

State of the School

November 6, 2024



**CASE WESTERN RESERVE
UNIVERSITY**
School of Medicine

Centers and Institutes

- 31 Centers for research and education, 18 presented today
- Collaborative innovative research and multi-PI grants, (P30s etc)
- Transdisciplinary, cross-institutional collaboration
- Education programs (UME, PhD, MS, UG, GME)
- Translational impact and new therapeutics
- Multi-Institutional support

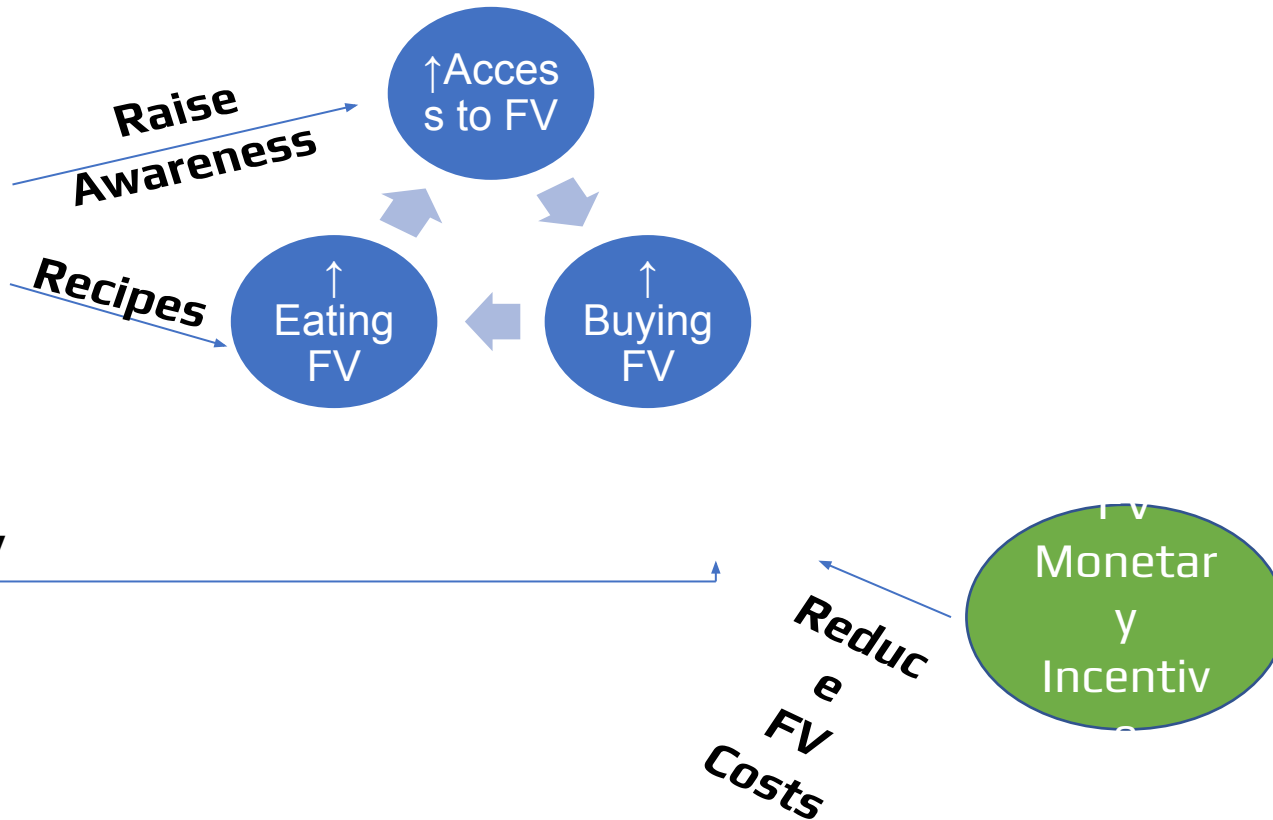
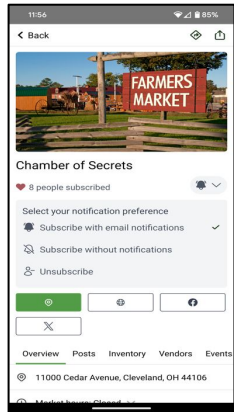
Community Engaged Research Centers



Leveraging Technology to Improve Community Nutrition



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Mary Ann Swetland Center for Environmental Health



Darcy Freedman,
Director

IMPACT:

Produce Path App connects people receiving SNAP to healthy, lower cost foods. Used for 10 years at Cuyahoga County farmers markets.

The app is used at **500 farmers markets nationally** and is the most widely used **data portal for impact of related federal policies**.

Co-Developing Strategies to Improve Health in Underserved Communities



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Prevention Research Center
for Healthy Neighborhoods



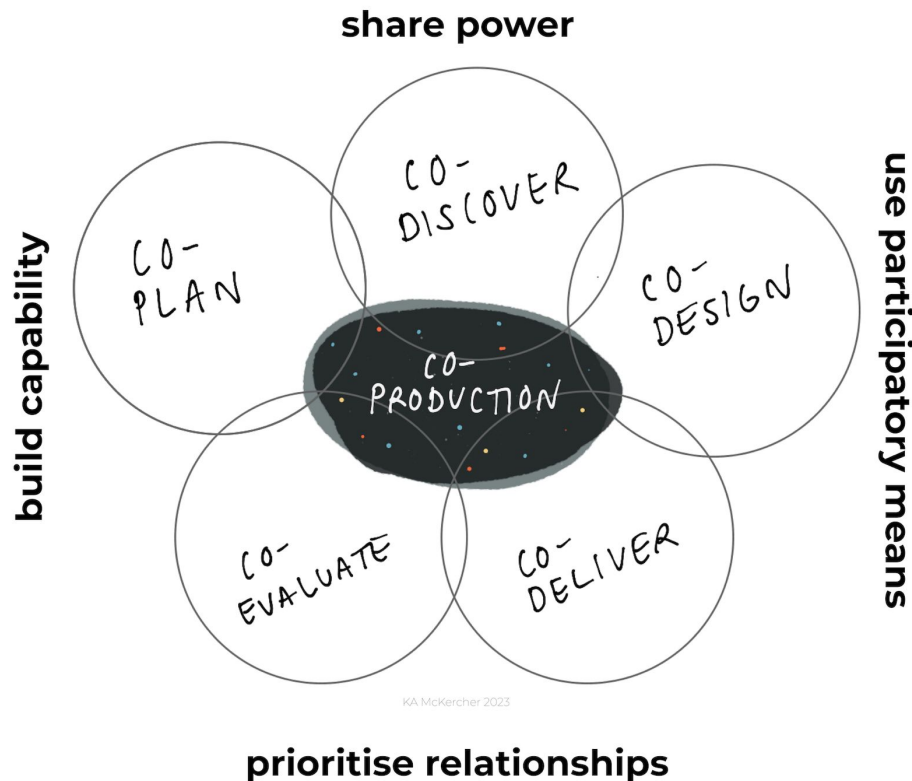
Erika Trapl, Director

IMPACT:

Novel approaches to support smoking cessation at the intersection of tobacco use and food insecurity.

