



ROLE SPECIFICATION

DIRECTOR, CENTER FOR BIOMEDICAL DATA SCIENCES

Contact

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Center for Biomedical Data Sciences



The amount and types of data generated in biomedical research are expanding at an unprecedented pace. From large-scale genomic sequencing to metabolomic and high-dimensional imaging analyses, expertise and leadership are needed to enable more effective integrated, systems-level analyses to gain biologically and clinically meaningful insight from complex data. Comprehensive data analytics involving biostatistical methods, data modeling, and visualization tools are utilized in all types of research at the Oklahoma Medical Research Foundation, from basic model organism studies to clinical investigations.

In response, OMRF is launching its Center for Biomedical Data Sciences. The center's inaugural director will have significant support and resources to establish this new center. The ideal candidate will be a driving force for collaborative, multi-investigator funding initiatives.

Mission

The Center for Biomedical Data Sciences will bring cutting-edge, integrated data analytic knowledge and support to the OMRF community.

- (1) The center will serve as a hub for recruiting experts who will work collaboratively across a range of scientific disciplines in all research programs to develop and deploy innovative data science support. This activity will expand collaboration between and within research programs at OMRF.
- (2) The center will function as an educational resource to train the OMRF scientific community on how to implement data analytic tools to advance scientific goals.
- (3) The center will provide leadership in organizing computational and related resources, in strategic planning to support basic and clinical research, and in expanding the research opportunities at OMRF.

The Role



Job Purpose

The Director of the Center for Biomedical Data Sciences will work with OMRF senior leadership to develop and execute a comprehensive strategy for advancing biomedical data analytics with research teams throughout OMRF.

They will recruit and manage center members, oversee research-focused computational and analytic resources, and contribute to strategic planning at OMRF. Working closely with OMRF's program chairs and investigators, the director will build a team of collaborative center members that support diverse, biomedical research programs. As the founding director, the successful candidate is expected to provide leadership in defining the best practices for high-dimensional data utilization and required resources (tools and training) to help OMRF thrive in an expanding data-intensive research environment.

The Role

Key Accountabilities

Participates in establishing strategic plans and objectives

Provides high-level guidance and support to center team members and OMRF scientists

Regularly interacts with leadership on matters affecting the organization

Anticipates and recognizes data analytic challenges and makes recommendations for solutions and allocation of resources needed to meet the research goals of OMRF investigators

Maintains a nationally-recognized reputation in biomedical data sciences through collaborative scholarly activity, including multi-investigator publications and extramural funding, participation in national meetings, and development of new data analytic techniques and approaches

Leads, mentors, evaluates, and recruits a motivated and talented team, including biostatisticians, computational scientists, and data visualization experts

Works closely with information technology and other relevant technology cores
Develops strong partnerships with regional research-intensive universities and undergraduate-focused institutions to foster collaborations, develop local talent pipelines, and grow biomedical data science resources in Oklahoma

Key Experiences and Competencies

Associate professors or other mid-career individuals from the nonprofit or industry sectors

A minimum of 12 years of related experience, including at least 5 years of successful leadership experience and a Ph.D. in bioinformatics, statistics, clinical science, biological science, or equivalent combination of education and experience

Values team-based research utilizing data analytic tools and expertise to strengthen and expand biomedical discoveries

Record of contributions demonstrated by successful completion of multiple collaborative projects addressing a variety of biological problems, highly cited publications, impactful tools, products, or data sets used by the scientific community, presentations at international conferences, and awards

Record of successful NIH and/or other extramural grant applications (including multi-investigator) in relevant fields

Deep understanding of systems biology, bioinformatics, clinical informatics, and/or modern statistical and machine-learning tools for analysis of various datasets

Exceptional communication skills with ability to collaborate, seek constructive feedback, build relationships, promote teamwork, and remain adaptable to change

The Role

Reporting To

The director will report to the Vice President of Research and the Vice President of Clinical Affairs. The director and center members will be evaluated through a new collaborative data science career ladder emphasizing multi-investigator and co-investigator activity.



