FACILITIES AND OTHER RESOURCES

The goal of the Clinical and Translational Science Collaborative is to provide full service integrated clinical & translational research capabilities within the Cleveland community that will improve the health of patients in Northeast Ohio through patient-based research. The CTSC also provides career development support, clinical research navigation, and research participant resources. The coordination of existing resources encompasses CWRU, Cleveland Clinic (CC), MetroHealth (MH), University Hospitals (UH), and the Louis Stokes Cleveland Veteran's Affairs Medical Center (VA). The resources of all five institutions are fully available to the CTSC and provide the necessary environment to fulfill the goals of the CTSC.

Case Western Reserve University

CWRU was founded in 1826 and connected with the CWRU School of Medicine, which was established in 1843. The medical school is the largest biomedical research center in Ohio, with affiliations to UH, CC, MH, and the VA. The campus includes the Case School of Engineering, College of Arts and Sciences, Frances Payne Bolton School of Nursing, Mandel School of Applied Social Sciences, School of Dental Medicine, School of Law, School of Medicine, and Weatherhead School of Management. It enrolls roughly 5,000 undergraduate students and 6,000 graduate and professional students annually from all 50 states and over 90 countries. There are about 3,200 faculty members and 3,100 staff members.

The Breadth and Depth of Research

CWRU is rated the top research university in Ohio and receives in excess of $500,000,000 in external awards yearly. The following table shows the research funding attributable to the major CWRU schools and hospital affiliates (excluding the VA) that participate in the CTSC.

Research Funding to CTSC partners. Data include SOM, SON, SODM, BME Dept, UHMC, Metro and CC

Fiscal Year	Total Research	Federal	NIH	Other Govt	Industry	Foundations
2012	386,174,199	42,614,957	268,366,734	14,085,755	12,697,031	48,409,722
2013	366,456,388	34,664,588	269,815,348	2,145,291	11,441,871	48,389,290
2014	378,235,604	34,096,033	267,661,833	8,159,360	14,166,052	54,152,327
2015	363,842,027	37,640,558	260,357,758	519,611	13,292,171	52,031,929
2016	390,212,090	34,549,132	278,954,801	2,523,513	15,113,940	59,070,703
Totals	**1,884,920,307**	**183,565,268**	**1,345,156,472**	**27,433,530**	**66,711,066**	**262,053,971**

CWRU School of Medicine (SOM)

The **CWRU School of Medicine** is the leading medical research and training institution in Ohio, ranking 25th among 140 U.S. medical schools in research (USNWR, 2017) and 17th in NIH funding (when SOM and CCLCM-CWRU are combined). The full-time faculty of the SOM number 2,824 and consist of basic and clinical/translational researchers and physicians based at the SOM and the 4 clinical partner institutions. CWRU SOM is the home for many NIH, CDC, and foundation supported research centers, including the Case Comprehensive Cancer Center, Center for AIDS Research, Prevention Research Center for Healthy Neighborhoods, Cleveland Digestive Diseases Research Core Center, GI Cancer SPORE, BETRnet for upper GI cancer, Visual Sciences Research Center, Skin Diseases Research Center, National Center for Regenerative Medicine, and the Cystic Fibrosis Therapeutics Development Center, among others. National leadership in clinical trials is documented in the overall section. Although the programmatic and administrative functions of these Centers are based at the SOM, subject participation occurs within the clinical and clinical research facilities of the four clinical partner institutions, including their expansive community sites throughout northeast Ohio. Many technology and support cores at the SOM provide services to our basic, translational, and clinical research programs throughout the city. The Institute for Computational Biology (ICB), jointly supported by CWRU, CC and UH, is housed at the SOM, and directed by CTSC Informatics lead Dr. Haines. The ICB designed and manages the centralized databases used to support C/T research for the CTSC. In addition to Dr. Haines, other CTSC leadership based at the SOM include Drs. Borawski and Stange (Community and Collaboration), Dr. Chance (Translational Endeavors Lead and Associate-PI), as well as Drs. Konstan (PI) and Davis (Associate-PI). CWRU SOM training programs for MD students include a large MSTP and CTSTP program, 160 students through the CCLCM who spend an additional year in research, and many students who obtain the MS or MPH in addition to the MD degree (anatomy, bioethics, clinical research are most popular), over 1000 graduate students (MS and

PhD), as well as longstanding pipeline programs for undergraduates from underrepresented minority groups. The SOM stands among the top 10% of US medical schools in graduating African American physicians, and among the top 15% for contributing medical school faculty. The School of Medicine has 536,447 square feet of research space including the Biomedical Research Building, the Wood Medical School Building, and the Wolstein Research Building.

The **Department of Biomedical Engineering's** top-ranked research program is innovating new approaches to core-health issues and debilitating disease. The department spans both the Case School of Engineering and the School of Medicine, and leverages partnerships with other leading medical research organizations, including Cleveland Clinic, University Hospitals and Louis Stokes Cleveland VA Medical Center and major academic centers across the globe. This collaborative environment fosters natural research collaborations between fundamental scientists, engineers and clinical practitioners. The department is home to 27 primary faculty, more than 70 secondary and adjunct faculty, nearly 500 students in the BS program, and 150 students in the graduate program that comprise the dynamic and comprehensive Department of Biomedical Engineering at Case Western Reserve University. The BME department was founded in 1968 as one of the first in the world. It pioneered rigorous BS, MS, and Ph.D. educational programs that have long served a wide range of career aspirations and prepared our graduates to be leaders in academia, industry, and medicine . The department continues to lead BME curricular innovation, and provide cutting edge research opportunities and hands-on industrial/translational research experiences. The Case BME department has added its unique quantitative and technical skills to this amazingly rich environment to forge innumerable l research collaborations and cross-disciplinary centers that have made its faculty national research thought leaders in biomedical imaging and analytics, biomaterials, neural engineering, metabolic systems, and biosensors. These techniques are applied to many clinical challenges, including cancer, cardiovascular and metabolic diseases, neurological disorders, and musculoskeletal disorders. The BME faculty and students are entrepreneurial, as illustrated by the Case-Coulter Translational Research Partnership and several educational programs focused on translational research and commercialization.