Findings on flavored tobacco use have informed federal tobacco control policy.

Innovation in medically tailored groceries to mitigate food insecurity and improve birth outcomes among low-income pregnant individuals.

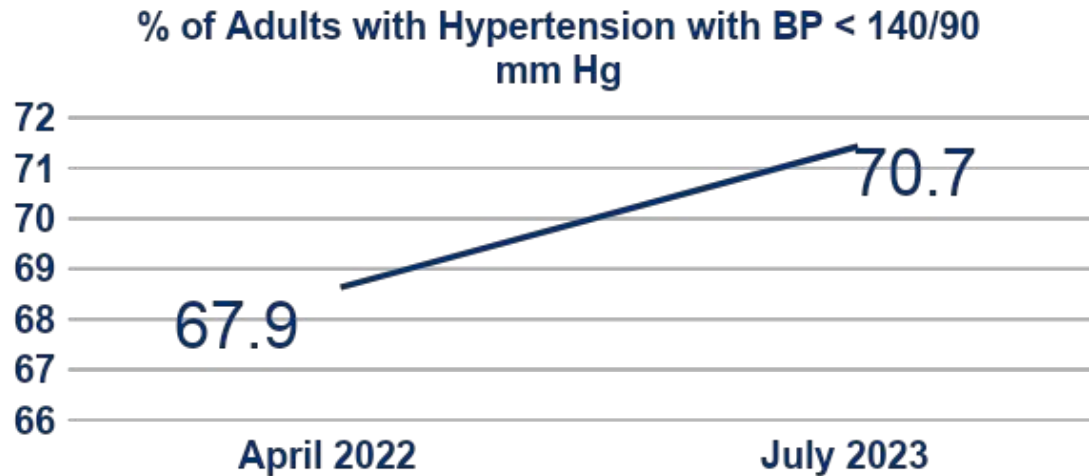


Our Approach

- CONNECT-Pantries: Leveraging Community-based food pantry settings for provision of tobacco cessation treatment.
- Nourish: an innovative approach to Type 1 Diabetes. A “food kills” Intervention for adults at risk for food and nutrition insecurity Diabetes Inspired Culinary Education (DICE).

Credit: <https://www.beyondstickynotes.com/what-is-codesign>

Reduction of HT in Ohio



Implementation strategies:

1. Monthly Quality Improvement (QI) Coaching
2. Quarterly webinars – peer to peer learning, didactic presentations by experts
3. EHR Data dashboard for continuous QI
4. Toolkits with evidence-based resources
5. Collaborations with payers and community



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School of Medicine
Center for Health Care
Research and Policy



**Shari Bolen,
Director**

IMPACT:

Established an expanded statewide primary care quality improvement collaborative infrastructure.

Improved blood pressure control across Ohio in over 100,000 adults.

Triple Drug Regimen Reduces Lymphatic Filariasis (LF) in Papua New Guinea



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School of Medicine
Center for Global Health & Disease



Adam Burgener
Director



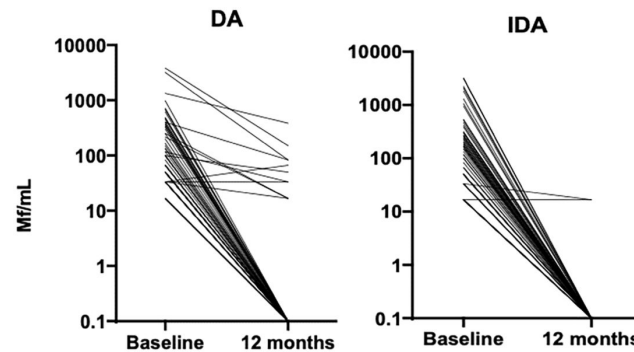
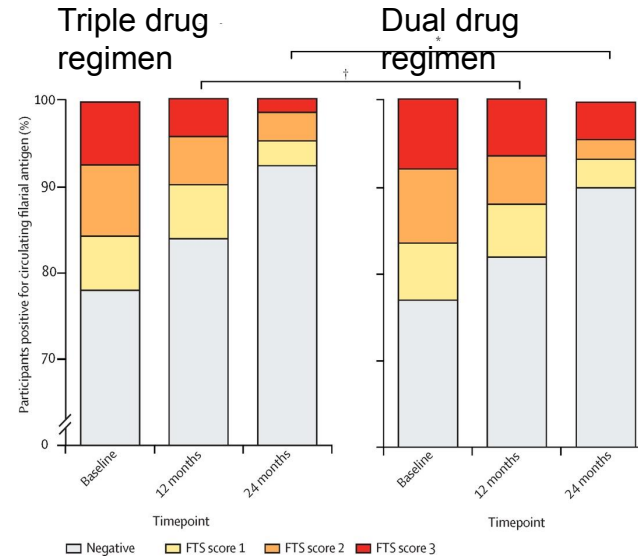
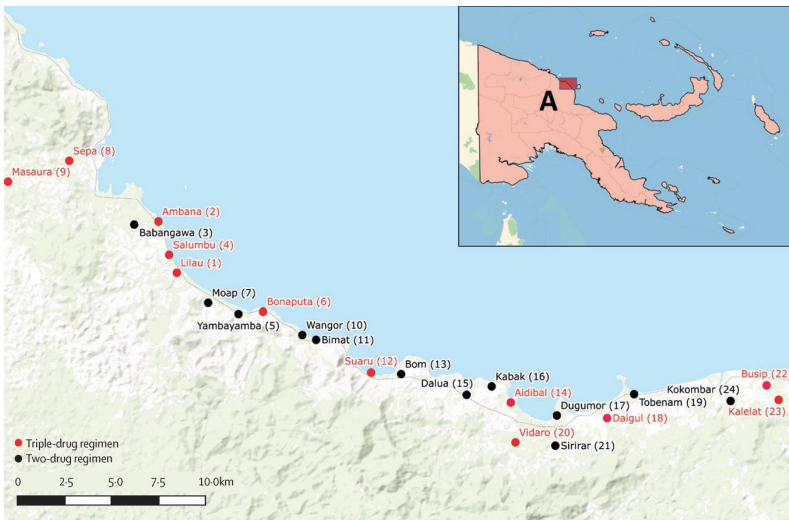
Chris King

IMPACT:
Mass administration of the triple-drug regimen was more effective in reducing microfilariae prevalence in communities to less than the target level of 1%, which support this approach to accelerate **elimination** of lymphatic filariasis.

