to determine which patients did not have either ADC maps or T2W images, had ADC maps only, or had T2W images only. A script was generated to determine whether those patients were supposed to have their respective missing image types. Prostate segmentation was performed on the images to create prostate masks through a deep learning model, and intensity standardization of T2W images was conducted through a MATLAB script. Resampling of ADC maps was achieved via a Python script. Scripts to register ADC maps to the same dimensions as T2W images were modified and run. MRQy was run on the standardized T2W images of the directory, and metadata values were determined.

Results:
In the directory, nine patients did not have ADC mapping, 42 patients did not receive T2W imaging, and 115 patients did not receive either ADC mapping or T2W imaging. After employing MRQy onto the directory, several metadata values that represented different artifacts within the images were significantly altered. Particularly, the Peak Sound to Noise Ratio (PSNR) value increased for the intensity standardized T2W images, meaning that the variation of randomly generated brightness in the images was removed. The Coefficient of Variation of the Foreground Patch (CVP) was significantly reduced, indicating that shading artifacts in the images were removed by MRQy.

Conclusions:
The pre-processing steps of ADC resampling, ADC registration, T2W intensity standardization, and processing by MRQy for intensity standardized T2W images result in ADC maps and T2W images with a standardized level of quality across an entire directory of patients. As a result, the accuracy of processing steps taken is drastically improved. For example, Prostate Imaging-Reporting and Data System (PI-RADS) scores can more accurately determine the likelihood of clinically significant prostate cancer in patients using these pre-processing QC steps.
Pranav Sompalle is a Sam Miller Scholar

ABSTRACT #87

Effects of PGC-1alpha modulation in Alzheimer's Mice model

Diya Swain, Shaker Heights High School; Yubing Lu; Sandra Siedlak; Xiongwei Zhu, PhD, Department of Pathology, Case Western Reserve University

Background:
Alzheimer's disease (AD) results in the loss of memory and other cognitive functions. There is extensive neuronal loss in selective brain regions such as the hippocampus and cortex in the brains of AD patients. Mitochondrial dysfunction and oxidative stress are prominent features in the AD brain, which likely play a critical role in neurodegeneration. Peroxisome proliferator-activated receptor-gamma coactivator (PGC)-1alpha, a transcriptional coactivator, is a master regulator of mitochondrial biogenesis and links a complex reactive oxygen species defense system to mitochondrial oxidative metabolism. Prior studies demonstrated reduced PGC-1alphae xpression in the AD brain which could contribute to mitochondrial dysfunction and oxidative stress.

Goals:
To determine whether activation or over expression of PGC-1α rescues AD-related deficits in AD mouse models.

Materials and Methods:
The wildtype and 5XFAD Alzheimer mouse models were used for the experiments. Mice were fed either Bezafibrate-containing diet or a normal diet starting at 3 months before being sacrificed at 6 months for the experiment. Bezafibrate is a PPAR agonist that is known to activate PGC-1α and mitochondrial biogenesis. An immunostaining study was performed (N=2/group) to observe the pathological changes in the brain of Alzheimer's mice, when PGC-1α was activated by Bezafibrate, to see if there were any changes of inflammation, oxidative stress, mitochondria, and amyloid levels. Also, 5XFAD mice overexpressing PGC-1alpha were studied. Novel Object Recognition (NOR) analysis was conducted (N=5/group) to observe the behavioral changes between Alzheimer's mice with an overexpression of PGC-1alpha, Alzheimer's mice, and normal mice (wildtype) at 6 months. The time that it took for the mice to identify new objects was recorded by timing exactly how long they interacted with each object.

Results:
There is an increase of amyloids, microglia, and inflammatory response in Alzheimer's mice models compared to the wild type mice. However, the relationship between Alzheimer's mice fed Bezafibrate and those fed normally are inconclusive in regard to amyloids, microglia, and inflammatory response due to the low number of samples included. Furthermore, levels of oxidative stress and mitochondria require further research before forming conclusions between the Bezafibrate Alzheimer's mice and the Alzheimer's mice. The NOR analysis results suggest that PGC-alpha may improve behavior in AD mice models.

Conclusions:
The question of whether or not an expression of PGC-1α will benefit those diagnosed with AD still needs further research. However, from previous papers and ongoing experiments, it is suggested that activation or overexpression of PGC-1α, through Bezafibrate or genetic modification, can alleviate AD-related deficits, suggesting thatPGC-1α is a therapeutic target for AD.

Diya Swain is a Martha Holden Jennings Scholar

ABSTRACT #88

Does treatment for psoriasis decrease the risk of developing comorbidities, such as cardiovascular disease?

Hans Swain, University School; Neil Korman, MD, PhD, Department of Dermatology, Case Western Reserve University

Background:
Psoriasis is described as "a chronic, systemic immune-mediated disease characterized by development of erythematous, indurated, scaly, pruritic and often painful skin plaques". In a more basic description, it is a skin disease that causes red, itchy, scaly patches, mainly on the knees, elbows, trunk and scalp of humans. Psoriasis is one of the most frequent chronic inflammatory skin diseases. Psoriasis is called a "chronic disease", which means it is often long-lasting, and difficult to "cure". Psoriasis and its immune effects occur in up to 3.2% of the United States population. Worldwide, about 2-3% of the population have psoriasis, according to the world psoriasis day consortium. Other medical conditions that often show up at the same time, considered comorbidities - known as diseases that can impact a patient's overall prognosis and risk of death - are hypertension (1.1% to 27.8%), diabetes mellitus (7.0% to 13.9%), cardiovascular diseases (4.2% to 8.1%), and even tonsillitis (3.5% to 5.4%)". Treatment options include a variety of topical, oral, and subcutaneous medications. In this research, I propose that treatment of psoriasis leads to a decreased risk of developing comorbidities known to be related to the disease.

Goals:
The overall goal of this project is to gain knowledge and understand if treatment for this disease decreases risks of developing diseases associated with psoriasis.