Case School of Engineering

The Case School of Engineering is nationally ranked as one of the top engineering schools with a 125-year history of excellence. The School offers through seven departments: 14 undergraduate degree programs, 14 Master of Science degrees and their related Doctor of Philosophy degrees, as well as the Master of Engineering and Master of Engineering and Management degrees. Case is the best small private university for engineers "plus"-those whose interests and abilities allow them to excel beyond engineering. Dual majors in the humanities, joint degrees in management and medicine, and laboratories shared with world class institutions like the Cleveland Institute of Art and NASA Glenn Research Center let Case engineers go as far as their imaginations will take them.

Case Comprehensive Cancer Center

The Case Comprehensive Cancer Center (Case CCC) is one of only 41 National Cancer Institute-designated Comprehensive Cancer Centers in the country. The Case CCC integrates the cancer research activities of the largest medical collaborative in Ohio, Case Western Reserve University (CWRU), University Hospitals (UH) and Cleveland Clinic (CC) - under a single leadership structure. Our researchers dedicate themselves to improving cancer outcomes through basic studies into signaling pathways giving rise to cancer and its generic and epigenetic causes, pursuing novel therapeutic targets, and analyzing lifestyle interventions to prevent cancer and detect it earlier.

The Case CCC has over 360 collaborating scientists and physicians who have successfully competed for over $119 million in annual funding. These investigators are organized into eight interdisciplinary scientific programs and have access to 15 Scientific Core Facilities. A unified clinical research effort consisting of 12 multidisciplinary clinical disease teams develop and prioritize clinical trials among the partner institutions.

The Case CCC serves a population in Northeast Ohio with higher than average cancer rates. Research programs extend to CWRU affiliates MetroHealth (the region's safety-net hospital) and Louis Stokes Veterans Affairs Hospital and to 13 community medical centers operated by University Hospitals and Cleveland Clinic.

As a consortium cancer center, Case CCC has become a powerful example of the potential generated by complementary institutions coming together for the benefit of research and discovery, patient treatments and community impact. Through its partners, Cancer Center programs extend throughout Northeast Ohio to offer residents access to cancer care through participation in community outreach, cancer prevention, cancer

survivorship initiatives and a robust clinical trials operational effort coordinated across academic medical centers and community sites.

National Center for Regenerative Medicine
The National Center for Regenerative Medicine (NCRM) is a platform to facilitate translational research, clinical application, and commercialization of regenerative medicine, tissue engineering, and stem cell therapeutics across a consortium of institutions. NCRM is driven by four nationally ranked, medical research powerhouses, Case Western Reserve University, Cleveland Clinic, University Hospitals, and the Ohio State University. Through this network of researchers and clinicians, research discoveries are actively being translated into cell-based therapies for patient care.

NCRM is leading the way in Northeast Ohio in the following areas:

- Regenerative medicine and stem cell research
- Cellular manufacturing
- Clinical trials for cellular therapeutics

Global partnerships have been established with academic institutions and biotechnology companies to further expand research and discovery efforts.

NCRM goals include:

Translational Research: To support stem cell and regenerative medicine research across various disciplines, institutions and commercial entities.

Education and Training: To develop cutting-edge education programs for researchers, clinicians, trainees and the general public.

Strategic Partnership: To build networks across academic, clinical, commercial and public sectors.

Commercialization: To translate innovative technologies and cell-therapies into business opportunities.

Frances Payne Bolton School of Nursing
The Frances Payne Bolton (FPB) School of Nursing at Case Western Reserve University has earned a reputation as an innovator in nursing education, research and leadership. Taking an experimental approach to education was one of the key conditions of Congresswoman Frances Payne Bolton's 1923 gift of $500,000 to endow the school - the largest ever at the time for a university school of nursing.

The FPB School of Nursing at Case Western Reserve University provides leadership in innovative research, education, and practice to promote health and reduce the burden of disease. Dedicated to interdisciplinary scholarship, FPB SON is committed to the pursuit of excellence in service to local and global communities. The Frances Payne Bolton School of Nursing is a globally recognized leader in nursing education and research, and produces confident, dynamic health care professionals. The spirit of innovative collaboration has remained one of the hallmarks of Frances Payne Bolton School of Nursing, and FPB is at the forefront of discovery.

Aging across the lifespan research focuses on maintaining and improving health, functional status and quality of life. Emphasis is on successful aging, even in the face of morbidity and frailty. Utilizing an interdisciplinary perspective, FPB SON programs of research encompass a range of bio-psychosocial approaches, including psychological, cognitive, behavioral, physiological, genetic, sociological, and emerging, integrated models. Research models include racial, ethnic, gender, socio-demographic, and inter-generational influences. Aging research spans descriptive to intervention work and qualitative and quantitative methods.

School of Dental Medicine
The School of Dental Medicine at Case Western Reserve University was founded in 1892 as the Dental Department of Western Reserve University. The school has undergone many changes through the years, but since 1969 the facilities of the school of Dental Medicine have been located on and highly integrated into the Health Science Campus of Case Western Reserve University, adjacent to the schools of medicine and nursing and University Hospitals. Students select the school because of its reputation for excellence, first class pre-doctoral and post-doctoral dental educational programs that include the school’s preceptor model of clinical instruction, and strong commitment to patient care, research, collaboration, interprofessional education and community service. Upon admission, students are presented with a rigorous and fulfilling educational experience that features strong clinical experiences, an evolving and dynamic Relevant Experiential Active Learning (REAL)

Curriculum, state-of-the-art dental simulation clinics, extensive community service components, and opportunities to specialize in various post-doctoral programs, all delivered by highly skilled faculty and staff.

Mandel School of Applied Social Sciences
The Mandel School of Applied Social Sciences was founded by and for the Greater Cleveland community in the belief that a university-based school of social work would transform the work of people and organizations to achieve to their full potential. Its graduates are prepared to be future leaders who turn knowledge into action that furthers health, well- being, and social justice. The school is ranked #9 in the nation and #1 in Ohio for top Graduate Social Work Schools by U.S. News & World Report. The Best Schools also ranked the Mandel School #8 among social work programs. The School has partnerships with community agencies and field sites in Cleveland and around the U.S. The School receives over $9 Million in research and training grant awards.