THE LANCET
Infectious Diseases

Mass drug administration of ivermectin, diethylcarbamazine, plus albendazole compared with diethylcarbamazine plus albendazole for reduction of lymphatic filariasis endemicity in Papua New Guinea: a cluster-randomised trial

Moses Laman, Livingstone Tavul, Stephan Karl, Bethuel Kotty, Zebede Kerry, Stephen Kumai, Anna Samuel, Lina Lorry, Lincoln Timinao, S Cade Howard, Leo Makita, Lucy John, Sibauk Bieb, James Wangi, Jeffrey M Albert, Michael Payne, Gary J Weil, Daniel J Tisch, Catherine M Bjerum, Leanne J Robinson*, Christopher L King*



Clinical Based Research Centers

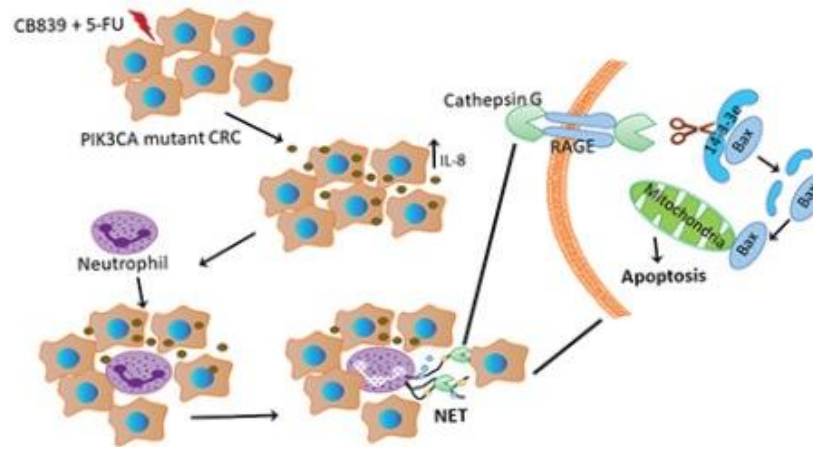
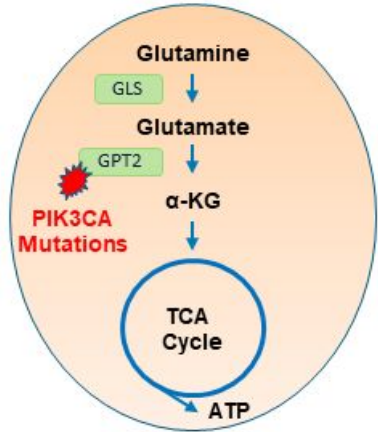


Chemo-Induced Neutrophil Extracellular Traps (NET) Kill Colorectal Cancer Cells

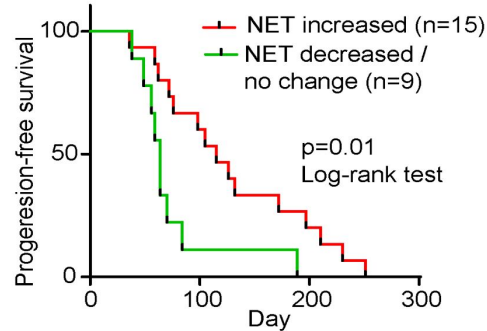
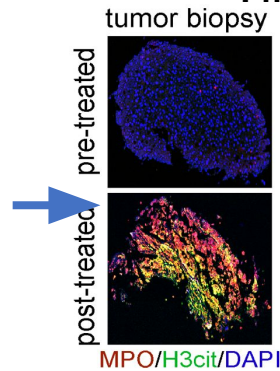


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Case Comprehensive Cancer Center

Mutation driven glutamine dependency



Phase II Clinical Trial



Gary Schwartz, Director



Wang (CGE)



Bajor (DT)



Markowitz (CGE)



Willis (CGE)



Selfridge (DT)



Dubyak (IO)



Hatzoglou (MO)



Conlon (CGE)



Khorana (DT)

IMPACT: Novel cancer cell killing by neutrophil extracellular traps (NET) which could represent a new therapeutic approach to treat CRC.

Community Health Research and Education Programs



Grace McComsey,
Director



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Clinical Translational
Science Collaborative



- Education
- Leadership training
- Collaborative Science
- Cross institutional
- ATLAS team science
- Informatics Tools
- (faculty and students)

CTSC Grant Number: UM1TR0045282023

2023 Annual Pilot Awards - \$233,631

2023 Core Utilization Pilot Awards - \$130,000

2024 Equity Diversity & Inclusion -\$196,853

2024 Public Health Pilot - \$50,000

2024 Voucher Awards - \$144,159

2024 Research Projects - \$292,522

RECOVER-long COVID (McComsey, Singer)

HEALing communities study (Konstan, Bolen) -combating opioid crisis

NCATS AIM-AHEAD program to train in utilizing informatics tools:
Dave Kaelber, Craig Jarrett

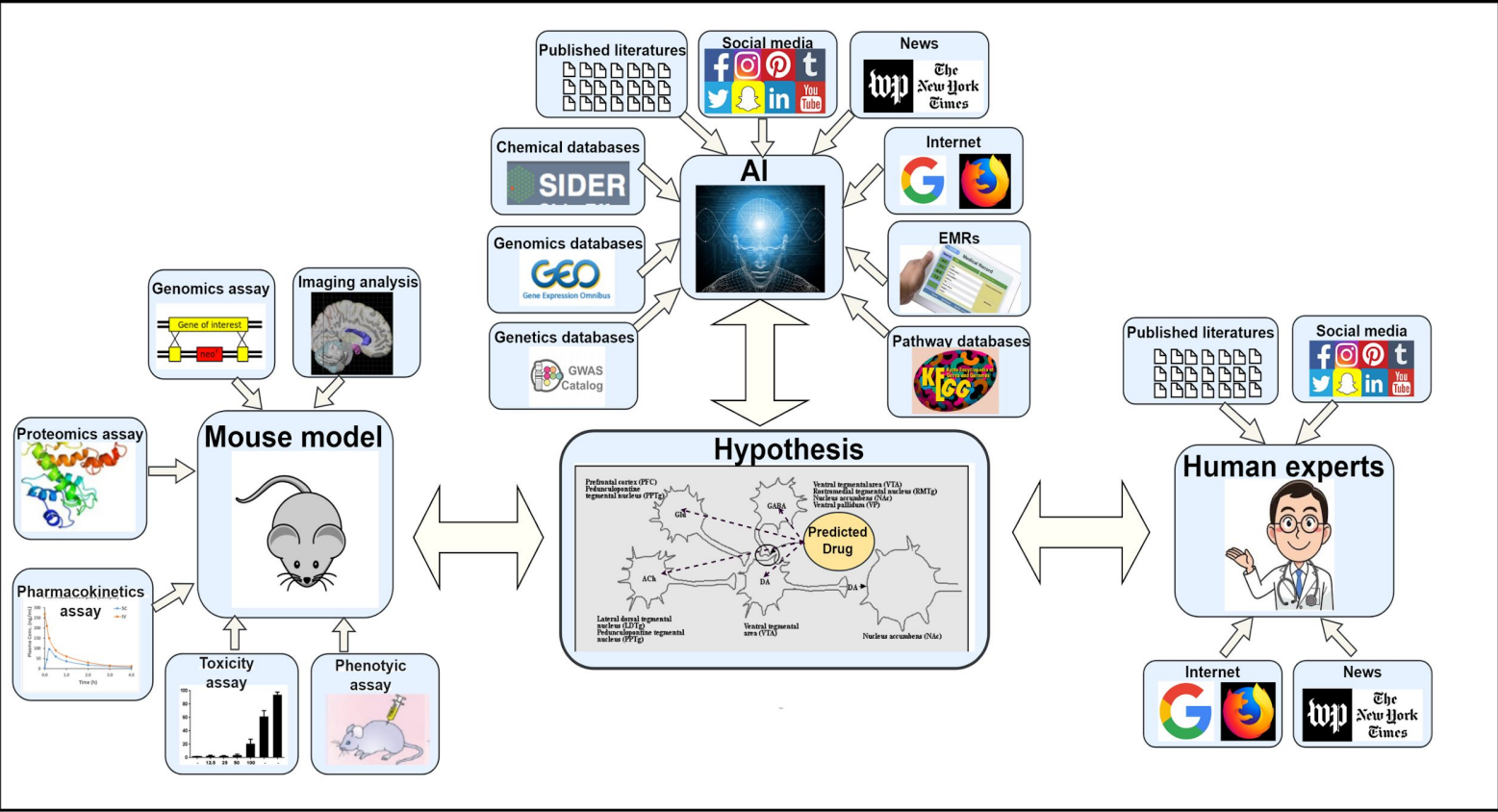
JAMA Oncol. 2024 Feb 1;10(2):256-258.