Rodger McEver, M.D. **Vice President of Research**

Dr. Rodger McEver is OMRF's chief scientific officer, maintaining the excellence of scientific output of the research programs and core facilities. A cardiovascular biologist board certified in internal medicine and hematology, he headed OMRF's Cardiovascular Biology Research Program from 2007 to 2016. His lab discovered the protein P-selectin, and his work with the adhesion molecule led to the creation of Adakveo, the first targeted therapy for sickle cell disease. He received his medical degree from the University of Chicago and completed a fellowship at Washington University School of Medicine in St. Louis. He joined the faculty at the University of Texas Health Science Center at San Antonio before establishing his lab at OMRF in 1987. Dr. McEver got his first taste of medical research as a high school student when he was selected to participate in OMRF's Sir Alexander Fleming Scholar program in 1965.



Judith James, M.D., Ph.D. **Vice President of Clinical Affairs**

The head of clinical affairs, Dr. Judith James oversees OMRF's Multiple Sclerosis Center of Excellence, Rheumatology Research Center of Excellence, biorepository, clinical immunology lab and infusion center. A board-certified rheumatologist, Dr. James also leads the Arthritis & Clinical Immunology Research Program. She is best known for her work in predicting and preventing lupus. She earned her doctorate in microbiology and immunology and medical degree from the University of Oklahoma Health Sciences Center. She holds numerous academic appointments at OUHSC, including associate vice provost for clinical and translational science. She first came to OMRF as a Sir Alexander Fleming Scholar in the summer of 1988 and joined the foundation's scientific staff in 1994. She was named to her current role in 2017.

Organization Background



An Introduction to OMRF

The Oklahoma Medical Research Foundation is one of the oldest, most respected independent research institutes in the United States. For 75 years, OMRF's mission has remained constant: conducting biomedical research that enables more to live longer, healthier lives.

With an annual budget of almost \$100 million, OMRF focuses its research on cardiovascular biology, diseases of aging, and immunology and autoimmune disease. The National Institutes of Health has three times designated OMRF an Autoimmunity Center of Excellence, one of only 10 in the U.S. In partnership with the University of Oklahoma Health Sciences Center, our scientists have also secured two NIH Nathan Shock Center of Excellence in the Basic Biology of Aging grants, making Oklahoma home to one of just eight Shock Centers.

Since its inception, OMRF has also emphasized the practical application of basic discoveries, converting scientific insights into therapeutics for human disease. To this end, OMRF holds more than 200 active patents for discoveries made in its labs. Three of those discoveries have led to medications that have been approved by the Food and Drug Administration and are now being used to treat patients. Discoveries at OMRF have also given birth to more than a dozen spin-off biotechnology companies, the largest of which has a market capitalization of nearly \$40 billion.

Home to a pair of clinics that serve thousands of patients and a massive biorepository of patient samples built with an NIH construction grant, OMRF also offers scientists the opportunity to engage in all facets of translational research. Currently, physician-scientists are leading 50 clinical trials, and researchers have gathered more than 1 million biological samples from research subjects with autoimmune illnesses. This sample collection has contributed to more than 200 papers, helping OMRF scientists to identify the genetic bases and mechanisms of diseases like lupus, Sjögren's syndrome, sarcoidosis and multiple sclerosis.

Today, OMRF stands at an exciting crossroads, an intersection that offers the opportunity to marry traditional strengths in basic laboratory research with a burgeoning clinical footprint. And with a record of consistent budget surpluses, a strong portfolio of extramural grants and philanthropic fundraising, an endowment of \$150+ million, and another \$150+ million held in trusts for its benefit, OMRF stands on the kind of firm financial footing that will enable scientific growth for decades to come.

Organization Background

History and Philanthropic Support



A 501(c)(3) public charity, OMRF was chartered in 1946 with the mission of “conducting scientific investigations in medicine.” The following year, Oklahoma Governor Roy J. Turner launched a fund drive that spanned all 77 of the state’s counties to raise capital for the fledgling research institute. The effort, which included a statewide “Research Week,” yielded more than 7,000 pledges and gifts. Construction of OMRF’s first research building began in 1949, and OMRF opened its doors in 1950.

That same year, Tulsa oilman J.A. Chapman designated OMRF as one of the beneficiaries of a charitable trust he and his wife, Leta, established. The Chapmans later named OMRF as a beneficiary of two additional trusts. Since 1950, those trusts have been a bedrock source of funding, paying out more than \$350 million to OMRF, including over \$12 million in 2020.