Institute for Computational Biology
The Institute for Computational Biology (ICB) is a joint venture between CWRU, CC, and UH, led by genetic epidemiologist Jonathan Haines, PhD. This infrastructure of shared resources provides specialized biostatistics expertise to efficiently analyze vast amounts of clinical data. Established in 2013, ICB facilitates high-level analytic and computational methods across the intersection of computational, biomedical, and translational research. It has developed a successful process for translating patient information across health systems and electronic health records.

ICB uses **CLEARPATH (The Cleveland Area Research Platform for Advancing Translational Health),** a data warehouse that represents a centralized, limited data set that aggregates and normalize EHR data, various disease registry databases, and biobank databases from the multiple contributing health systems. CLEARPATH utilizes a novel, federated, de-identified and hashed technology to provide patient de-duplication capabilities across all the contributing health systems. Unlike other centralized, de-identified or limited data-set research data warehouses, this technical innovation allows for CLEARPATH to merge patient health records for a single person across multiple health systems to a high degree of certainty offering a true patient-centered record. This provides a substantial advantage over other research data warehouses that are unable to perform patient de-duplication across their contributing member-base. Researchers are able to utilize several enterprise platform capabilities for patient cohort identification across the aggregate data. For studies with IRB approval, CLEARPATH supports utilizing an honest broker process to take the researcher's identified patient cohort, perform a re-identification process, and then migrate the patient records into the OnCore and Labmatrix systems to support on-going research data collection and analysis.

High Throughput Sequencing Core Facility/Case Genomics Core
The Department of Genetics and Genome Science and the CASE Comprehensive Cancer Center operate a High-Throughput DNA Sequencing Facility that offers Illumina Next-Generation Sequencing (NGS) services to the entire Cleveland research community. This technology has broad application across many fields including re-sequencing to discover novel variants in human genetic studies, de novo sequencing of pathogens, quantitative gene expression and identification of the distribution of histone modification patterns, clinical panel screening and binding of transcription factors along the genome. Customized genotyping and methylation solutions allow researchers to optimize the number of loci per sample and throughput level to best suit their study goals using either the BeadArray or Veracode technology. Large-scale genome-wide SNP association studies are performed using Illumina's Infinium assays which can be run on the iScan module. The mission of the Core is to provide better data at a reduced cost and turn-around time to the research community.

Center for Proteomics and Bioinformatics (CPB)
The Center for Proteomics and Bioinformatics is fully available to CTSC investigators. This core is comprised of 9000 sq. feet of laser, spectroscopy, spectrometry, cell culture, and biochemistry laboratory space on the 9th floor of the BRB Building. The core is equipped with laboratory benches, cabinetry, central air, gas and vacuum hook-ups, as well as internet connections. This core is equipped with protein electrophoresis apparatus, refrigerators, freezer, analytical balances, pH meter, micropipets, glassware, pipettes, and -70□C freezers. In addition, the applicant has access to the departmental dark room, a walk-in cold room, a cell culture room, preparative ultracentrifuges, and HPLC and FPLC chromatography apparatus.

Case Center for Imaging Research
The Imaging Research Core is housed within the Case Center for Imaging Research (CCIR) and is located within the Department of Radiology at CWRU/UHCMC. In close proximity to the main CWRU ARC, the CCIR provides state of the art imaging capabilities spanning the entire range from molecular and preclinical imaging services to clinical and translational imaging research studies. The preclinical CCIR imaging laboratory is a 2,500 sq. ft. lab including multiple preclinical MRI scanners to be utilized heavily during this proposal. In addition to the MR scanners there are multiple optical imaging capabilities including bioluminescence and fluorescence capabilities, and a novel cryoimaging system that provides whole animal *in situ* high resolution (10µm) fluorescence and brightfield images. Preclinical PET/CT, SPECT/CT, and planar X-ray capabilities are also available as needed. All systems are equipped with dedicated workstations and the necessary software to perform intended experiments. Clinical imaging systems are also available within the CCIR (i.e., 3T Siemens Skyra 3T MRI) to enable translational imaging research studies.

Light Microscopy Imaging Core
The Light Microscopy Imaging Core Facilities on the Case Western campus are shared resources that offer a wide range of imaging services to the research community. Our facilities are committed to enhancing and expanding collaborative capabilities of research in northern Ohio. Our range of instruments allows for most types of modern imaging techniques from basic widefield imaging to very high spatial and temporal resolution imaging of fixed and live cells, tissues or small organisms.
Those instruments are often used for analyzing human and animal cells under pathological conditions such as cancer, neuronal degeneration, and metabolic disorders. By allowing high-resolution and dynamic analysis of biological tissues under pathological status, this core supports translational research. An additional application includes optimization of cell-based fluorescence assays for drug screening. Moreover, the slide scanning capability allows completely automated, high-throughput analysis of fixed human pathology specimens while the image processing capabilities allow unbiased comparison of samples from healthy and diseased tissues.

Gene Expression and Genotyping Core
The Gene Expression & Genotyping Facility occupies 740 sq. ft. of Cancer Center space in the Wolstein Research Building. This space houses an area dedicated to RNA and DNA isolation and dedicated space for Affymetrix and ABI instrumentation. In addition the Facility has a 150 sq. ft. amplicon-free room for set-up of PCR-based assays. Staging room, which contains 2 PCR hoods, dedicated pipettors, small microfuges and mini-thermocyclers. This room also contains a liquid handling system from Matrix, the PlateMate 2x2, which has X-Y stage movement with 8, 12 and 96 channel pipetting capability.

High Performance Computing Cluster (HPCC)
In late 2004, CWRU deployed a high performance computing cluster for research use. Since the summer of 2008, the cluster has been operated using a business model in which usage fees and direct hardware contributions partially fund growth and operations. The CWRU High Performance Computing center provides local supercomputing cycles and services for researchers whose needs do not scale to the level of national resources such as XSEDE and who require very fast turnaround for their jobs. The HPCC provides personalized service to its users and is highly responsive to requests for specialized software required for CWRU faculty to continue to carry out world-class research. The center leverages many staff within the entire Division of Information Technology Services to continue to improve its service offerings in HPCC, research storage, data visualization, specialized networking, and data intensive computing as new technologies emerge.