Lancet Diabetes Endocrinol. 2024 Aug;12(8):523-534

Circulation. 2024 Mar 26;149(13):993-1003



Knowledge-driven AI-Human-Animal Reinforcement Learning for Biomedical Discovery



Goals:

- Develop new systems of AI
- Improve Understanding of the pathogenesis of disease
- Design new therapies

- Health outcomes Research
- Collaborate to test the generated hypotheses



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 Center for AI in Drug Discovery



Rong Xu, Director

MISSION: To develop/apply AI to understanding and treating important diseases (e.g. Alzheimer’s disease, cancers, drug addiction).

IMPACT:

CDC Guideline: Studies from CAIDD on COVID-19 were included in CDC guidelines.

FDA & EMA (European Medicine Agency): CAIDD study of Ozempic, Wegovy, and suicide contributed to FDA and EMA drug label changes.

85 publications including *Nature Medicine*, *JAMA*, *JAMA Oncology*, *JAMA Pediatrics*, *World Psychiatry*, *Nature Communications*

CTN0153 (PI: Xu)(24-27)
 CTN0114 (PI: Xu): (21-24)
 CDC contract: \$ 200,000 (2024-2025)

RF1AG07664 (PIs: Xu & Davis): (22-25)
 AA029831 (PIs: Xu & Davis):(21-25)
 5T32CA094186 (PI: Xu) (23-28)

Innovation in Neurogenomics and Biomedical Health Informatics



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Cleveland Institute for Computational Biology

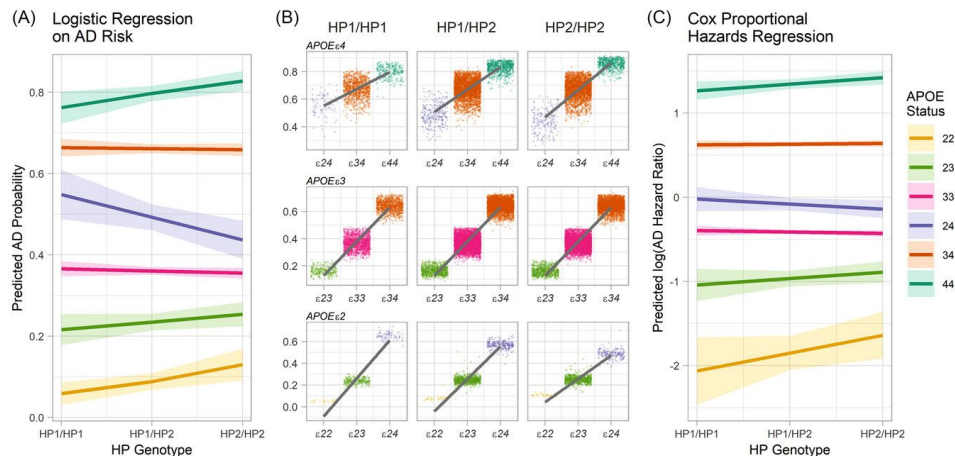
Illuminating genetic architecture of disease to advance precision medicine:

Examination of Genetic Risk Variability for Alzheimer Disease Across Genetic Ancestries across 10 countries (2023-2024)*

Will Bush, Scott Williams, Jonathan Haines

- Ascertainment of 4K African Americans, 4K Hispanics, 5K Africans
- Collect phenotype, whole genome sequence, biomarkers, SDOH
- Analysis of multiple data types for ancestry specific effects
- Increased risk of the APOE-e4 allele varies significantly by ancestry
- Expression of APOE varies by cell type and ancestry
- Gene expression profiles vary by ancestry
- Gene x gene interaction shows the risk of APOE alleles is attenuated by Haptoglobin alleles

Figure showing interaction of haptoglobin alleles and APOE alleles in Alzheimer disease



Creating clinician-driven computational phenotypes to inform critical and primary care:

Sepsis Pilot (2024)** - Biomedical Health Informatics

Jessica Goldstein, MD (CMO, UH Ahuja), Mark Beno

1.7 million annual sepsis cases in US accounting for 6% of all hospitalizations and 35% of hospital deaths

Computational phenotype algorithm run daily against Epic EHR patient data (structured and clinical notes) to find patients matching the CDC definition of sepsis – currently shared with hospital leadership and coding.



Jonathan Haines, Director

IMPACT:

Haines et al have identified novel genes for Alzheimers disease that lay the foundation for developing new and critically needed drugs.

****Biomedical Health Informatics:** UH Center to Improve Clinical Diagnosis, AHRQ R18HS029358 (2022-2026), \$4 million total costs, CWRU Schools of Medicine & Nursing & UH Family Medicine, Peds, Emergency Medicine.



***Neurogenomics:** AG072547, AG058654, AG070864, AG074865, AG058066, AG070935, AG084545

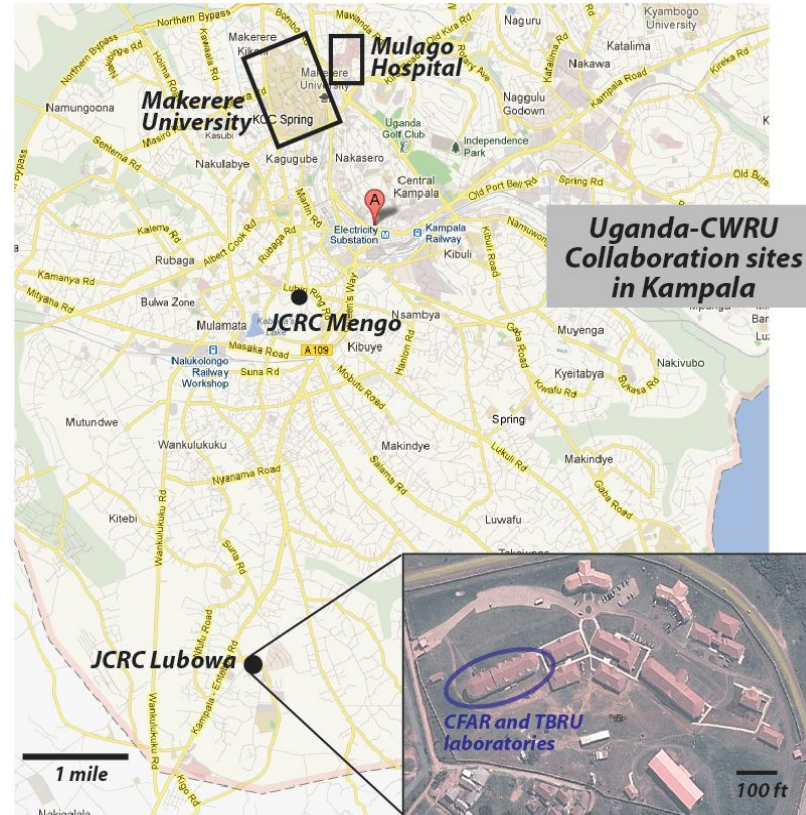
Rustbelt Center for AIDS Research – HIV Cure-related Initiative in Uganda