Materials and Methods:
To conduct this literature research project, I will use the following search engines: Google, Pubmed, and OhioLink. Search terms will include "psoriasis" alone and also combined with one or more of the following terms and phrases: "risks", "risk factors", "disease(s)", "treatments", "severity", "susceptibility", "comorbidities", "cardiovascular", and "associated medical conditions". The number of hits (results) will be recorded. I will find research studies that used human subjects, but I will also not exclude studies that used animals like mice and rats. For any studies that did not use humans, I will be sure to make a clear note. I will not restrict my study in terms of past years or decades since publication, but I will prioritize studies done in the past 20-30 years.

Results:
Several studies, such as Churton et al., 2014, have described that there is a relationship between the risk of developing cardiovascular disease. We expect that relationship to be an inverse correlation. The results of my literature review will include scientific research and data that will also help answer my research question and evaluate my hypothesis. I anticipate finding that my results will support those patients who receive treatment and have less psoriasis also have a lower risk of developing cardiovascular disease and other diseases versus those who are not treated and have large amounts of psoriasis.

Conclusions:
Overall, we found that treatment of Psoriasis impacts the risk for developing comorbidities, such as cardiovascular disease. We expect our findings to support the following: Psoriasis is a common disease worldwide and there are many treatment options available. They not only help to decrease the skin disease, but also lower the risk of developing other disease.

ABSTRACT #90

An evaluation of microbiome changes in women in the THRIVE study undergoing treatment for bacterial vaginosis

Mackensie Thompson, Andrews Osborne Academy; Adam Bergener, PhD,
Department of Pathology, Case Western Reserve University

Background:
Bacterial vaginosis is a common condition worldwide, about 30% of women will have had BV in their lifetime. There are several factors that contribute to risk of BV and vaginal health, one factor is the makeup of the vaginal microbiome. The vaginal microbiome varies for each person, however, there are some common bacterial species. One optimal bacterial species in the vaginal microbiome is the *Lactobacillus* species, which is commonly most prominent in the vaginal microbiome. It increases the pH in the vagina by producing lactic acid and releasing antimicrobials. The lack of *Lactobacillus* could raise the chance of acquiring diseases, poor reproductive health, and infections, one of those infections being BV. There are several different ways to treat BV; two common treatments are clindamycin in the form of a cream and metronidazole in the form of a gel.

Goals:
The goal of this research is to evaluate a form of treatment for this condition titled metronidazole in the THRIVE clinical trial and to monitor for any changes in the bacterial species that could have relation to the treatment along with changes in the vaginal microbiome. The THRIVE; The Study of Host-bacterial Relationships and Immune function in different Vaginal Environments clinical trial was conducted over the course of 6 months with an initial check in prior to treatment after being diagnosed with BV and a check in at the end of the 1st month after treatment. The objective was to determine how effective treatment was and if significant changes could be seen in the vaginal microbiome.

Materials and Methods:
Using 16s rRNA sequencing the data was able to be prepared and processed. This is an 11-step process that begins with the setup, in a 94-well plate(s) that will have 1 positive and negative control, and sections with the samples and index primers inside. Then the samples go through the Lysis step, which is essentially transferring the sample into smaller tubes, pipetting, putting the samples into an incubator, extracting the buffer and then pipette again to mix, incubate and add Proteinase K to the samples. After this process, the samples go through DNA extraction, and then go through post-extraction quantification, which will allow for a standard curve to determine the amount of DNA. Samples also go through an amplicon to amplify the 16s rRNA gene target region, a Post-PCR check, a way to make sure the samples are fully mixed and a Post-amplicon clean up. The last few steps are the Index PCR to transfer 5 microliters (uL) into a new plate to store and add in the designated primers, do the clean-up process, complete the last amplicon, then normalize the samples and the library dentering and load into the MiSeq samples.

Results:
The clinical data shows, there were 54 patients in the study and on the initial check in, 20% of the participants had been diagnosed with BV. By the end of the trial about 1% of the participants still had BV or had been diagnosed with it. The women who still had BV and those who didn't still had a wide variety of bacteria in their microbiomes, the most prominent being Garnerella, Lactobacillus and Prevotella just to name a few. The predominant bacterial species was the Lactobacillus.

Conclusions:
There are more complex factors that contribute to the patient being diagnosed BV including; environment, limited access to healthcare and the inconsistent use of contraceptives. When it comes to metronidazole as a form of treatment, it is showing to be reliable for treatment. As shown by the significant decrease in patients diagnosed with BV in the trial, the data is yielding a positive effect on their conditions.

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ABSTRACT #91

Analyzing the Impact of Pc 4-PDT on Candida Auris

Owen Tolbert, Shaker Heights High School; Thomas S. McCormick, PhD, Department of Dermatology, Case Western Reserve University

Background:
Candida auris **is an emerging fungus that has caused many different outbreaks in hospitals. It has grown to become a problem in many hospitals and is an emerging global health threat.** ***Candida Auris*** **is a very resistant fungus, and is often multidrug-resistant.** ***Candida Auris*** **is a yeast that can enter through a patient's bloodstream, and can cause invasive infections. Skin is a natural place for** ***Candida Auris*** **to colonize and it transmits throughout cutaneous contact. Photodynamic therapy(PDT) is a form of therapy using light that is used to destroy abnormal cells, and some skin and eye conditions. Photodynamic therapy is a form that can be used to try and limit the cutaneous contact of** ***Candida Auris*****. Silicon Phthalocyanine IV(Pc 4) is the photodynamic therapy used in this project to test the resistance of** ***Candida Auris*** **to certain doses of Pc 4-PDT.**

Goals:
Due to the high resistance of Candida Auris to different types of antifungal therapies, the objective of this study is to test the resistance of ***Candida Auris*** **to Pc 4-PDT and how it mutates to combat it. The objective is also to find a reasonable dosage amount of light that best combats** ***Candida Auris*****, and limits its spread rate.**

Materials and Methods:
A literature review was conducted of both photodynamic therapy, and ***Candida Auris*****, to assess the validity of using photodynamic therapy to best control the spread of** ***Candida Auris.*** **In the lab, photodynamic therapy was used against Pc4 treated** ***Candida Auris.*** **1mj of light was used upon untreated, Pc4 treated (0.5m), Pc4 treated (0.4m), and Pc4 treated (0.3m)** ***Candida Auris.*** **Pc4 was also used as an antifungal against Candida Auris without the light. Testing the untreated, Pc4 treated (0.5m), Pc4 treated (0.4m), and Pc4 treated (0.3m).**