Training Programs
The Biomedical Sciences Training Program (BSTP) offers a common entry point to most of the biomedical Ph.D. programs with over 200 faculty members in a wide range of research areas. The program identifies accomplished, creative young scientists to work with dynamic faculty researchers. The faculty value their interactive relationships with students and view mentoring young scientists as an important part of the mission of the School of Medicine.

Medical Scientist Training Program (MSTP) Case Western Reserve University has offered MD-PhD training since 1956 for students aspiring to careers combining academic medicine and biomedical research. This program was among the first to be awarded NIH funding and carry the designation Medical Scientist Training Program over 30 years ago. The CWRU MSTP provides an outstanding opportunity for students to obtain combined MD-PhD training and launch careers as physician-scientists.

The **CWRU Clinical and Translational Scientist Training Program (CTSTP)** was launched in 2007 to expand opportunities for combined degree training in clinical and translational research. The CTSTP is a branch of the MSTP with full MSTP status and support for CTSTP students, but CTSTP students will have a distinct set of training areas related to clinical and translational research. The overall structure of training is the same in the MSTP and CTSTP, with graduate courses integrated into the first two years of medical school, and clinical training integrated into the PhD phase, to create a truly integrated physician-scientist training program. The CTSTP represents the T32/TL1 component of the CTSA Education Module, which supports MD-PhD and DNP-PhD training (options for DDS-PhD training are under development).

The **Master's Programs** of Case Western Reserve University School of Medicine offer a wide variety of programs in both Allied Health and the Basic Sciences, including everything from Anesthesia and Genetic Counseling to Bioethics and Public Health.

Office of Translational Workforce Development
The Office of Translational Workforce Development (TWD) was established to inventory, connect, and coordinate workforce training. The office provides educational consultation and integrates efforts to provide training and develop talent to enhance translation across Cleveland.

Continuing Medical Education (CME): CWRU in partnership with UH established a Continuing Medical Education (CME) Program to provide continuing medical education to health professionals. Services include sponsorship of grand rounds, series, live conferences, seminars, workshops, self-study vehicles such as monographs, CDs, audio/video tapes and courses from the Internet. The CME Program helps learners identify gaps in their professional practices related to recent research findings, the release of new clinical practice guidelines, and/or the identification of opportunities for improvement and by developing, delivering, and assessing high quality post graduate education activities that are designed to address these gaps. There is also a specific credentialing process everyone involved in clinical research must complete. There are also educational courses for patients and employees that are offered online.

Office of Research and Technology Management
Case Western Reserve's Technology Transfer Office (TTO) serves its innovators with full-spectrum intellectual property services. For both faculty and students, the office provides support for intellectual property and commercialization that spans the research & development continuum. They serve researchers by assessing and building upon the commercial potential of new ideas and inventions. Through interaction with inventors, regional and national networks, including our affiliate healthcare systems, and potential commercial partners, the office endeavors to determine the best path of translation and ultimate commercialization for University intellectual assets.

Bioethics
The Department of Bioethics focuses on emerging ethical issues in clinical translational research where clear regulatory standards or professional points of agreement concerning the conduct of research may be lacking. It serves as a critical resource for addressing ethical issues, such as those regarding the ethical conduct of stem cell research, large genomic studies, and bio repositories. A key component of the Bioethics Office is the network of Research Ethics Consultation Services. This network of experts provides CTSC investigators with convenient access to high-level specialists with the knowledge and expertise required to manage ethical issues in translational research, that is, issues which go beyond mere regulatory compliance or transcend available professional guidance.

Bioethics supports the work of the CTSC Research Subject Advocates (RSAs). Our RSAs conduct protocol reviews, monitor adverse events, evaluate HIPPA compliance, and review consent documents and procedures. RSAs schedule direct observations of subject recruitment and consent conversations on request or as needed, such as for studies involving high-risk or vulnerable populations. Furthermore, RSAs provide education and training on human research ethics generally and specific issues such as informed consent to investigators, study coordinators, research assistants, community members, and other clinical translational researchers in the Cleveland metropolitan area.

This office provides expanded educational opportunities in research ethics for clinical and translational scientists, young investigators, and trainees. Education and training include: (a) conflicts of interest; (b) collaborative research (including research with industry); (c) policies surrounding human subjects and animal research; (d)

data acquisition, management, sharing, and ownership; (e) mentor/mentee relationships and responsibilities; (f) responsible authorship and publication; (g) research misconduct and the policies for handling research misconduct; (h) responsible peer review; and (i) the role of scientists in society, including reflections on the ethical, environmental, and societal impacts of scientific research.

Office for Inclusion, Diversity & Equal Opportunity
The mission of the office of inclusion, diversity and equal opportunity is to provide support and guidance and to promote equitable and fair treatment in employment, education. The office serves as a resource to the university in the interpretation, understanding and application of federal and state equal opportunity and affirmative action laws and regulations.

Ultimately, the office supports the university's mission by providing strategic leadership in the development of policies, procedures and programs that will help foster diversity, inclusiveness and a welcoming environment for faculty, staff, students and others. Case Western Reserve University values excellence by advancing diversity through inclusive thinking, mindful learning and transformative dialogue.

Council to Advance Human Health Accelerator Fund
The Council to Advance Human Health (CAHH) was developed as a catalyst to provide a focused model of translation. The CAHH consists of alumni and industry leaders in pharmaceuticals, devices, ventures, law, finance, and entrepreneurship. This group collectively possesses the knowledge and perspective required for rigorous assessment of projects. The CAHH Program directly links to the Accelerator Fund. Support through the philanthropic Accelerator Fund provides small targeted grants for investigators to follow through on CAHH advice and move projects to the next stage.

Animal Resource Center
The Animal Resource Center (ARC) of Case Western Reserve University has programmatic responsibility for veterinary and husbandry care of all animals used at CWRU. The ARC provides state-of-the-art husbandry, health care and procedure space for investigating mice submitted to the MMPC.