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Center for AIDS Research

- Transferred advanced digital PCR equipment and technology to CFAR Clinical Core to measure HIV reservoirs.
- CRDF Global Grant to Immaculate Nankya: “Interplay between Estrogen, immune activation and HIV persistence during pregnancy.”
- Developed a pipeline of new projects on HIV reservoirs:
 - Establishment in young (18 to 25 year) newly-infected people;
 - Dynamics in PWH with chronic viremia despite ART;
 - Impact of TB coinfections; and
 - Clade-specific differences in viral reactivation.



Jonathan Karn,
Director



Sharon Hillier
(Pitt)

IMPACT:

Intensive two-year experience providing start-up funds, pilot grant awards, salary support and mentoring in Uganda and through exchange visits to Rustbelt CFAR laboratories and cores.

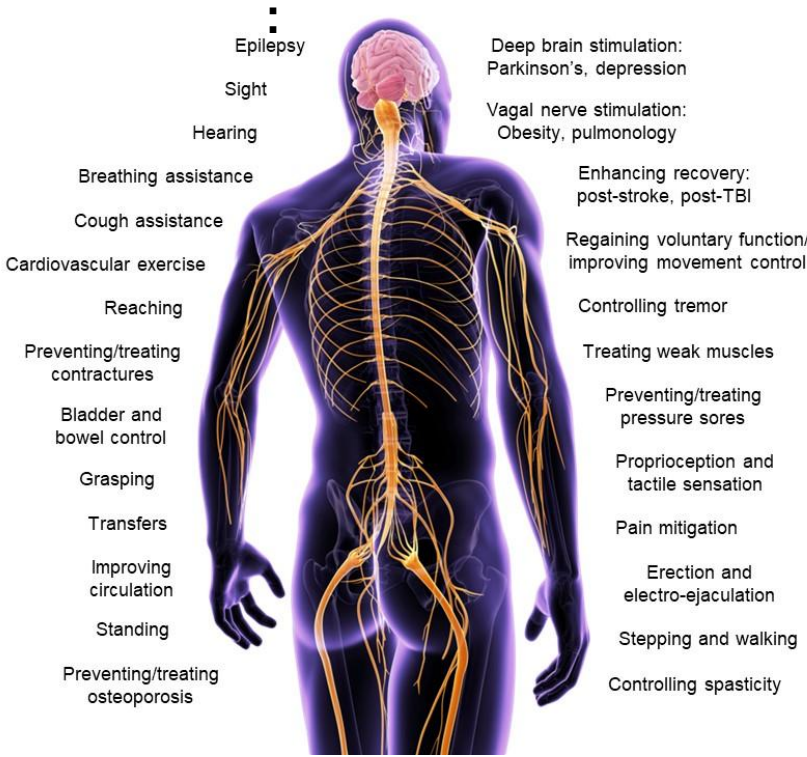
\$1.5 M/yr supplemental funding for Training initiatives in
Uganda and Puerto Rico

Bench Research Centers and Institutes



Center for Functional Electrical Stimulation (FES Center)

Applications



Research thrusts:

CLINICAL AND BASIC RESEARCH



Brain Health

Targeted activation of neural systems to replace or modulate brain structures



Pain Mitigation

The use of specific neuromodulation and neurostimulation regimens to treat pain



Movement Restoration

Coordinated activation of paralyzed muscles to improve motor functions

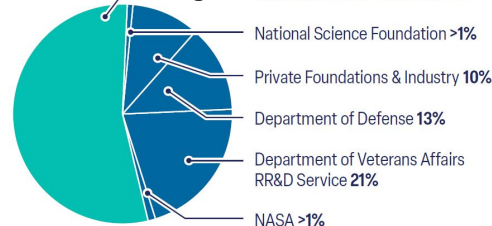


Autonomic Restoration

Modulation of autonomic systems to regulate internal body and visceral functions

Total funding:

To FES Center
 Investigators and for
 core funding



Robert Kirsch,
Director



Ronald Riechers,
Medical Director

IMPACT:

Develop interventions based on external modulation of nervous systems to replace or compensate for natural neural function lost due to neural disease or injury.

Advancing Medicine through Imaging Science



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Center for Imaging Research



Agata Exner,
Director

IMPACT:



Lower-Cost, Better Access



Reducing Invasive Procedures



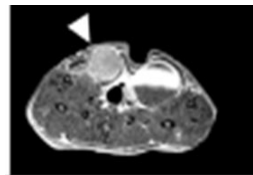
Eliminating Unnecessary Treatment



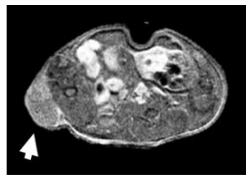
Improving Accuracy of Diagnosis



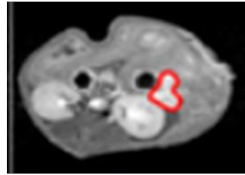
Targeting disease through image-guided therapies