Results:
Candida Auris **was heavily impacted by the Pc 4-PDT. 23.59% was the survival ratio for the** ***Candida Auris*** **when using Pc 4-PDT compared to just using Pc4 as the antifungal. The ratio of survival for the Candida Auris when using Pc 4-PDT to the untreated cells was 11.43%. The ratio of survival for the** ***Candida Auris*** **colonies when only using Pc4 as an antifungal compared to the untreated was 48.57%.**

Conclusions:
The data shows that Pc 4-PDT had a major impact on the spread of ***Candida Auris*****. When only light was used without the Pc4 it did not make a significant impact on the amount of colonies. When Pc 4-PDT was used it caused a big difference in the amount of colonies. When 0.5m of Pc4 was used with light it completely eradicated all of the** ***Candida Auris*** **colonies. 0.4m of Pc 4-PDT, turned out to be the amount of dosage that we were looking for in killing off enough of the** ***Candida Auris*** **colonies.**

Supported in part by NIH, NCI, R25 CA221718

ABSTRACT #92

The Positive Aspects of Sunscreen in Regards to the Benzene Contamination

Mythili Ungarala, Shaker Heights High School; Devin K. Barzallo; Christina Wong MD, Department of Dermatology, Case Western Reserve University

Background:
Skin cancer is the most common form of cancer in the United States. It is the uncontrolled growth of abnormal skin cells. While healthy cells grow and divide normally, cancer cells grow and divide in a hazardous manner. This rapid growth causes tumors that are either benign or malignant. Basal cell and squamous cell cancer account for 95% of all skin cancers and are curable when treated early on. Melanoma is the deadliest skin cancer and frequently metastasizes. If left untreated, it can spread to other organs and cause substantial damage. Recently Valisure LLC has detected Benzene in several batches of sunscreen. Benzene is an organic chemical compound with the molecular formula C_6H_6. It is colorless and very toxic. Benzene is known to cause cancers, such as leukemia and other blood disorders. It is an industrial chemical used to make plastics, resins, synthetic fibers, rubber lubricants, dyes, detergents, drugs and pesticides. It ranks in the top 20 chemicals for production volume in the U.S.

Goals:
The goals of this project are to analyze the positive effects of sunscreen on the skin to protect against potentially harmful skin cancers, and acknowledge the negative effects of Benzene contamination in regards to sunscreen and public health.

Materials and Methods:
We investigated sunscreen's benefits through numerous articles and papers that discussed how applying sunscreen when exposed to UV radiation is a critical part of preventing skin cancer. PubMed and Valisure's research, concerned with the chemical Benzene, which is detected in many sunscreen products, known to cause cancer. We discovered multiple lawsuits against major sunscreen corporations and analyzed the difference between the positive results of using sunscreen daily, and the negative results of Benzene on the skin.

Results:
Sunscreen is a widely used product that protects against the sun's ultraviolet rays, and has been shown to reduce the risk of developing melanoma by 50%. There are two forms of sunscreens, mineral based and chemical based. Mineral sunscreens act as a physical barrier to the skin blocking all ultraviolet radiation. Chemical sunscreens are absorbed into the skin and change the UV rays into heat. On May 24th, Valisure had reported that they had found Benzene in 78 out of 294 tested sunscreen and after-sun products like Neutrogena, Banana Boat, and Fruit of the Earth. Benzene is a known carcinogen that causes bone marrow failure, DNA strand breaks, and affects the liver, kidney, lungs, heart, and brain. This caused consequences within the public regarding the safety of using sunscreen. Many thought that benzene was an ingredient of sunscreen, which it was not, and had disregarded the benefits of using sunscreen completely.

Conclusions:
In statements to CBS News, Johnson & Johnson, Sun Bum, and CVS have all denied including benzene in their products. They all guaranteed reevaluation in their testing and sourcing from now on. Sunscreen is still an important part of reducing cancer and protecting the skin. It is important to note that not all sunscreen products were tainted with benzene, and there are available products that are uncontaminated and should continue to be used to protect against potentially harmful sun radiation.

Mythili Ungarala is a Martha Holden Jennings Scholar

ABSTRACT #93

Optimizing Cytarabine and BAFF Doses to Maximize the Reduction of Cytarabine's Effect on JEKO Proliferation

Zoie VanHuffel Gouldlock, Bedford High School; Daniel Feinburg; Reshmi Parameswaran, PhD, Case Comprehensive Cancer Center, Case Western Reserve University

Background:
Mantle cell lymphoma (MCL) is a type of non-Hodgkin's lymphoma cancer that specifically targets the lymphatic system. It's a very invasive form of cancer that is resistant to most modern types of treatment. An example of the poor outcome for patients with relapsed or drug-resistant MCL, research done by Dr. Fensek has shown that with treatment by a specific drug (Ibrutinib), the average effectiveness of the drug was about 17 months and once treatment failure occured, the average overall survival for patients was about 2 and a half months. JEKO is a type of B-cell lymphoma that has a high expression of a BAFF-R (BAFF ligand receptor). BAFF means B-cell activating factor and it is specific to B-cells, and it has no advantage in normal states. When drugs or treatments like Cytarabine are introduced, the BAFF to BAFF-R interaction gives the cancer cells protection from the drugs/treatment. Cytarabine is a type of chemotherapy used to treat cancer.

Goals:
The goal of this experiment is to optimize the dose of Cytarabine and BAFF to maximize the reduction of cytarabine's effect on JEKO proliferation. By doing this, it will make it easier to study BAFF inhibitors that may block BAFF-BAFF R interaction. Moreover, it will further prove BAFF's critical role in lymphomas under stress.

Materials and Methods:
RPMI Media (Sigma-Aldricch)
Cytarabine
BAFF ligand (Sino Biologicals)
JEKO cells (ATCC)
Methods: We treated the JEKO cells with differing amounts of BAFF and Cytarabine and studied the cells using a cytoflex flow cytometer machine to get the data.

Results:
After 3 days of conducting the experiment, the results show that there is a rescue that is shown in the 20nM Cytarabine group. If more days are conducted, hopefully the results will show a substantial rescue with the BAFF ligand at 250 nM and 500 nM. No dose-dependent rescue has been seen between the 250nM and 500 nM BAFF addition. The results at 10 nM of Cytarabine, although showing a significant reduction of proliferation, were not substantial enough to allow for a rescue. These will continue with a higher dose of Cytarabine.