The ARC employs three full time veterinarians who are responsible for providing veterinary care and preventative medicine programming for all animals. All three veterinarians review Institutional Animal Care and Use Protocols (IACUC) and provide researchers advice in designing experimental procedures to ensure that humane needs of the animals are considered in experimental design. The veterinarians have twenty-four hour access to all central and satellite animal facilities.

Animals are housed in two central animal facilities. The main central facility is the Health Sciences Animal facility which is located in the basement of the Biomedical Research Building (BRB) in the School of Medicine. This is a conventional 83,000 square foot facility. The facility underwent major renovation in 2007. This restricted access facility houses several operational units specializing in housing and care of animals used in all aspects of research at CWRU. A high level rodent barrier, integrated BSL2/BSL3 suite, quarantine facilities, large and farm animal housing units, large animal surgery area and specific pathogen free rodent housing areas are included in the facility. The Wolstein Animal Facility is a 25,000 sq. ft. rodent barrier facility located in the sub-basement of the Wolstein Research Building.

CWRU was granted full accreditation by AAALAC in 1990. The program was granted **CONTINUED FULL ACCREDITATION** in 1993, 1996, 2000, 2002, 2005, 2009, 2012 and 2015. An assurance letter (PHS Assurance A3145-01) is on file with the Office for Laboratory Animal Welfare at NIH. Reports of surveillance findings are available in the ARC office, on the ARC web site and posted in the animal housing rooms.

The Program for Animal Care and Use is conducted under the supervision of the Institutional Animal Care and Use Committee in accordance with applicable federal animal welfare regulations. All animal related research is conducted under the highest standards of humane animal care.

Cleveland Clinic (CC)
Cleveland Clinic was founded in 1921 as a not-for-profit group practice, integrating clinical and hospital care with research and physician education. In 2002, the Cleveland Clinic and Case Western Reserve University formed an academic partnership for teaching and research by establishing the Cleveland Clinic Lerner College of Medicine of Case Western Reserve University (CCLCM). Medical students apply to and are accepted into either program by one admissions committee and are awarded medical degrees from CWRU.

The initial cohort of 32 medical students enrolled in 2004 in a 5-year program designed to emphasize small class learning and physician-investigator training. With that affiliation agreement came the opportunity for all investigators and educators at Cleveland Clinic to become CWRU faculty.

Cleveland Clinic Lerner Research Institute (LRI) is administrative home to laboratory-based biomedical research at the Cleveland Clinic. More than 150 principal investigators and their teams pursue a wide range of biomedical questions. The Institute is comprised of 10 Departments: Biomedical Engineering, Cancer Biology, Cell Biology, Genomic Medicine Institute, Immunology, Molecular Cardiology, Molecular Genetics, Neurosciences, Pathobiology, and Stem Cells and Regenerative Medicine.

Cleveland Clinic consistently ranks as one of the nation's five best hospitals in USNWR annual America's Best Hospitals' survey. The heart program has ranked number one in America for 22 consecutive years. CC also ranks among the nation's top ten in thirteen of 16 subspecialties. Patients come from all 50 states and 147 countries to receive care at CC. In addition to its main campus (contiguous with the campus of CWRU), CC has a network of community hospitals and outpatient centers in Northeast Ohio, and maintains sites in Florida, Nevada, Toronto, London, and Abu Dhabi. Cleveland Clinic is a pioneer in internet-based medicine and internet-based research tools. CC leads the nation in information technology for research, many of which benefit our CTSC, including eResearch, Knowledge Program (KP) and Explorys, the latter licensed to IBM/Watson for advances in healthcare technology. CC offers clinical services through eClevelandClinic. The Lerner Research Institute (LRI) coordinates and oversees laboratory-based C/T research at CC. More than 1,200 scientists and support personnel work directly within the LRI's 700,000 sq ft of lab and C/T research space. In addition to research within the LRI, CC's Clinical Institutes conduct translational and clinical research, including the Cole Eye Institute, the Heart and Vascular Institute, the Neurologic Institute and the Taussig Cancer Institute (associated with the SOM's NCI designated Case Comprehensive Cancer Center). CC also is one of three NIH Centers for Accelerated Innovations, and partners with CWRU, Ohio State University, University of Cincinnati, and Cincinnati Children's to accelerate the translation of NHLBI-supported discoveries and technologies into new products. The strong commitment of CC to education, particularly C/T research education, is manifest not only in its fellowship program and many applicants for KL2 scholars, but also by the track in the SOM that CC supports, the CC Lerner College of Medicine of CWRU – a five year program dedicated to training the next generation of physician-investigators.

The Breadth and Depth of Research

Cleveland Clinic is a top-rated hospital in research and receives in excess of $250,000,000 in total research awards yearly, with over $90,000,000 in NIH funding alone. The Clinical Research Unit (CRU) at CC is a 7-bed research inpatient/out-patient unit that provides research nursing and laboratory support. The Education Institute is the world's largest continuing medical education program, with 70 accredited residency training programs and one of the largest graduate medical education centers in the United States.

Knowledge Program System

The Knowledge Program® (KP) is a scalable electronic platform to systematically collect patient-reported data through a mobile ready web-based data collection system. Started in 2007, the goals of KP are to incorporate the collection and tracking of patient reported outcomes (PRO) into existing clinical workflows, and to use PROs and health information technology to help optimize healthcare management and delivery, as well as research applications. KP provides the ability to communicate and obtain information from Cleveland Clinic patients at the time of their clinic visit, and remotely at pre-specified time-points independent from clinical encounters. Invitation(s) to complete questionnaires are sent to patients' email with a link to questionnaire content individualized to the patient and the project. The system is independent of, but integrated with, Cleveland Clinic's Electronic Health Record (EHR) through Health Level 7 (HL7) and web services feeds.

Core features of the system include the ability to identify patients using demographic, clinical or administrative data, to send information (such as education material) to the patients, and collect and store patient-reported data. KP sends automated reminders and collects management and performance statistics per-study and across all studies. The questionnaires are response-driven, so questions may vary from patient to patient within a given questionnaire set, depending on patient responses. When each question is completed, the data is sent in real-time to the KP data warehouse. All questionnaires are synchronized, so patients do not repeat previously answered questions within pre-specified time intervals. Data is accessible to researchers through a self-service web-based query tool, and through direct data feeds and manual data pulls. KP has collected patient-reported data on over 70,000 encounters each month throughout the Cleveland Clinic.