With a unique state tax credit for donations, OMRF also continues to enjoy broad funding support from the general public and a robust stream of planned gifts. In 2020, OMRF received more than 9,000 donations, including a dozen bequests from estates and trusts. All told, in 2020, OMRF secured almost \$10 million in contributions from sources beyond the Chapman Trusts, bringing total annual support from private contributions to over \$22 million.

For more on OMRF’s history, watch “Cultivating a Dream” at omrf.org/Video.



Organization Background



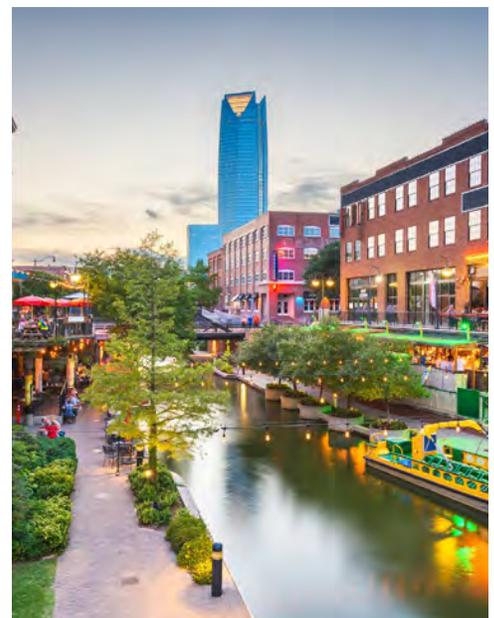
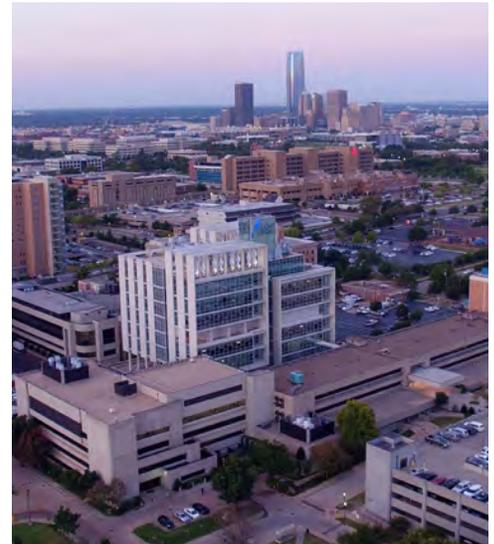
Research Campus

OMRF's campus houses more than 500,000 square feet of laboratory, clinic and administrative space. The campus consists of seven adjoining buildings that include 65 wet labs, a vivarium, a zebrafish facility and two patient clinics.

The newest addition to OMRF's campus is its research tower, which opened in 2011. Crowned by 18 wind turbines, the 186,000-square-foot facility won the 2014 S-Lab ("safe, successful, sustainable") award for best new research laboratory. The LEED-gold-certified facility was also named a finalist for the Renewable Energy World North America 2012 building of the year.

OMRF sits next to the VA Medical Center, where several of its investigators also hold appointments. Across the street is the University of Oklahoma Health Sciences Center, where nearly all OMRF faculty members hold adjunct titles, allowing for the training of OUHSC graduate students in their labs. OUHSC is home to a school of medicine and six other professional colleges that, together, serve 4,000 students. It is also home to Stephenson Cancer Center, which holds a National Cancer Institute designation.

OMRF is located in the Oklahoma Health Center, a 325-acre complex that houses more than 20 health-related institutions and businesses in Oklahoma City. With a population of more than 650,000, Oklahoma City is now the 25th largest city in the U.S. It not only consistently ranks among the country's most affordable cities for living and home-buying, but in 2020 Zillow named it as the number one city for start-up and tech businesses to expand, and *Travel and Leisure* chose it as one of its top 50 destinations in the world.



Organization Background

Areas of Discovery

OMRF is currently home to almost 60 principal investigators who lead independent research programs, publish in peer-reviewed journals, apply for external funding, and educate and train students and postdoctoral fellows in their laboratories. In total, OMRF employs more than 400 people, including more than 150 scientists with MD and/or PhD degrees.