Conclusions:
The findings conclude that there is a rescue shown in the 20nM Cytarabine group and there is a potential rescue with the BAFF ligand at 250nM and 500 nM. There are no dose-dependent rescues which is what we hoped to see. The experiment was not fully completed; other conclusions cannot be made without the additional data.

Supported in part by NIH, NCI, R25 CA221718

ABSTRACT #94

Substrate Charge Distribution Modulates the Activity of the GalNAc-Transferase-Catalyzed Initial Mucin-Type O-Glycosylation

Mantas Viazmitinas, Westlake High School; Collin Ballard; Miya Paserba; Dayna Nguyen; Kaitlyn Moore; Thomas Gerken, PhD, Department of Biochemistry, Case Western Reserve University

Background:
Mucin-type O-glycosylation is one of the most ubiquitous, diverse, and complex posttranslational modifications of secreted and membrane-bound proteins in metazoans. This quasi-regulated process is initiated via a large family of homologous genes encoding the polypeptide N-acetylgalactosamine transferases (GalNAc-Ts), 20 of which have been identified in humans. The GalNAc-Ts are involved in the covalent attachment of the sugar N-acetylgalactosamine (α-GalNAc) to the hydroxyl group of a peptide chain's serine or threonine residues. The GalNAc-Ts play an important role in normal physiology and in many disease states, including cancers, due to mutation, overexpression, and underexpression of specific GalNAc-Ts. Previous studies from the Gerken lab have characterized multiple GalNAc-T specificities that vary with isoform, including preferences for 1) serine or threonine residues, 2) specific peptide sequences, and 3) specific prior remote and/or neighboring glycosylation. Ultimately, these unique specificities serve to regulate the glycosylation of residues in polypeptide substrates.

Goals:
Recent studies have shown that flanking charged residues altered the rates of peptide glycosylation, and therefore, the focus of this research was to systematically investigate and understand how substrate protein charge distributions modulate mucin-type O-glycosylation.

Materials and Methods:
The analysis was performed using a series of synthetic peptide substrates possessing all possible, different flanking charge combinations, including positively charged arginine (RRR) repeats, negatively charged aspartic acid repeats (DDD), and neutral glycine/alanine repeats (GAG). The activities of 11 isoforms of GalNAc-T against these charged peptide substrates were then determined. In addition, surface charge calculations (APBS Software in PyMOL) were performed on known and homology-modeled (SWISSMODEL) GalNAc-T isoform structures to further evaluate these preferences.

Results:
Several isoforms demonstrated preferences for a net negative charge (h-GalNAc-T1, T2, T6, T11 & T16) or net positive charge (h-GalNAc-T3 & tg-GalNAc-T3), while other isoforms displayed preferences for unique combinations of N- and C-terminal charges (h-GalNAc-T4, T5, T12 & T13). Furthermore, the surface charge calculations showed that peptide charge distributions correlated well with GalNAc-T surface charge preferences, thus explaining their preferences at a molecular level.

Conclusions:
These findings reveal flanking charges are another factor that can modulate mucin-type O-glycosylation in a GalNAc-T isoform manner. Thus, the initiation of O-glycosylation is modulated by multiple properties of the target peptide. These findings will be useful in predicting sites of glycosylation for the interpretation of O-glycoproteomics data and our understanding of GalNAc-T isoform specificity in relation to disease.

Mantas Viazmitinis is a Sam Miller Scholar

ABSTRACT #95

Biomarker and re-purposable drug identification in endometrial cancer

Damon Wallace, Stefanie Avril, Cheryl Cameron, Mark Cameron

Background:

In the United States, African American women have a 2-fold higher mortality rate due following diagnosis with endometrial cancer; their survival being significantly lower for all histologic subtypes even after stratifying by age, stage, and tumor grade at presentation. While anti-tumor immune responses have emerged as strong predictors in most malignancies, the biological and molecular mechanisms that underlie endometrial outcome disparities are poorly understood. There also isn't much known about the genes that determine immune subgroups within endometrial cancers, especially amongst African American women. In my SEO/YES program project, I became familiar with the published literature in endometrial cancer outcome disparities and a bioinformatic method being applied in the Cameron lab, called drug perturbation Gene Set Enrichment Analysis (dpGSEA), that can both assess anti-tumor immune response genes that drive endometrial cancer outcomes in African American women as well as perform in silico drug screening for re-purposable drugs that might be able to target these genes and treat patients with endometrial cancer.

ABSTRACT #96

Risk, incidence, and disparities of COVID-19 vaccine breakthrough infection among patients with multiple myeloma in the U.S. between December 2020 and July 2021

Lindsey Wang, William Wang, Orange High School; Nathan Berger, MD, Case Comprehensive Cancer Center; Rong Xu, PhD, Center for Artificial Intelligence in Drug Discovery, Case Western Reserve U.

Background:
Patients with multiple myeloma (MM) are at an increased risk for COVID-19 infection. Three FDA-approved vaccines are highly effective against COVID-19 in the U.S. The compromised immune status of patients with MM, the exclusion of cancer patients in vaccine clinical trials, high vaccine hesitancy, and the emergence of new SARS-CoV-2 variants make it imperative to evaluate real-world COVID-19 immunity among vaccinated patients with MM.

Goals:
To examine overall risk, time trend of incidence rate, and disparities of vaccine breakthrough COVID-19 infection in patients with MM during the seven-month period between Dec. 1, 2020 and July 1, 2021; (2) to compare COVID-19 immunity among patients who received Pfizer-BioNTech vs. Moderna mRNA vaccine; (3) to investigate how different types and timing of cancer treatments impact COVID-19 immunity among vaccinated patients with MM.

Materials and Methods:
This retrospective cohort study used the cloud-based TriNetX Analytics network platform, which allows access to de-identified data of more than 83 million unique patients from 63 health care organizations in the U.S. The study population comprised of 740,332 vaccinated patients who had a recent encounter with a healthcare organization during the seven-month period from Dec. 1, 2020 to July 1, 2021 and had no COVID-19 infection prior to December 2020, including 1,490 vaccinated patients with MM and 738,842 without MM. The overall risk of COVID-19 infection in patients with MM was examined and compared to that of propensity-score matched patients without MM. Time trends of the incidence rates of COVID-19 infection during the seven-month study period were examined among vaccinated patients stratified by age, gender, and race.