Center for Online Medical Education and Training (COMET)
COMET, currently transitioning to its new name, the Center for Technology-Enhanced Knowledge and Instruction (cTEKI), is used to provide free online continuing education for clinicians, caregivers, and all Cleveland Clinic employees. Started in 2002, it helps provide system-wide courses that can train employees on necessary information and modules, with completion tracking and reporting. It supports the strategic development of web-based training to supplement the medical education of physicians, house staff, medical students, and nursing personnel, as well as to train employees, vendors, and guests with a diverse catalog of courses. The overall goal of COMET is to help improve efficiency and effectiveness of eLearning, and to provide expertise in the development of web-based education and training materials. Services include learning management systems, course design and development, portal development, classroom training, emerging technologies, and consultation. Some notable courses include holographic and 3D imaging courses for anatomy education, spaced learning for incoming residents, point-of-care learning, blended learning for residents, interactive case studies for healthcare workers, interactive exercises for nurses on defibrillation, and porting clinical knowledge to academia for nursing students.

Research Core Services/Cleveland Clinic

The Lerner Research Institute's Core Services seek to facilitate and advance research throughout Cleveland Clinic by providing technologies that support basic, translational, and clinical research. Services range from those that support common requirements such as glassware sterilization, web design and computing services, to more specialized services such as confocal microscopy, mass spectrometry, or DNA sequencing. An additional level of expertise uses biomedical engineering to transform new medical device ideas into functional prototypes, fostering innovation.

Cell Culture Core
The Core provides Cell Culture and Cell Banking resources to Investigators and has the capacity to freeze and store 10,000 vials. Any cells received for culturing will be quarantined until tested and found to be free from mycoplasma. The Cell Culture Core offers a cell authentication service with special discounted prices.

Digital Imaging Microscopy
The Digital Imaging Microscopy Core is part of the LRI Imaging Core. Experienced staff members are ready to help with the planning of imaging experiments, use of the microscopes, and the processing and analysis of data.

Electron Microscopy
This division of the Imaging Core provides investigators with a full range of electron microscopy services — from expert advice to sample preparation and observation in high quality instruments. Electron Microscopy services comprise both transmission and scanning electron microscopy (TEM and SEM).

Flow Cytometry Core
The Flow Cytometry Core provides investigators with a resource for analytical and preparative studies of cells using flow cytometry. The Core offers FACS acquisition and analysis, cell sorting, and consultation for experimental design, interpretation and troubleshooting. Applications include immunophenotyping, intracellular staining, molecular and cellular probes such as Ca flux and GFP, CBA (Cytometric Bead Array), DNA cell cycle, TUNEL and Annexin V for apoptosis, sterile sorting for cloning and more. Both the LSRFortessa and Aria II have a green 561nm laser, which is optimal for detection of "mFruit" fluorescent proteins.

Genomics Core
The Genomics Core offers a wide range of services, including Capillary sequencing and Genotyping, Illumina Microarray-based Gene Expression profiling and Genotyping, and Next-Generation Sequencing (NGS). Our lab is equipped with the Illumina MiSeq and HiSeq2500 sequencer, which enables rapid and effective targeted and whole genome analyses. We prepare and normalize libraries for RNA-seq, miRNA-seq, DNA-Seq, targeted exome sequencing, amplicon sequencing, bacterial 16S metagenomics and whole genome sequencing. In addition we also have an Illumina NeoPrep which is an automated, easy to use system for NGS Library Preparation. Currently we offer mRNA and DNA library preparation on the NeoPrep. Other services include DNA and RNA quality check using the Agilent Technologies Bioanalyzer, DNA and RNA quantification using Qubit, shearing of DNA and chromatin using Covaris, and Illumina microarray and genotyping data analysis support using Genome Studio. We also collaborate with the Genomic Medicine Biorepository to extract DNA and RNA for our users.

Hybridoma Core
The Hybridoma Facility was established to provide investigators at CCF and the Cleveland biomedical community with a resource for monoclonal and polyclonal antibody production. The facility also provides consultation services to assist the investigator in all aspects of monoclonal/polyclonal antibody production. The services are performed under strict QC guidelines appropriate for antibodies that may have commercial potential.

Immunohistochemistry
Immunohistochemistry (IHC) allows investigators to visualize the expression levels and distribution of specific cell or tissue antigens. Due to the variability among antibodies and techniques, IHC requires significant knowledge of basic histology, available immunological reagents, antigen retrieval techniques and immunohistochemical procedures. It can be time consuming and may require considerable titration and optimization of antibodies before research samples can be stained. It may also require experimentation with different antigen retrieval methods for paraffin tissues as well as experimentation with different fixatives for fresh frozen tissues.

Laboratory Diagnostic Core
The Laboratory Diagnostic Core offers investigators a large menu of automated clinical chemistry assays, elisa based testing, hematology and phlebotomy services. The LDC has maintained accreditation with the College of American Pathologists and CLIA for more than fifteen years. The Core has been a CDC Lipid Standardization Laboratory since 2001. The laboratory test menu includes assays for both human and animal samples.

Media Preparation Core
The Media preparation lab offers a wide variety of quality controlled media at economical prices. Media is prepared in large batches ranging from 50L-250L from commercially produced powders. All of our products go through a strict QC program. Custom plates and media are offered by request and are usually available within 1-3 days. All other orders placed on-line can be picked up on the next business day.

Molecular Biotechnology Core
The Molecular Biotechnology (MBT) Core offers consultation and services in the areas of customized peptide synthesis, peptide modification, purification and quality analysis. The Core also offers CD Spectroscopy and biomolecular interaction analysis and equilibrium and kinetic measurements using Surface Plasmon Resonance (SPR), Isothermal Titration Calorimetry (ITC) and Microscale Thermophoresis (MST).

Molecular Screening Core
The MSC is a facility at CCF and Cleveland wide to provide access to high throughput screening technology (HTS), including the expertise and reagents, necessary for screening of libraries of small molecules in a variety of readout systems for identification of active drug like compounds. The goal is to provide validation of screening assays and proof of concept that the proposed therapeutic target can be attenuated by chemical entities. In addition, the facility provides access to shRNA and CRISPR reagents through a partnership with Sigma for molecular validation of signaling pathways and molecular targets.