OMRF's research is concentrated in five major areas:



Aging & Metabolism

Scientists in this program share an interest in the metabolic basis of age-related disease and in extending the health of our aging population. Investigators study a variety of age-related conditions integrated across multiple organ systems, including heart failure, diabetic cardiomyopathy, macular degeneration, osteoarthritis, sarcopenia and neurodegenerative disorders. Common among these afflictions are alterations in cellular metabolism and energy production. Laboratories in this program investigate distinct aspects of these processes, identifying alterations that occur with age exacerbated by obesity and diabetes. They explore associated defects in energy homeostasis, cellular and mitochondrial quality control, production and removal of toxic free radical species, and the inflammatory response to define underlying causes of diseases that primarily afflict the elderly.



Arthritis & Clinical Immunology

This research program focuses on understanding the etiology, pathogenesis and molecular mechanisms of systemic autoimmunity, as well as understanding immunologic responses to infection and vaccination. Using genetic, genomic, proteomic, immunologic and molecular approaches, researchers work to understand complex human diseases such as systemic lupus erythematosus, Sjögren's syndrome, rheumatoid arthritis, inflammatory myositis, multiple sclerosis and thrombotic thrombocytopenic purpura. They also seek to decipher mechanisms of immune protection after influenza or anthrax vaccination. To facilitate these patient-oriented research activities, scientists in this program develop and utilize novel methods and algorithms to mine large datasets and evaluate complex human genetic diseases.



Organization Background

Areas of Discovery

Cardiovascular Biology

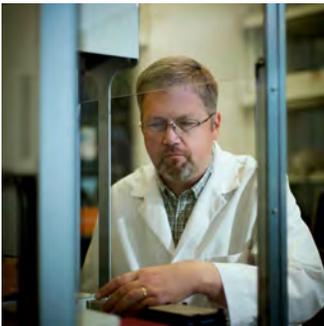
Researchers use a multidisciplinary approach to investigate fundamental mechanisms involved in blood and lymphatic vessel function, atherogenesis, blood coagulation, inflammation and sepsis at a molecular level. This approach encompasses all aspects of modern vascular biology, including structural biology, structure-function analysis of enzymes and receptors, regulation of the relevant genes, in vivo studies using transgenic and gene deletion approaches, cell biology, protein chemistry and physiological studies. The multidisciplinary approach allows identification of new factors and the mechanisms that regulate coagulation and inflammation and enables translation of these findings into an appreciation of their physiological role and clinical relevance. In addition to contributing to a fundamental understanding of these systems, the studies have clinical relevance to heart attack, stroke, septic shock, cancer and inflammatory bowel disease.