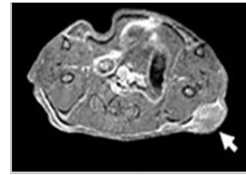
Breast cancer



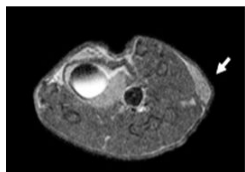
Head & neck cancer



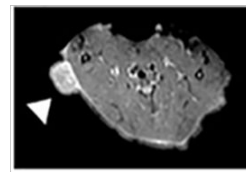
Pancreatic cancer



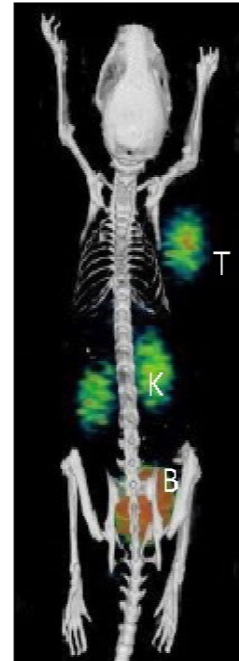
Colorectal cancer



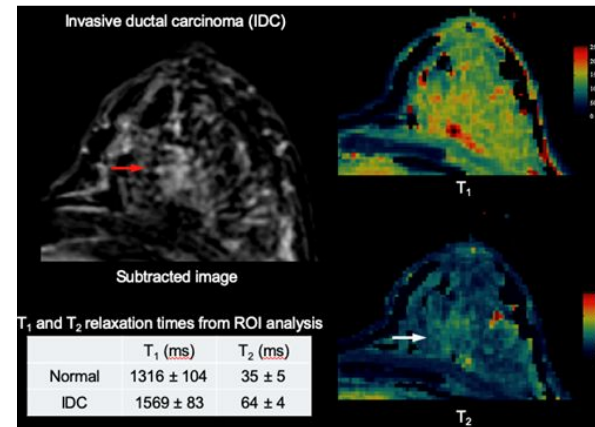
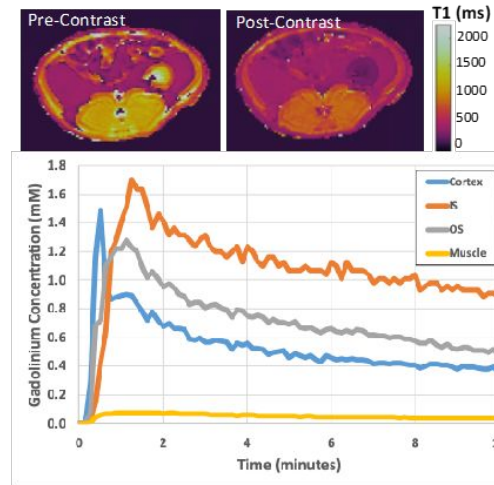
Lung cancer



Prostate cancer



ZD2 peptide PET probe



*grants awarded as PI, MPI, co-PI; grants enabled as co-I & collaborator

\$51.9
Million across 21 grants awarded* in FY23-24

\$17.5
Million across 4 grants enabled* in FY23

20
Issued Patents in calendar year 2023

Wilson, JACC: Advances (2024) IF 21.7
Ma & Badve, Investigative Radiology 59 (2024) IF 6.2
Li, Medical Image Analysis 97 (2024) IF 10.9
Exner, Bioactive Materials 35 (2024) IF 18.9

14 R01s
1 NSF
R21/43/44/56

U01EY034693
SPARC 75N98022C00018
JobsOhio and others

Affiliated Cores: Imaging Research Core, Light Microscopy Imaging Core
Affiliated Centers: Case CCC, AID2B, CCF Mellen Center, Interactive Commons

The structural basis of NINJ1-mediated plasma membrane rupture in lytic cell death



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Cleveland Center for Membrane
and Structural Biology



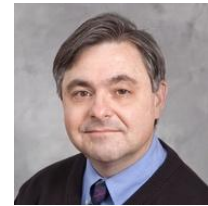
Sudha Chakrapani, Director



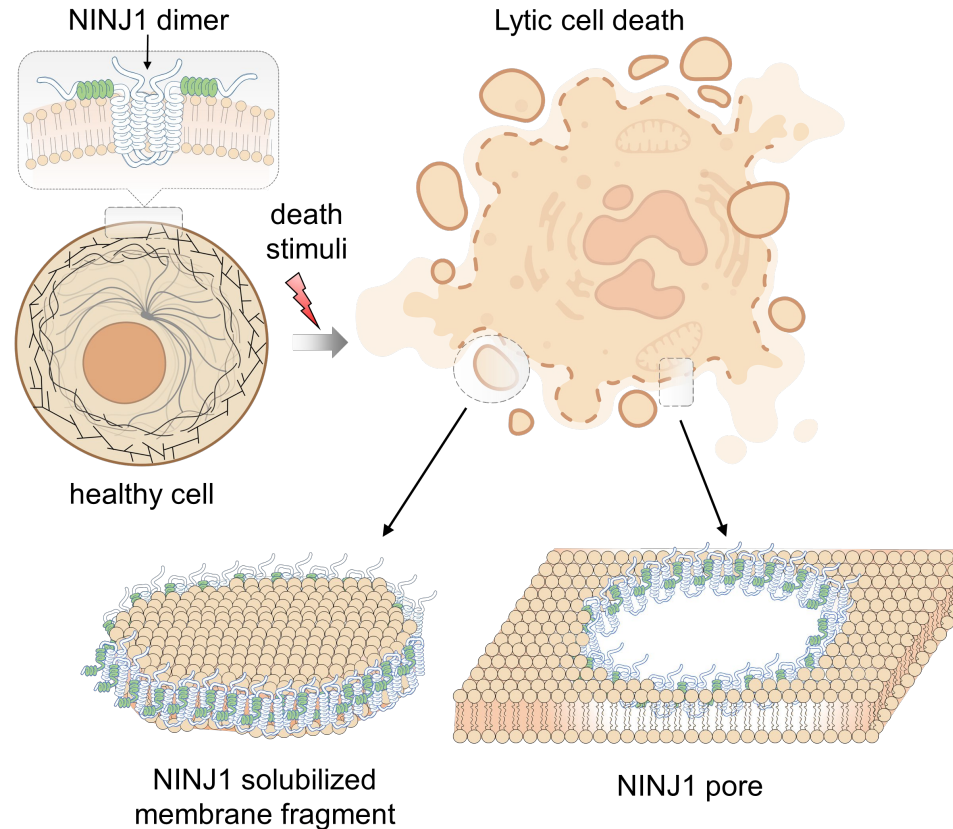
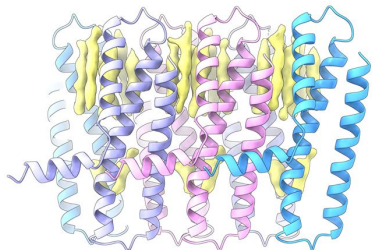
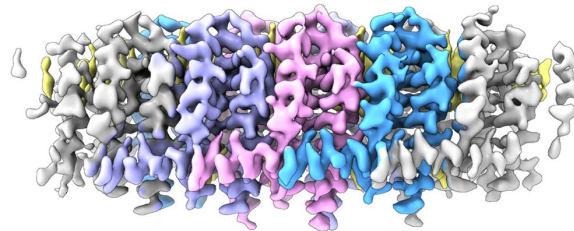
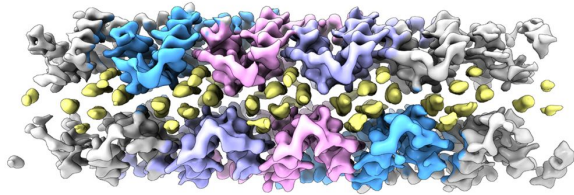
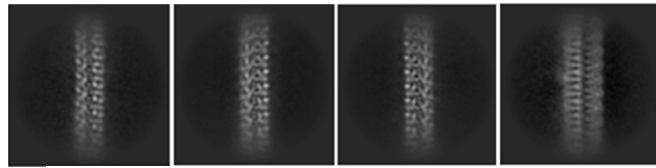
Bibekananda
Sahoo



Xinghong
Dai



George
Dubyak



IMPACT:
Mechanistic understanding of the last
step in lytic cell death.

Point to new directions of therapeutic
development against sepsis and many
inflammatory diseases.