Proteomics and Metabolomics Laboratory
The Proteomics and Metabolomics Laboratory uses advanced mass spectrometry methods for the sequencing of proteins and the analysis of small molecules. The goal of the core is to help investigators with the qualitative and quantitative characterization of proteins and small molecules in biological matrices such as plasma/serum, urine, tissues, cell lines, along with other biological materials. The Proteomics applications include the identification of protein from gel bands or in-solution, identification and quantitation of post-translational modifications, and the global quantitative analysis of proteomes. The Metabolomics applications include both targeted and untargeted quantitative analysis of metabolites.

MetroHealth System (MH)
MetroHealth, Cuyahoga County's safety-net hospital, located on the west side of Cleveland 8 miles from CWRU is an integrated health system with an acute care hospital housing the area's only Burn Center and a Level 1 Adult Trauma Center. The Emergency Department is among the busiest in the country (>275 visits per day); Metro Life Flight air ambulance service is internationally recognized. Not surprising that the MetroHealth Trauma Research Institute of Cleveland (MeTRIC) is one of MH's research strengths. MH was the first of the CWRU affiliated hospitals to establish a formal research track in its internal medicine residency and is committed to C/T research training. MH was the first public safety-net hospital system in the U.S. to install an electronic health record (EHR) for clinical care (1999), and has been recognized by several national organizations for its

early adoption and sustained value of its EHR. Over 40% of MH's socioeconomically diverse patient population is enrolled in Epic's MyChart personal health record.

MetroHealth maintains primary site status for ECOG operations for CWRU. A small number of Cancer Center members maintain their research labs on the MetroHealth campus. Negotiations between Case CCC and MetroHealth to integrate the clinical research programs into the Case CCC are underway, with MH expected to participate fully in the single PRMS, DSMP, and IRB that takes place under the auspices of the Case CCC and to utilize the Case Cancer IRB. Initiatives are underway to expand programs in minority accrual to clinical trials, studies of aging and cancer in minority populations, and studies of the impact of co-morbid conditions on therapeutic outcomes. The teaching programs in cancer at MHMC are closely integrated with the Medical School curriculum and there are combined postgraduate training programs in medical oncology and general surgery. In addition, MetroHealth is the home of the program providing clinical research training to medical fellows. Cancer Center members participate in 16 course hours of formal classroom training in the "Bench to Bedside" course, a formal 4 credit course required by all KL2 trainees in the NIH KL2 award of the CTSA to CWRU, Cleveland Clinic, MetroHealth, and University Hospitals.

The Breadth and Depth of Research

MetroHealth has an 80,000 square foot Center for Education and Research (CER). There is also the Center for Health Research & Policy, the Center for Reducing Health Disparities, the Functional Electrical Stimulation Center (FES), and a specific focus on stroke trials and stroke research. MH has strong research programs in renal disease, perinatal medicine, rehabilitation medicine, and health services research. The Clinical Research Unit (CRU) at MH, is a 6 bed unit for inpatient visits and 8 "swing" rooms catering to inpatient or outpatient needs, and provides research nursing and laboratory support.

Center for Health Care Research & Policy

The mission of the Center for Health Care Research & Policy is to: 1) improve the health of the public by conducting research that improves access to health care, increases the quality and value of health care services, and informs health policy and practice; and 2) lead education and training programs that promote these goals. Formally established in 1994, the Center's mission is carried out by a cross-disciplinary faculty who both lead and collaborate with other scholars in Northeast Ohio and beyond. A core faculty of 17 is extended by affiliated Senior Scholars throughout the university, assisted by an able staff and over 30 grant-supported research associates. The Center's home at MetroHealth's Rammelkamp Research and Education Building is an outstanding venue for collaborative research, mentoring of students and junior faculty, and cross-disciplinary seminars.

The Center's research and training focuses in programmatic areas that reflect national health care priorities as well as high impact problems in adults. Center Programs pertain to chronic conditions, especially stroke, obesity and diabetes, and kidney disease. Programs are supported by methods units, including biostatistics and evaluation, health care decision making, and health economics and health policy. Research using clinical informatics capitalizes on growing institutional capacities in electronic medical records (EMR) and clinical decision support. Center faculty view Northeast Ohio as a laboratory for research, recognizing the national relevance of regional challenges and opportunities. For over four years, the Center has served as the administrative home for Better Health Partnerhsip, an EMR-catalyzed initiative to measure, publicly report, and improve health outcomes for the region's residents with chronic medical problems. Center faculty also assume leadership roles in federally-supported degree programs in Health Services Research and Clinical Investigation and teach in the core curriculum of the School of Medicine.

Charles H. Rammelkamp, Jr., M.D., Center for Education and Research

This center houses education and research programs, including laboratories, support areas, classrooms, and a 10,300-square-foot medical library. MHS has established a Learning Center that provides ongoing education for employees, providers, and health professionals. Operated through eLearning platforms, there is a specific Learning, Engagement and Performance system that helps support performance management and leadership development processes. The Learning Center also provides educational tools for patients and hosts seminars and classes.

University Hospitals

University Hospitals (UH) was founded in 1866 and is the affiliate of CWRU. The UH Cleveland Medical Center includes Rainbow Babies & Children's Hospital, MacDonald Woman's Hospital, and the Seidman Cancer Center, which is affiliated with the Case Comprehensive Cancer Center (CCCC). The UH Health System has 1,032 beds and 24,000 physicians and employees. UH also has 17 community hospitals and 32 outpatient health centers, including 3 surgery centers. UH also includes a network of specialty care physicians, skilled nursing, elder health, rehabilitation and home care services, managed care and insurance programs, occupational health & wellness, and the most comprehensive behavioral health services in the region. UHCMC has been closely affiliated with the School of Medicine since 1928 and shares a contiguous campus with CWRU that is the principal site for medical students and residency training for the School of Medicine, and has a long history as a partner with CWRU in sponsoring NIH Centers.