Cell Cycle & Cancer Biology

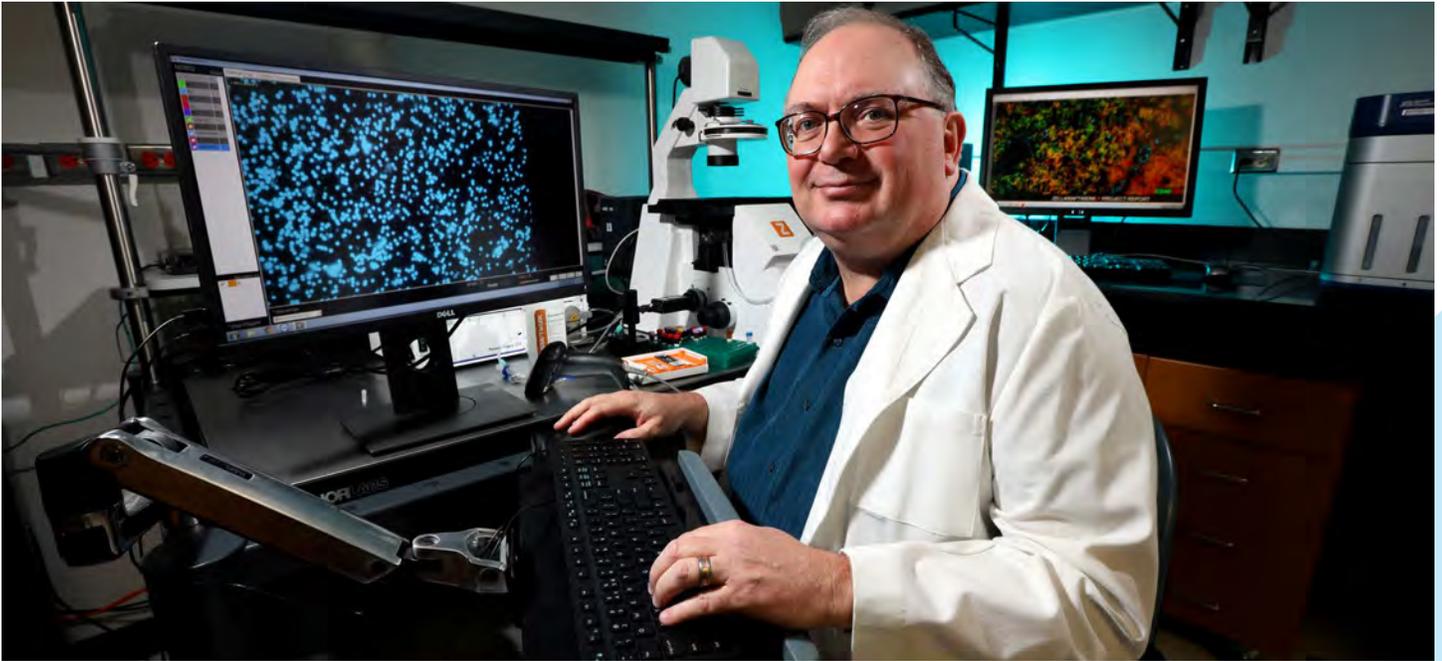
OMRF's Cell Cycle & Cancer Biology Research Program focuses on basic biological processes that control cell growth and cell division. Researchers within this program use cutting-edge technologies in molecular biology, genetics, and advanced microscopy to investigate the factors that regulate genome stability in experimental systems such as budding yeast, *Xenopus laevis* and cultured mammalian cells. The contributions made by members of this program in illuminating the normal pathways of cell division and the malfunctions that lead to chromosome abnormalities have important implications for human diseases, including birth defects and cancer.

Genes & Human Disease

This program is devoted to identifying and understanding how genetic variations cause human diseases. While all investigators in the program share this focus, each has their own specific interests, including determining the function of non-coding RNA, and understanding how the complex, three-dimensional organization of the genome, disease-associated non-coding variants, and the epigenome regulate gene expression in health and disease. Faculty in this program are also developing and applying new machine and deep-learning approaches to identify new disease-associated genetic variations and define disease-associated gene networks. The program works closely with OMRF's CLIA-certified clinical genomics center, CAP-accredited biorepository and quantitative analysis core, all established with funding from the NIH Institutional Development Award (IDeA) program.



Organization Background



Faculty

OMRF's principal investigators join our faculty following postdoctoral fellowships or faculty appointments at institutions throughout the U.S. and, occasionally, beyond. They include a member of the Association of American Physicians, a fellow of the American Association for the Advancement of Science, three former Pew Scholars, and the current Chief Advisor for Clinical Development of the Lupus Foundation of America. Numerous OMRF PIs serve as permanent and *ad hoc* editors of scientific journals and members of NIH study sections.

While OMRF does not grant tenure, it does employ a rolling appointment system that provides senior faculty (equivalent to associate or full professors at universities) who meet performance expectations with renewable, rolling three- or five-year appointments. Renewal is determined through an annual review process that evaluates scientific productivity.