Advancing Research for Children's Health and Conditions such as Cystic Fibrosis

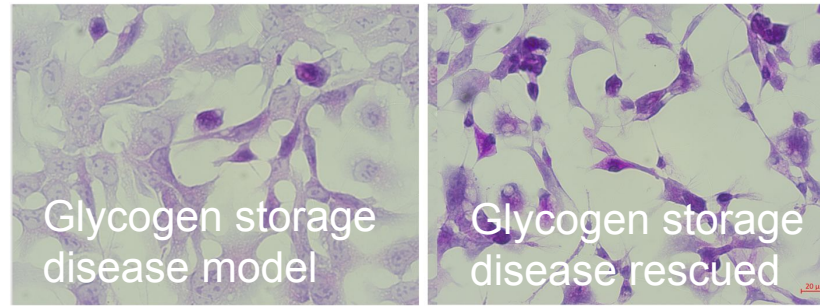


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Research Institute
for Children's Health



Mitchell Drumm,
Director



Science
GENE EDITING

Landmark Cystic Fibrosis Research

In vivo editing of lung stem cells for durable gene correction in mice

Yehui Sun^{1†}, Sumanta Chatterjee^{1†}, Xizhen Lian¹, Zachary Traylor², Sandhya R. Sattiraju³, Yufen Xiao¹, Sean A. Dilliard¹, Yun-Chieh Sung¹, Minjeong Kim¹, Sang M. Lee¹, Stephen Moore¹, Xu Wang¹, Di Zhang¹, Shiyong Wu¹, Pratima Basak¹, Jialu Wang³, Jing Liu³, Rachel J. Mann², David F. LePage², Weihong Jiang², Shadaan Abid⁴, Mirko Hennig³, Anna Martinez³, Brandon A. Wustman³, David J. Lockhart³, Raksha Jain⁴, Ronald A. Conlon², Mitchell L. Drumm², Craig A. Hodges², Daniel J. Siegart^{1*}

IMPACT:

~\$3.5 million raised since 2015.
Investments of those funds have
contributed to > \$30 million in grants.

Promising genetic research in mice
holds potential for future Cystic Fibrosis

\$32,661,904 DC in CF-related grant support 2019-2024
CF RDP (infrastructure grant), \$700K annual direct costs
CF Mouse Resource Center, \$1M annual direct costs

>\$400K in industry contracts since 2021
>30 CF-related manuscripts from 2022-2024

Core services for CF research

Histology, pathology and microscopy
Common cell culture facilities

Multifaceted Approaches to Developing Mitochondria-Targeted Therapies for Neurological Disorders

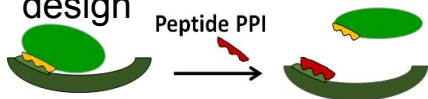


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Center for Mitochondria Research and Therapeutics

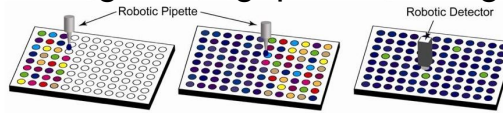
Therapeutic Discovery

Biologic peptides design



Peptide PPI

High throughput screening



1. Dispense Library 2. Dispense Target/Reagent 3. Assay Readout

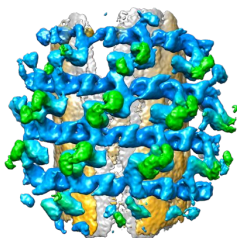
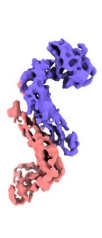


Mitochondrial enhancer development



Therapeutic candidates

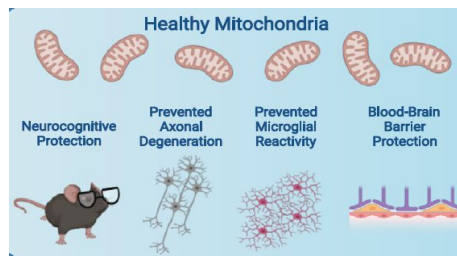
Structural & Functional Studies



Structure defines function

Mechanistic insight

Translational science



Novel therapy for neurodegenerative diseases



Xin Qi, Director



Jason Mears, Director

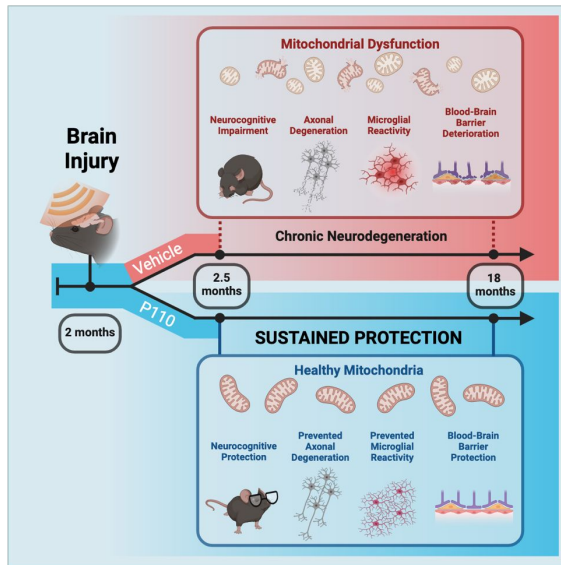
IMPACT:

Mitochondrial impairment in neurological disorders represents a key factor in disease progression, offering a target for innovative therapeutic approaches to improve patient health.

Discovery Led Therapeutics



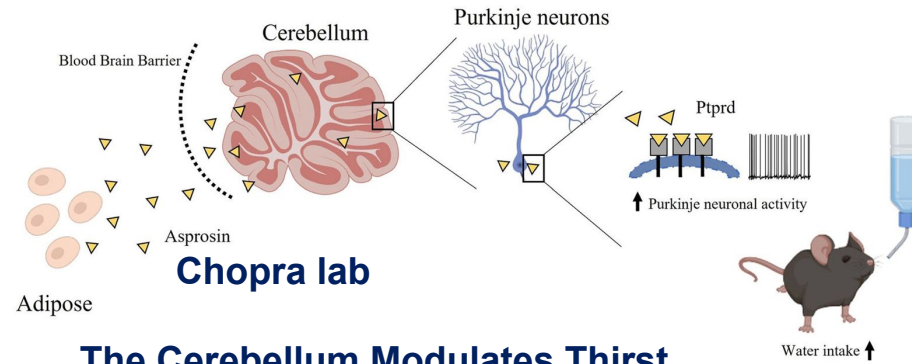
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Pieper lab

Acutely blocking excessive mitochondrial fission prevents chronic neurodegeneration after traumatic brain injury.

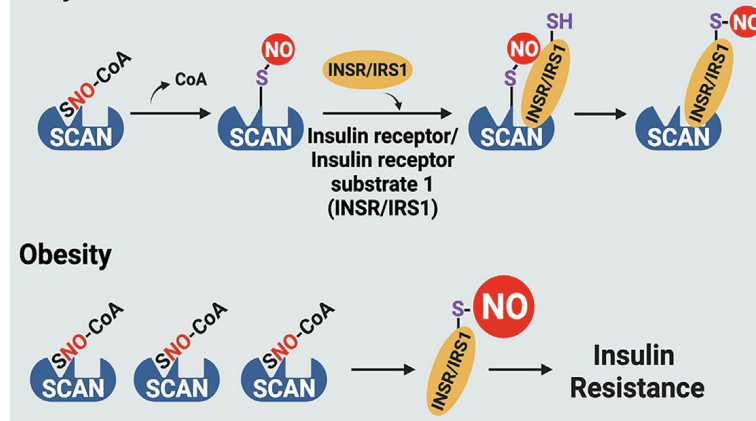
Sridharan et al., 2024,
Cell Reports Medicine **5**, 101715
10.1016/j.xcrm.2024.10171509



The Cerebellum Modulates Thirst

Mishra et al., 2024, *Nature Neuroscience* **9**, 1745-1757
10.1038/s41593-024-01700-9

Enzyme mechanism



Stamler lab

An enzyme that selectively S-nitrosylates proteins to regulate insulin signaling.