Results:
The overall risk of vaccine breakthrough COVID-19 infection among patients with MM is 8.1%, significantly higher than the risk of 2.8% in patients without MM ($P < 0.001$) and 3.6% in matched patients without MM ($P < 0.001$). The risk of COVID-19 infection is 6.6% in patients with MM who received the Moderna mRNA vaccine and 8.4% in those who received the Pfizer-BioNTech vaccine ($P = 0.27$). The incidence rate of COVID-19 infection among vaccinated patients with MM steadily increased from 0 cases/person-day in December to 0.00025 cases/person-day in February 2021, 0.00103 cases/person-day in April 2021, and 0.0018 in June 2021. Similar increasing time trends were observed for patients stratified by gender, race, and age. The risk of COVID-19 infection among vaccinated patients with MM who have received cancer treatment any time in the past two years is 10.2%, significantly higher than the 5.8% in those who received no recent cancer treatments ($P < 0.001$).

Conclusions:
We showed that among the vaccinated population, patients with MM were at a significantly increased risk for COVID-19 infection than those without MM. Nonetheless, the overall risk of COVID-19 infection among vaccinated patients with MM remains low, demonstrating the high efficacy of vaccines against COVID-19 and the importance of vaccination for patients with MM. The incidence rate of COVID-19 infection in patients with MM is low but steadily increased during the seven months from Dec. 2020 to Feb. 2021, especially after February 2021, highlighting the value of vaccination and the continuous preventive measures given the emergency of the Delta variant and the vulnerability of patients with MM to COVID-19 infection.

ABSTRACT #97

COVID-19 Vaccine breakthrough infection among vaccinated patients with colorectal cancer in the U.S. between December 2020 and July 2021: a retrospective cohort study using electronic health records

William Wang, Lindsey Wang, Orange High School; Nathan Berger, MD, Case Comprehensive Cancer Center; Rong Xu, PhD, Center for Artificial Intelligence in Drug Discovery,Case Western Reserve U.

Background:
Colorectal Cancer (CRC) is the third most common cancer diagnose in both men and women, and diagnosed patients are often immunocompromised. Though data from earlier on in the pandemic pointed out those un-vaccinated patients who had been diagnosed with Cancer, e.g. CRC, are at a heightened risk for COVID-19, it is still unknown what the COVID-19 immunity is among the vaccinated patients with CRC after the vaccine's approval in December.

Goals:
To evaluate overall risk, time trend of incidence rate, and disparities of vaccine breakthrough COVID-19 infection in patients with CRC during the seven-month period between December 1, 2020 and July 1, 2021; to compare COVID-19 immunity among patients who received Pfizer-BioNTech vs. Moderna mRNA vaccine; and to investigate how different types and timing of cancer treatments impact COVID-19 immunity among vaccinated patients with CRC.

Materials and Methods:
This retrospective cohort study used the cloud-based TriNetX Analytics network platform, which allows access to de-identified data of more than 83 million unique patients from 63 health care organizations in the United States. The study population comprised of 744,079 vaccinated patients who had a recent encounter with a healthcare organization during the seven-month period from December 1, 2020 to July 1, 2021 and had no COVID-19 infection prior to their vaccination, including 3,458 vaccinated patients with CRC and 740,621 without CRC. We examined the overall risk of COVID-19 infection in patients with CRC compared to that of propensity-score matched patients without CRC. Time trends of incidence rate of COVID-19 infection during the 7-month study period were examined among vaccinated patients stratified by age, gender and race.

Results:
Of the population of patients who had been diagnosed with CRC, the overall likelihood of vaccine breakthrough COVID-19 infection is 7.6%. Of the population who had not been diagnosed with CRC, the overall likelihood was significantly lower, only 2.8% ($P<0.001$) - for the matched population, the overall risk was 4.7% ($P<0.001$). The population of patients who had the Pfizer vaccine (7.1%) were less likely to contract COVID-19 than those who had the Modern mRNA vaccine (9.2%) ($P = 0.533$). The incidence rate of COVID-19 infection among the vaccinated population with CRC steadily grew from 0 cases / person-day in December, to 0.00225 in June, 2021. Similar time trends were observed from populations stratified by gender, race, and age. Of the vaccinated population with CRC who underwent any cancer treatments (e.g. chemotherapy, radiation therapy, or target therapy) after December 2020, the risk of contracting COVID-19 was 9.9%, higher than those who received no cancer treatment (7.0%, p-value = 0.018)

Conclusions:
Though patients with CRC are at a heightened risk of contracting COVID-19 than those without CRC, the overall risk is still low (7.6%), highlighting the efficacy of the vaccines. The incidence rate of COVID-19 infection in the population with CRC is low, but still growing during the 7-month period, especially after May 2021. This highlights the importance of vaccinations and the need to take preventive measures against the emergence of the delta variants in vaccinated populations.

ABSTRACT #98

Manipulation of gut-resident bacteria to influence changes in gut microbiota within the brain tissue

Gwendolyn Weagraff, Avon High School; Jonathan Duncan; Jeffery Capadona, PhD, Department of Biomedical Engineering, Case Western Reserve University

Background:
Hydrocephalus is an illness distinguished by excess cerebrospinal fluid within the fluid-containing ventricles of the brain. The primary treatment of hydrocephalus is to insert a ventricular shunt into the fluid-filled ventricle of the brain. The distal end of the shunt drains the excess cerebrospinal fluid to other body cavities, such as the chest cavity or the abdomen. Unfortunately, failure rates associated with obstruction and infection reach nearly 100% given enough time. More specifically, up to 27% of ventricular shunts result in cerebrospinal fluid infections and bacterial colonization on the shunt surface, accelerating the rate of inflammatory-mediated obstruction. The use of antibiotic-loaded shunts have become more common to attenuate infection rates. Recent evidence suggests the role of disruptions in the microbiome in neurodegenerative inflammation in the brain. Growing evidence suggests that changes in the gut microbiota can alter brain physiology and behavior. Therefore, we hypothesize that treatment of hydrocephalus with drainage tubes connecting the gut to the brain can facilitate gut-resident microbiome implications on brain health and shunt performance.