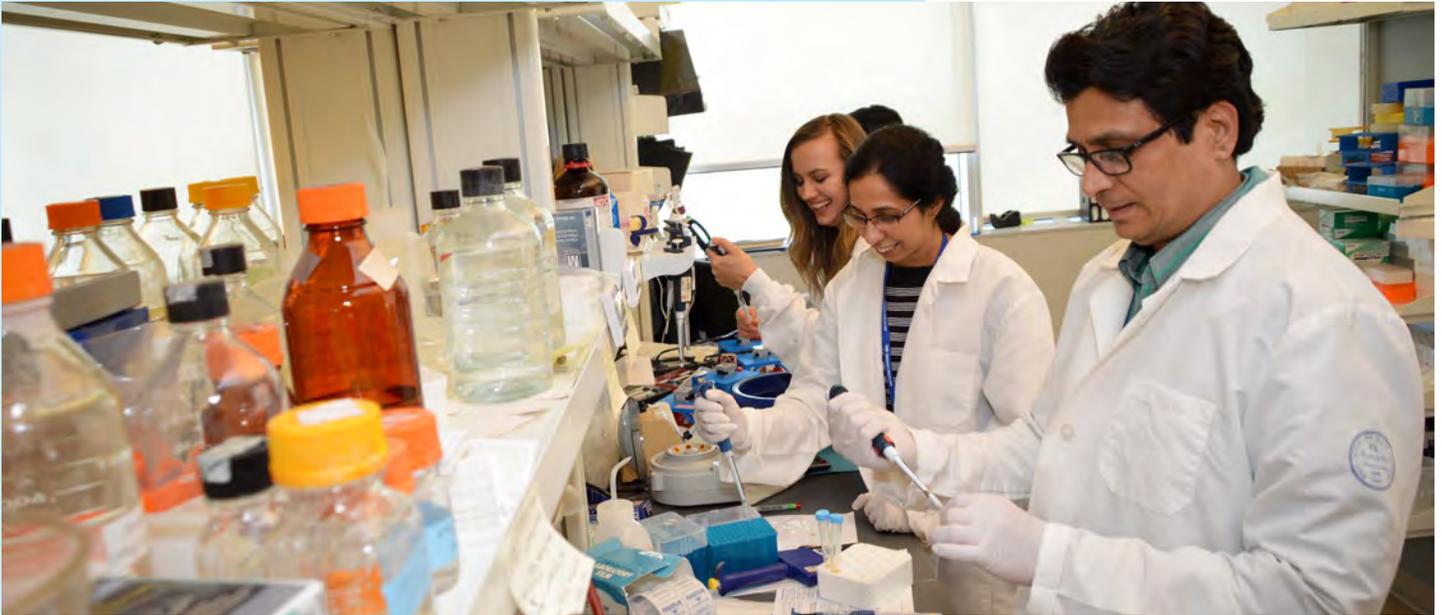
This process also results in a yearly award of institutional funds to support each scientist's lab. Funds are distributed according to a formula consisting of three components: a fixed award, a distribution tied to annual performance scores, and an amount determined based on grant funding secured by the investigator. Annual distributions now average almost \$200,000 per investigator. They provide a flexible source of funding that PIs can use to help pay their own salaries, support salaries of lab personnel, and pay other research expenses. As part of this system, OMRF allows investigators to set their own salaries (within broad ranges) based on available funding sources.

Each year, a scientific advisory board consisting of distinguished senior researchers from across the U.S. also visits OMRF to review one of our research programs. This rigorous evaluation by key opinion leaders, most of whom are department or center heads at leading academic research centers, ensures OMRF investigators maintain standards of research excellence and competitiveness at national and international levels.

You can learn more about OMRF's principal investigators at omrf.org/Scientists.



Organization Background



Extramural Funding

OMRF currently holds more than 150 active extramural research grants from the NIH and other federal and non-federal sources. During the most recent fiscal year, expenditures on those grants totaled more than \$31 million, with the lion's share (over \$24 million) coming from the NIH. In addition to research program grants, OMRF has a significant portfolio of active NIH program project and centers grants:

- Center for Cellular Metabolism Research in Oklahoma (P20): National Institute of General Medical Sciences (Centers of Biomedical Research Excellence award)
- Expanding Excellence in Developmental Biology in Oklahoma (P20): NIGMS (COBRE)
- Interdisciplinary Research in Vascular Biology (P30): NIGMS (COBRE)
- Molecular and Immunologic Analysis of the Pathobiology of Human Anthrax (U19): National Institute of Allergy and Infectious Diseases
- Oklahoma Autoimmunity Center of Excellence (UM1): NIAID
- Oklahoma Nathan Shock Center of Excellence in the Basic Biology of Aging (P30): National Institute on Aging (joint grant with OUHSC)
- Oklahoma Rheumatic Disease Research Cores Center (P30): National Institute of Arthritis and Musculoskeletal and Skin Diseases
- Oklahoma Shared Clinical and Translational Resources (U54): NIGMS (subcontract with OUHSC)

Since the NIH launched its Centers of Biomedical Research Excellence (COBRE) funding initiative through its IDeA program, OMRF has built a two-decade track record of competing successfully for these three-phase grants. With total awards that can exceed \$30 million over a 15-year period, COBRE grants provide sustained funding to develop research infrastructure and support junior investigators. Since the program began in 2001, OMRF has secured five COBRE P30 awards, including a new award in 2021. This funding has proven invaluable for mentoring junior PIs to independence and supporting research cores at OMRF.