Stamler Lab: Zhou et al., 2023, *Cell* **186**, 1–14, 10.1016/j.cell.2023.11.009.
R01 DK137973, R01 DK119506, R01 DK137973, R01 DK128347, P01 HL158507,
R01 HL126900, AHA 19PABH134580006

Institute for Transformative Molecular Medicine



Jonathan Stamler,
Director



Atul
Chopra



Andrew
Pieper

IMPACT:

Physician-scientist faculty with translational interests provide academic leadership for the Harrington program to accelerate discoveries to medicines.

The Harrington track record includes 39 companies, 21 clinical trials, 15 licenses to pharma. All local faculty have started new companies to advance discovery.

Shared Resources:

CCMSB CryoEM Core (NIH 1S10OD032437)
Core Facility for Advanced Research Computing

Pieper Lab: Sridharan et al., 2024,
Cell Reports Medicine **5**, 101715
10.1016/j.xcrm.2024.10171509

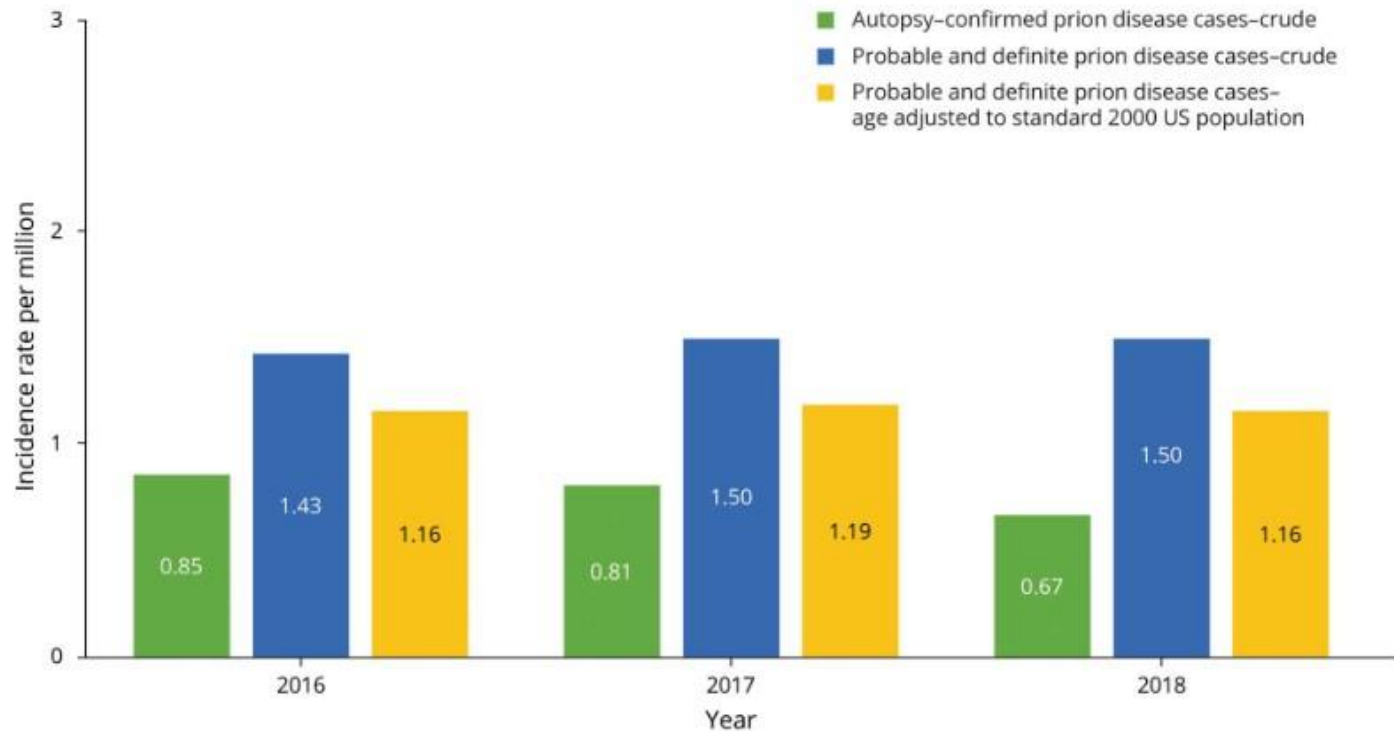
Monitoring Prion related neurodegeneration in the US



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School of Medicine
National Prion Disease Pathology Surveillance Center

Prion Disease in the United States

Figure 2 Comparison of annual incidence rates of prion disease in the United States as determined by neuropathology only vs including probable cases of prion disease as detected by positive CSF RT-QuIC results



RT-QuIC = real-time quaking-induced conversion.



Brian Appleby,
Director

IMPACT:

Providing laboratory-based surveillance of human prion diseases.

Guiding and participating in clinical trials for human prion diseases.



Lia Logio, Director

IMPACT:

EPIC Training (Lyceum)

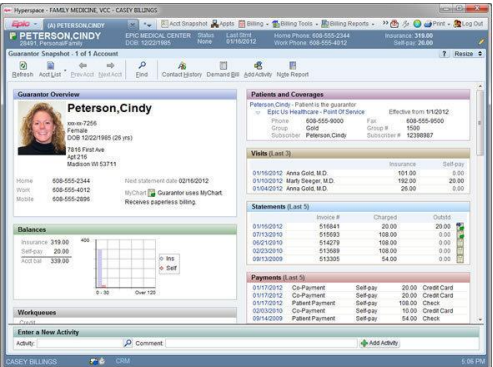
Students learning EMR = readiness

Generative AI as Curricular Partner

Faculty and students using new tools for learning = modeling life-long learning

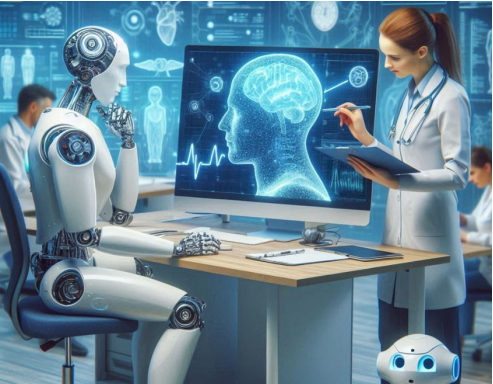
Geriatrics Education

Preparing for the gray tsunami



EPIC Training (Lyceum)

- Smoking cessation
- Changing pronouns
- Medication reconciliation
- Documenting vital signs



Generative AI as Curricular Partner

- Map learning objectives
- Identify gaps
- Create board-like questions that link to curriculum



Senior Advisors in Geriatrics Education

Relationship based learning about

- 4Ms of Age-friendly healthcare
- Health systems science
- Early role as doctor, advocate