Goals:
The goal of this project is to investigate if gut-resident bacteria can be manipulated to influence changes in gut microbiota within the brain tissue. Then, we will investigate if this change is exacerbated following device implantation.

Materials and Methods:
To date, fifteen C57/BL6 mice have been separated into three groups of five and housed individually for two weeks. Group 1 was fed a normal diet to serve as controls. Group 2 was treated with antibiotics in their drinking water to reduce bacteria, while group 3 was provided probiotics to selectively promote healthy bacteria growth. Weekly stool samples and post-mortem intestine (cecum) and brain tissue were harvested for quantification of microbiome content.

Results:
Animals will be euthanized and samples collected for analysis during the last week of my internship. Therefore, no results can be included in this manuscript.

Conclusions:
No conclusions can be drawn at this point. However, I will continue working in the Capadona Lab throughout the next academic year to see this project to the end.

ABSTRACT #99

Does cholesterol depletion alter the size of lipid raft micro domains of T-Cell Signaling proteins in Jurkat T Cells

Isaiah Whatley, Mayfield High School; Jeffrey A. McCausland PhD; Alan D. Levine PhD, Department of Molecular Biology and Microbiology, Case Western Reserve University

Background:
It is understood that on the membrane of eukaryotic cells, there are distinct areas of the membrane called lipid rafts. Recent studies have conveyed that lipid raft heterogeneity exists implying certain proteins can actively function in certain rafts. This is important during the immune response process of T cells. Cholesterol, a major component of the lipid raft, can regulate lipid raft function by altering protein functioning in the raft and therefore potentially regulate the process of T cell signaling and activation.

Goals:
The goal of this project was to determine if the size of a lipid raft is a factor to consider when evaluating the effects of different cholesterol depleting drugs (Methyl Beta Cyclodextrin (MBCD) & Cholesterol Oxidase) on the functioning of raft associated proteins. We specifically characterized lipid raft dimensions of T cell signaling proteins not only to help understand the role that lipid rafts play in the immune response but to potentially begin seeing the effect that cholesterol has on T cell function.

Materials and Methods:
Cells were cultured under sterile conditions without antibiotics using RMPI 1640 supplemented with 10% FBS and 20 mM HEPES. Cells were then separated into three conditions: either control, cholesterol depleted using 20 mM MBCD, or cholesterol depleted using 1 activity unit/ml of Cholesterol Oxidase. The cells were then unroofed, subsequently immunolabeled, and stained as previously established in the lab on 200 mesh Formvar coated electron microscopy grids. Micrographs were collected on a Tecnai T12 Electron Microscope with an accelerating voltage of 100 kV. Image analysis was performed in the NIH developed suite of Software known as FIJI. Area of the lipid rafts were measured selectively for two T cell proteins, p56LcK and the Linker for the Activation of T cells (LAT). Protein expression would be identified by measuring the size of gold conjugated immunolabeled secondaries that targeted either LAT or p56LcK antihuman antibodies.

Results:
In my time, although I was not able to associate the proteins Lck and LAT with certain rafts based on features of rafts and therefore was not able to measure the correlation of raft size and protein expression due to time constraints and methodological inconsistencies. I was however able to gather statistical data and analysis by measuring lipid raft sizes across approximately 60 micrographs (20 each condition). After producing histograms based on raft size for each condition, the average, median, and standard deviation of the raft sizes were all determined for each condition. Control: Avg .00421, Med .00372, standard deviation .00259; MBCD: Avg .00575, Med .00346, .00786; Cholesterol Oxidase: Av. .00253, Med .00168, standard deviation .00273. These areas are consistent with other measurements established in literature.

Conclusions:
Based on the results from the data that was gathered, I concluded that although the standard deviations for both the cholesterol oxidase and MBCD treated rafts both overlapped with the control group in a box plot suggesting no significant difference in raft size, there was a higher average raft size for MBCD treated rafts in the histogram. In order to determine how this increase in raft size affects the proteins of rafts treated with MBCD, the Lck and LAT proteins will have to be associated with certain rafts based on their features, then protein expression would have to be measured via methods like flow cytometry, immunolabeled secondary size analysis, sucrose density gradient utilization, etc.

Supported in part by NIH, NCI, R25 CA221718

ABSTRACT #100

Family Income and its Impact on Family Resilience

Matthew Wilson, Solon High School; Peter Hovmand, PhD; Center for Community Health Integration, Case Western Reserve University

Background:
Resilience research is typically centered around an individual and the factors that allow that individual to succeed despite adverse circumstances. However, in recent history there has been a surge of interest in family resilience which revolves around interpersonal relationships and how those relationships impact resilience and personal success. Family resilience has been proven to play a large role in developing social and emotional competence in children as well as adults. In this study, we will be approaching family resilience using Community Based System Dynamics (CBSD). System Dynamics is a research approach for understanding complex relationships and behaviors using stock and flow, table functions, time delays, and internal feedback loops. However, Community Based System Dynamics uses this approach and applies it to changing systems within communities. By using a CBSD approach, we can develop our research to encompass the most important community factors that are impacted by family income and how the relationship between family income and community factors ultimately affects family resilience.

Goals:
The goal of this project is to test the hypothesis that increasing family income would subsequently cause an effect on key determinants of family resilience resulting in increased resilience as a function of time and personal success in the long term.

Materials and Methods:
We identified three major community factors that are impacted by income. Those factors are Family and Community Platform (indicating the strength and support family and community offer), Systemic Barriers (meaning obstacles restricting the success of an individual or family), and Differences in Power and Privilege (indicating advantages available to a particular individual). Each of these factors impact other variables to create a system of connected feedback loops. Other variables impacted include institutional norms, Informal and Formal Sanction, Trust, Hopefulness, Sense of Future, Spirituality, Healing, Professional and Individual Accountability, Justice, Obfuscation and Collusion, Trauma, Citizenship Tax, Core Values and Culture, Double Consciousness, and lastly Family Resilience. To analyze the effect of family income on resilience, we used Stella Architect to create a model of all the specified community factors and how they are affected by the previously mentioned variables. From the model built, a simulation was then created to graph the effect of differences in income and how those differences ultimately affected resilience over a period of time.