Organization Background

Key Scientific Core Facilities and Resources

Biorepository: Offering more than 10,000 cubic feet of -20, -80 and liquid nitrogen storage, this CAP-certified facility stores more than 1 million biological samples from research volunteers and provides OMRF scientists with a unique resource to facilitate translational research.

Clinical Genomics Center: Using Novaseq, NextSeq and Miseq instruments, this facility provides investigators with massive amounts of sequencing, genotyping and gene expression data in a timely, cost-efficient manner.

Clinical Immunology Lab: This CAP/CLIA-certified autoantibody and testing reference laboratory performs a variety of tests to identify autoantibodies for the diagnosis and treatment of autoimmune and other diseases.

Flow Cytometry Core: With training, analysis and multi-parameter, high-speed cell sorting, this facility offers access to state-of-the-art flow cytometry.

Comparative Medicine: With three separate barrier-level facilities, OMRF's animal care program manages an average of 6,500 cages of mice and 1,200 tanks of zebrafish, as well as frogs, rats and other species as needed. OMRF's cage rates rank among the lowest in the country, and the program is accredited by AAALAC International and is a member of the Vivarium Operational Excellence Network.

Gnotobiotic Mouse Core: These centralized germ-free and gnotobiotic mouse services include access to small experimental isolators for a variety of *in vivo* studies utilizing germ-free mice.

Human Antibody Core: OMRF is home to one of the few laboratories in the world that produces fully human, full-length, antigen-specific antibodies for use in studying human immune responses.

Human Phenotyping Core: This core provides analysis of human biofluid biomarkers, genetic variant analysis, gene expression analysis, single-cell proteomic/single-cell high-content immune phenotyping and single-cell transcriptomics/epigenetics.

Imaging Core: From basic histology, immunofluorescence and electron microscopy to digital image processing and analysis, this facility assists researchers with imaging needs of all kinds.

Nuclear Magnetic Resonance Center: With a 7-Tesla magnet, researchers can obtain *in vivo* non-invasive functional, morphological and molecular information on various disease models in mice and rats.

Quantitative Analysis Core: This broad array of analytical support includes assistance with genetics, genomics, bioinformatics, qualitative data modeling, biostatistics and statistical modeling.

Translational Informatics Core: This facility offers technical expertise in information systems development and management, data science and analytics, and computational and data visualization.



Organization Background



Clinical Centers

OMRF is home to a pair of clinics, the Multiple Sclerosis Center of Excellence and the Rheumatology Research Center of Excellence. Each year, care providers in these clinics conduct 6,000 patient visits with people living with MS, lupus, rheumatoid arthritis and other autoimmune diseases. The physician-scientists in these clinics also provide their patients with access to investigational new drugs through clinical trials, with 50 such trials currently underway. These treatment resources, which generate approximately \$20 million in revenues each year and are run on a break-even basis, exist to support clinical and translational efforts at OMRF. In particular, investigators at OMRF recruit volunteers for research studies focused on autoimmune diseases. Through clinics, OMRF has established world-leading collections of well-characterized biological samples of patients with MS, lupus, Sjögren's syndrome and sarcoidosis that have served as the basis for hundreds of collaborations with academic scientists and industry.



Organization Background



Education Programs

Through predoctoral and postdoctoral training programs, approximately 75 graduate students and postdoctoral fellows train at OMRF each year. Nearly every OMRF principal investigator maintains adjunct faculty status at the neighboring OUHSC, enabling them to train graduate students in their labs. Postdocs come to OMRF from across the U.S. and worldwide, and a training committee consisting of PIs from throughout the institution leads OMRF's postdoc training program.

In partnership with the Fulbright Commission, OMRF is one of four institutions (along with the University of Chicago, University of Virginia and University of Texas Southwestern Medical Center) that participates in the Visiting Research Graduate Traineeship Program. This program provides one-year research traineeships to students enrolled in master's degree programs in biomedical sciences in Poland.