Rainbow Babies & Children's Hospital has 244 beds with 16 medical divisions and 12 surgical specialties. It consistently sees ~700,000 patients per year. The MacDonald Women's Hospital is the state's only hospital dedicated solely to women's health. Its resources include maternal fetal medicine, obstetrics and gynecology, female pelvic medicine and surgery, gynecologic oncology, reproductive endocrinology and infertility, behavioral medicine, midwifery, and breast care.

The Breadth and Depth of Research

University Hospitals had $61,000,000 sponsored research funding in 2016. Its total research was $257,000,000. The Harrington Discovery Institute originated from UH and provides support for projects advancing translational research addressing unmet clinical needs. The Clinical Research Unit (CRU) at UH, is a 10-bed research inpatient/out-patient unit that provides research nursing and laboratory support.

The University Hospitals Clinical Research Center

The University Hospitals Clinical Research Center consists of 7 offices and several core services dedicated to developing the responsible conduct of research for our patients through scientific, regulatory, legal, ethical and fiscal review. The UHCRC is directed by Grace McComsey, MD who also serves as a co-lead in Hub Research Capacity. The UHCRC includes:

Institutional Review Board (IRB) Administration Office

The UHCRC IRB is responsible for ensuring that all research involving human subjects is conducted in accordance with Federal & State Regulations as well as institutional policies. The IRB reviews protocols originating from:

- Any University Hospitals Health System entity involving UH patients or personnel, regardless of sponsorship
- Case Western Reserve University School of Medicine, Nursing, Dentistry or any Case department that involves patients or personnel at UH
- Multi-site research conducted at non-UH performance sites, when requested by the entity (with an IRB Authorization Agreement)

Research Compliance and Education

The Office of Research Compliance and Education (ORC&E) offers regulatory support and research education to UH/UHRBC/Case research community. The ORC&E promotes Good Research Practice (GRP) through the following services:

- Research protocol monitoring (prospective & retrospective)
- Responsible Conduct of Research Education Seminars
- Informed Consent Observations
- Regulatory Audit (FDA/Sponsor) support

Grants and Contracts Pre-Award

The Grants and Contracts Pre- Award Office provides oversight of the legal and budgetary aspects of grants and contracts for the purpose of:

- Verification and negotiation of research agreements that addresses legal issues and are consistent with FDA and UHCMC/ UHRBC policies
- Support investigators and coordinators in the development and negotiation of adequate study budgets
- Responsible for the review, approval and submission of grant applications (non-NIH research studies)
- Ensuring regulatory compliance with research subject billing

Grants and Contracts Post-Award
The Grants and Contracts Post- Award Office provides oversight of all fiscal aspects of grant management including the following:

- Creation of grant accounts
- Review and approval of grant expenditures
- Reconciliation of grant awards including cash application and grant closeout
- Labor distribution of grant accounts
- Financial reporting

Research Finance
The Research Finance Office provides oversight of research clinical billing to include:

- Creation of coverage analysis
- Development of the patient care portion of clinical research budgets
- Compliant management of research related patient claims to include accurate charge segregation, claim coding, and payment for services rendered while participants are on trial

Technology Management
The Office of Technology Management specializes in the utilization, creation, protection and commercialization of intellectual property including:

- Evaluation of new concepts for patentability and market potential
- Working with industry partners of the commercialization of new medical technology
- Assisting clinicians with the introduction of new technology into the clinical setting
- Assisting clinicians with the filing of patent applications to protect their medical inventions

William T. Dahms MD Clinical Research Unit (Dahms CRU)
William T. Dahms MD Clinical Research Unit (Dahms CRU), also a core resource of the Cleveland Clinical and Translational Science Collaborative (CTSC), is designed to support clinical and translational investigators by providing the following resources:

- Ten inpatient/outpatient beds with 2 outpatient recliner chair stations on the 7th floor of Horvitz Tower, RB&C
- Coleman Clinical Research Suite, a 4 room Phase 1 CRU to support cancer research (opened June 2011 on the 3rd floor of the Seidman Cancer Center)
- Additional 3 un-staffed exam rooms and a Developmental Testing Room in the Bolwell Health Center Suite 3400
- Community-Based CRUS are at UH Bedford Medical Center, UH Otis Moss Jr Health Center, and Ahuja Medical Center.
- Fee-based RN and non-RN Study Coordinator Core
- Metabolic Research Kitchen and Bionutritional support for research diets and analyses
- Sample processing and shipping support
- CLIA certified core analytical laboratory for research assays
- Informatics support, e.g. REDCap database utilization

The Center for Child Health and Policy at Rainbow Babies & Children's Hospital
Established in 2007, the Center for Child Health and Policy at Rainbow focuses on major health policy issues that are central to the well-being of children and youth. The Center recognizes that health policy forms a framework for all health care delivery, and that health policy is therefore essential to improving children’s health. In this way, the Center focuses on the nexus between policy and practice of pediatric medicine. The Center fills the need to amalgamate expertise in pediatric medicine and research with expertise in health policy. Operating as a think tank, the Center brings together experts in child health, health finance, law and policy to perform policy analyses, consultations, research, educational programming, and community outreach to advance child health through policy. Work is focused on several areas including: Maternal/Fetal/Newborn Health; Chronic Illness; Quality; and Care Delivery Systems.

Louis Stokes Cleveland Veterans Affairs Medical Center (LSCVAMC)

The LSCVAMC is a major teaching hospital affiliated with Case Western Reserve University's School of Medicine and is located ½ mile from CWRU. The LSCVAMC is highly regarded among VAs and is top-rated for its clinical service programs and its health services research. This is an extremely active VA with 1.38M outpatient visits each year, and 682 beds. Clinical activity at the VA is facilitated by the electronic medical system. Clinical trials including IRB, data safety monitoring and management are separate. The VA staff treating patients also engage in teaching and research and hold academic appointments at CWRU.

The Breadth and Depth of Research

The LSCVAMC has over 220 active research projects to enhance the medical center's ability to provide state of the art medical care and innovative techniques and treatments to Veterans. This site has two VA funded centers of excellence: Functional Electrical Stimulation Center and the Advance Platform Technology Center. The LSCVAMC has 41,400 square feet of recently renovated research space.