Results:
Pending

Conclusions:
Throughout this project, Family and Community Platform, Systemic Barriers, and Differences in Power and Privilege were analyzed with respect to household income to obtain a greater understanding of the effect of family income on family resilience. Although results are pending, we anticipate this project could be taken to a broader level to encompass a greater range of wealth other than family income alone. This might include stock ownership, real estate, or other assets owned by a family that may impact Family and Community Platform, Systemic Barriers, and Differences in Power and Privilege.

ABSTRACT #101

Neural Components contributing to the formation of the Perineuronal Net

**Gavyn Woo, Cleveland School of Science and Medicine; Lin Mei, MD, PhD,
Department of Neurosciences, Case Western Reserve University**

Background:
The Perineuronal Net(PNN) is a net-like structure of the extracellular matrix around certain populations of neurons in the central nervous system. It plays an impactful role in neural plasticity and brain maturation. The question posed in this research was what is the leading neural component to the formation of the perineuronal net. We have employed methods to inhibit gila and copy features of cellular activity through extreme depolarization to figure out the cellular source in specific components found in the perineuronal net and better acknowledge the activity-dependent nature of the Perineuronal Net expression by changing previous culture models.

Goals:
The goal of this project was to answer the question of what are the major neural components contributing to the formation of the Perinueronal net. The hypothesis that was formed was that aggrecan was the main neural component to the formation of the Perineuronal Net. This will be tested through analysis of the different proteins suspected to be neural components and thorough literature research on the topic.

Materials and Methods:
A literature review has been done to help prove that aggrecan is the main neural component to the formation of the perineuronal net. In addition, a variety of tests have been done to test the different proteins that have been suspected to play a role in the formation of the Perinueronal net.

Results:
Results showed that among the proteins that were theorized to be the main component in the formation of the perineuronal net, aggrecan shows the closest results supporting the hypothesis created. Furthermore, the results demonstrate an intriguing and complex interplay between neurons and glia in the formation of these structures and suggest that aggrecan is likely the key activity-dependent component of the Perineuronal Net.

Conclusions:
The conclusion that was reached at the end of this research paper was that agreccan was the leading neural component of the Perineuronal Net. Other conclusions that can be drawn from this paper was that PNN components are expressed by Gila.

Gavyn Woo is a Martha Holden Jennings Scholar

ABSTRACT #102

Stability of Indocyanine Green-Loaded Nanobubbles for Multimodality Imaging Applications

Victor Xie, Solon High School; Eric Abenojar; Agata Exner, PhD, Department of Radiology, Case Western Reserve University

Background:
Lipid-shelled nanobubbles (NBs) are used as ultrasound contrast agents for tumor imaging and detection. NBs are unique because of the benefits that stem from their small particle size. They are able to migrate from the vasculature to the extravascular target site and are able to accumulate in tumors via the enhanced permeability and retention (EPR) effect. This leads to potential theranostic applications such as its use as both an imaging and drug delivery agent. In this study, we incorporated indocyanine green (ICG) to the NBs to create a multimodal imaging agent. ICG is a near-infrared (>750 nm) fluorescent dye approved by the Food and Drug Administration (FDA), which acts as a photo absorber and can be used in biomedical imaging applications such as photoacoustic imaging in addition to ultrasound and optical (fluorescence) imaging. Using different imaging modalities to visualize the same agent in vivo provides comprehensive information about the NBs in applications such as drug delivery and cancer imaging.

Goals:
To determine the effect of ICG incorporation into NBs with regard to contrast-enhanced ultrasound (CEUS) signal, as well as NB size, concentration and stability.

Materials and Methods:
First, we created the NBs by dissolving the lipids DBPC (6 mg), DPPA (1 mg), DPPE (2 mg), and mPEG(2k)-DSPE (1 mg) in 0.1 mL of propylene glycol by heating and sonicating at 80 °C until the lipids were fully dissolved. Varying amounts of ICG (0, 0.2, and 0.3 mg per vial) were dissolved alongside the lipids. A 0.9 mL mixture of PBS and glycerol was added to the lipid solution and further sonicated at room temperature for 10 minutes. The lipid solution was transferred to a 3 mL vial and capped with a rubber septum and aluminum seal, and sealed with a vial crimper. We removed the air using a 30mL syringe and filled it with octafluoropropane (C_3F_8.) gas. The solution was activated using a VialMix for 45 s and centrifuged at 50 rcf for 5 min. The NBs were collected with a 21G needle and characterized with CEUS using an agarose phantom (1:100 dilution in PBS, 12 MHz, 0.1 MI, 1 fps). Bubble size and concentration were measured using resonant mass measurement (RMM) (1:1000 dilution in PBS), and dynamic light scattering (DLS) (1:10,000 dilution in PBS).

Results:
We found that incorporation of ICG did not significantly lower NB CEUS signal or bubble stability. After CEUS exposure for 8 min, bubbles without ICG had 89.63% of the initial signal remaining compared to the bubbles loaded with 0.2 mg ICG, which had 87.01% and the bubbles loaded with 0.3 mg ICG having 86.23% of the initial signal. When there was no ICG loaded, the NBs had a size of 255±110 nm and a concentration of $4.88\pm0.47\times10^{11}$ NBs/mL. When there was 0.2 mg ICG loaded, the NBs had a size of 239±98 nm and a concentration of $4.15\pm0.45\times10^{11}$ NBs/mL. When 0.3 mg ICG was added, the NBs had a size of 264±116 nm and a concentration of $3.80\pm0.37\times10^{11}$ NBs/mL. The DLS showed a consistent bubble size within all of the ICG concentrations.

Conclusions:
These findings show that addition of ICG did not impact NB stability under CEUS exposure and no large effects were noticed on bubble size and concentration.