OMRF also offers three training initiatives for undergraduate students. The Saxon and Sir Alexander Fleming Scholar Programs provide summer research experience to students from, respectively, U.S. military academies and colleges across the U.S. And in partnership with Langston University, Oklahoma's only historically Black college or university, OMRF has launched the Langston University Biomedical Research Scholars Program. This program is the first of its kind in Oklahoma. It aims to meld summer research internships with long-term mentoring to support students of color pursuing STEM degrees and encourage and assist them as they explore career paths in biomedical research.



Organization Background



Intellectual Property and Technology Transfer

OMRF's current intellectual property portfolio consists of 235 active U.S. and international patents. OMRF also has more than two dozen active licenses with industry partners. Through agreements with the Rajiv Gandhi Centre for Biotechnology in India and Rosalind Franklin University of Medicine and Science in North Chicago, OMRF also acts as a commercialization partner and licensing agent for technologies from these institutions.

In fiscal year 2020, OMRF's intellectual property revenues from royalties and licensing activities totaled \$1.75 million.

Since the passage of the Bayh-Dole Act, OMRF has aggressively patented technologies and worked to commercialize them through collaborations with industry and the formation of start-up companies. To that end, OMRF has spun off more than a dozen businesses, the largest of which, Alexion Pharmaceuticals, is in the process of being acquired by AstraZeneca for \$39 billion. Those efforts have also resulted in the commercialization of the following products, each of which is based on discoveries made at OMRF:

Adakveo: Approved by the FDA in 2019 and the European Commission in 2020, this Novartis drug is the first treatment for vaso-occlusive pain crises in sickle cell disease.

Ceprotrin: Baxter's FDA-approved treatment for protein C deficiency also was the first therapy approved for use under the European Union's centralized marketing procedure.

Soliris: Alexion's groundbreaking treatment for the rare blood disorder PNH has also been subsequently approved by the FDA to treat neuromyelitis optica and atypical hemolytic uremic syndrome.

Vectra DA: Recently acquired by Labcorp, rheumatologists have used this test throughout the U.S. for a decade to monitor disease activity in patients with rheumatoid arthritis.



Organization Background



Culture and Values

Independent yet interconnected. This seeming paradox stands at the heart of OMRF's culture. We are united in curiosity and a dedication to the pursuit of knowledge. But the path of that journey is one that each person at OMRF chooses. And as an organization, we strive to support each member of our community as they map their own paths toward a single goal of helping more to live longer, healthier lives.

OMRF is one of approximately 80 members of the Association of Independent Research Institutes. Like our AIRI peers, we are a single-mission research organization, which enables us to focus and remain nimble. We demand excellence, and we constantly reassess our systems and operations to ensure that all we do serves science in the most targeted and efficient manner possible.

These tenets seem to resonate with the people who make up OMRF. For eight consecutive years, in anonymous surveys, our employees have named OMRF a Top Workplace in Oklahoma. We've ranked in the top 10 every year since the annual contest began, one of only six employers in the state to do so.

Organization Background

Diversity, Equity and Inclusion

Diversity powers everything we do at OMRF. We recognize that each person's unique experiences and perspectives enhance the insights they bring to our laboratories and clinics, and we are committed to celebrating and honoring every voice at OMRF in our workforce, education programs, clinics and research.

One-third of our employees identify as Asian, Black, Latinx, Native American or multi-racial. Our staff members hail from over 30 different countries. And with our Langston University Biomedical Research Scholars Program, we joined with Langston University to train and mentor Black undergraduate students interested in careers in the biomedical sciences.

Through multiple NIH grants, our investigators have partnered with Oklahoma tribes to understand and remedy health disparities in our state's Native populations. Similarly, with funding support from the Department of Health and Human Services' Office of Minority Health, our clinical investigators have worked on a multi-year project aimed at increasing the participation of underrepresented minorities in clinical trials. In OMRF labs, our investigators have focused on understanding why certain diseases exact an outsized toll on Black people. Their insights also helped deliver a first-in-class drug to treat sickle cell disease, which disproportionately affects people of African descent.

We recognize that these efforts represent a starting point, not an end. As an organization, we are focused on continuing to support and elevate populations that have too often been neglected and mistreated.





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