Victor Xie is a Sam Miller Scholar

ABSTRACT #103
Role of IL-33 in inflammatory bowel disease-related fibrosis

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Background:
Inflammatory bowel disease (IBD) comprises a spectrum of disorders characterized by chronic inflammation of the gastrointestinal tract. Both ulcerative colitis (UC) and Crohn's disease (CD) fall under the "umbrella" of IBD, with an incidence of 1.3% of US adults (3 million). Many factors can contribute to IBD onset, including environmental factors, genetic predisposition, gut microbiota, and host immune response. IBD leads to chronic complications like colorectal cancer and fibrosis (as a reparative response to bowel injury or damage). The latter can cause bowel structuring and recurring bowel obstruction. Nowadays therapeutic armamentarium of IBD is limited, thus exploring the role of impactful molecules and proteins involved in the fibrosis process could lead to potential insights for additional new treatment options.

Goals:
The principal aim of the project is to elucidate fibrosis mechanisms in IBD. Particularly, my experiments have been focused on the role of IL-33 - an interleukin that is hypothesized to have a role in fibrogenesis - as a contributor to IBD fibrosis.

Materials and Methods:
Specific IBD mouse models have been used, namely AKR and SAMP mice populations. AKR mice are mice that aren't predisposed to inflammation, but have the same genetic background as SAMP mice, which are a product of selective inbreeding of the AKR/J strain that have a predisposition to Crohn's disease (CD)-like ileitis. Masson trichrome (tissue staining technique) has been performed to differentiate collagen tissue in AKR mice ilea. Quantitative real time PCR (rt-PCR) has been used to analyze expressions of genes involved in fibrogenesis in two populations of SAMP mice, treated or not with IL-33, K.O. (knock-out) or WT (wild-type) for SERPINE-1, a gene encoding for plasminogen activator inhibitor -1 (PAI-1), which also has been found significantly elevated in fibrotic tissue. More in detail, Masson trichrome has been used to identify levels of collagen in bowel tissue from AKR mice treated or not with IL-33 injections (according to already defined protocol). In order to extract samples of cDNA for rt-PCR, RNA extraction from the ileum of SAMP mice has been performed. Quiagen® protocol has been used for RNA extraction; NanoDrop has been used to measure A260/280 ratio and concentration; mini-gel was used to signify high quality RNA; cDNA obtained from reverse transcription of RNA was then used for rt-PCR.

Results:
When performing the Masson trichrome, we observed a slight difference (not significant) in amounts of collagen between tissue samples of the two differently treated AKR mice populations. Through rt-PCR (see graphs), we found that IL-33 treated population had a significant difference in expressing genes Col1a1 and Col3a1, as well as a slight difference in expression of Col1a2 compared to the untreated SAMP mice. IL-33injected mice showed very similar results in both K.O. and W.T. mice.

Conclusions:
IL-33 is an interleukin belonging to the IL-1 interleukin family with a role in fibrogenesis. Because of its ability to contribute to fibrosis as a consequence of inflammation, IL-33 has been hypothesized to play a pivotal role in initiating/perpetrating fibrosis in IBD. These inflammatory effects caused by IL-33 can also determine deregulation of the entire healing process that can eventually lead to anatomic complications such as stricturing. One of the reasons why we might have not observed a clear-cut difference in terms of ilea collagen expression between AKR mice treated and untreated with IL-33 might be related to the age of the mice, or the number of days the mice were stimulated with IL-33. However, in SAMP mice, it is clear that IL-33 influences expression of pro-fibrogenic genes in mice predisposed to ileitis.
Adam Yu is a Sam Miller Scholar

ABSTRACT #104
Employing 3D Choropleth Geospatial Maps to Evaluate Colorectal Cancer Incidence Rates

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Background:
Population-based cancer registry (PBCR) publications are a prominent and accurate source of data extensively referenced by the scientific community and public health departments to monitor cancer trends across time, detect cancer clusters, and identify cancer incidence/mortality disparities. However, PBCR reports commonly employ terminology difficult for the lay public and community partners to interpret. An enduring problem for health care providers and researchers is effectively communicating cancer risk and other PBCR-related statistics to local communities with the purpose of reducing health disparities and strengthening health policies. Common data visualization tools utilized by researchers include Excel, Tablaeu, Sisense, ArcGis, R, and SAS. The recent development of R graphical packages has harnessed this powerful language to create visually impactful plots of cancer statistics widely utilized by epidemiologists and other researchers. Despite the steep learning curve and lack of a graphical user interface (GUI) in R, this statistical software package enables researchers to easily document their code and conduct reproducible research—unlike other data visualization tools with GUIs such as Excel. Among the various cancers registered in PBCRs, colorectal cancer is one the most common causes of cancer morbidity in both men and in women. Colorectal cancer (CRC) is strongly influenced by sex, with mortality rates in males significantly higher than in females. However, the ratio of CRC incidence rates between males and females differs for different parts of the bowel and for different age groups; larger analyses conducted with consideration of CRC and sex may be necessary to further encourage preventative measures and specific screening.

Goals:
We aim to contrast the sex-specific CRC incidence rates across Ohio counties by employing choropleth geospatial mapping to determine statistically significant sex differences. Our secondary aim is to improve the graphical presentation of cancer incidence rates for the purpose of enhancing visualization and improve the dissemination of findings among community partners and the general public.

Materials and Methods:
We extracted data from the Ohio Department of Health and the United States Cancer Statistics (USCS). The data from the USCS included age-adjusted CRC incidence rates (per 100,000 people) in Ohio by county from 2014-2018. The data from the Ohio Department of Health included the age-adjusted CRC incidence rates in Ohio by county from 1996-2018, however, we restricted our analysis to only include CRC incidence rates from 2014-2018 in order to directly compare to data generated from the USCS. We used R (version 4.1.0) and Rstudio (version 1.4.1717) to manipulate and visualize the data. We used the R package 'rayshader' (version 0.24.10) to visualize the data in 3D.

Results:
The choropleth map generated within R was congruent with the choropleth map displayed by the United States Cancer Statistics' (USCS) interactive data visualization tool. Additionally, we were able to transform these choropleth maps into 3D, movable figures with R.

Conclusions:
3D visualizations in R should be used as a complementary tool to communicate PBCR publications, such as cancer incidence and mortality, to policy makers and local authorities. The method we used to generate 3D graphs in R could be implemented and built upon in the future to provide other researchers a convenient, reproducible, and visually impactful method of presenting data. In particular, these 3D visualizations could be incorporated into the Case Comprehensive Cancer Center website to better communicate with public partners.
Chelsea Zheng is a Sam Miller Scholar