



INDIANA UNIVERSITY
SCHOOL OF MEDICINE



INDIANA CENTER FOR MUSCULOSKELETAL HEALTH (ICMH)

EXECUTIVE SUMMARY
OCTOBER 2023

SCHOOL OVERVIEW

Founded in 1903, Indiana University School of Medicine has a long history of innovation and excellence in medical education, research and care. Our faculty developed the cure for testicular cancer, pioneered use of echocardiography and led the development of the electronic medical record, among other accomplishments.

That tradition continues today. Under the leadership of Dean Jay Hess and the school's executive team, IU School of Medicine has built on more than a century of success and is transforming the way health care is delivered in Indiana and afar.

RESEARCH GROWTH

The IU School of Medicine generates approximately \$460M in external research funding, including over \$220M in NIH funding. NIH funding increased more than \$80 million, or 70 percent, over the last four years, propelling IU School of Medicine to 14th out of 92 public medical schools that receive NIH funding and 31th out of 154 medical schools overall – demonstrating national leadership in critical fields like Alzheimer's disease, diabetes, and pediatric diseases.

STATEWIDE TRAINING

The school is capitalizing on its statewide footprint and the strengths of its nine campuses to graduate physicians who will serve all Hoosiers. More students are completing clinical rotations outside of Indianapolis, the school is partnering with community hospitals to add residency programs throughout the state, and campuses are developing scholarly concentrations that showcase their unique expertise.

LEADING-EDGE CARE

IU School of Medicine has moved more than 60 independent physician groups into a single faculty group practice, IU Health Physicians, to improve delivery of care and strengthen the alignment of clinical, education and research missions. As a result, more Hoosiers have access to advanced care and the most promising therapies in the form of clinical research studies.



ATTRACTING FUNDING

Grantmakers and individual donors have taken note of the school's ambitious vision and are investing generously in research and other programs. To date, IU School of Medicine has raised more than \$1.7 billion as part of For All: The Indiana University Bicentennial Campaign, including more than 100 endowed chairs and professorships and 150 endowed scholarships.

LEADERSHIP

Jay L. Hess, MD, PhD, MHSA, joined Indiana University School of Medicine in 2013 as its 10th dean. In addition, he serves as one of four executive vice presidents of Indiana University and is charged with guiding the university's clinical affairs strategy. Hess earned his medical and doctorate degrees from the Johns Hopkins University School of Medicine and completed residency training in anatomic pathology and fellowships in hematopathology and surgical pathology at Brigham and Women's Hospital. He holds a certificate in business administration from The Wharton School of the University of Pennsylvania, and a master's degree in health services administration from the University of Michigan School of Public Health.

The Indiana University School of Medicine, Indiana's only allopathic medical school, is the largest medical school in the United States, offering education to more than 1,600 medical and graduate students in pursuit of its tripartite mission to promote innovation and excellence in education, research and patient care.



EXECUTIVE SUMMARY

HISTORY AND COMPOSITION OF THE INDIANA CENTER FOR MUSCULOSKELETAL RESEARCH, ICMH

History of the ICMH

Indiana University has a long and rich history of musculoskeletal research. Dating back to the 1960's, **Conrad Johnston, MD** was the first person known to study osteoporosis in Indiana. As an endocrinologist by training, his work was critical to understanding the changes in bone mass that occur with age and the influence of inheritance on bone mass. He was recognized as a world-renowned expert with numerous awards. Another key figure in the history of musculoskeletal health research at IU is **David Burr, PhD** who served as the chair of the Department of Anatomy and Cell Biology in the IU School of Medicine from 1990-2010. Like Dr. Conrad, Dr. Burr's research impacted the field of bone research and the treatment of osteoporosis. It was his leadership and collaborative perspectives that led to the vision of founding the ICMH.

The Indiana Center for Musculoskeletal Health (ICMH) was established in 2017 to address the serious need to prevent and treat musculoskeletal disease. The mission of the ICMH is to harness the exceptional scientific talent of our members toward the discovery and development of new treatments, cures, preventative strategies, diagnostic tools, and new technologies to address the increasing burden of bone, muscle, mineral, and cartilage disorders among patients of all ages. This mission is being achieved by promoting and fostering collaborative research to accelerate discoveries in the field of bone and muscle science at our Institution. A major focus of the ICMH are the thematic research teams which include 1. Trauma, Regeneration, Rehabilitation 2. Mechanobiology and Muscle-Bone Crosstalk 3. Musculoskeletal Cancer 4. Lifestyle Modifications: Exercise and Nutrition 5. Musculoskeletal Medicine: Adults and Pediatrics. These teams are composed of basic, translational, and clinical researchers who share a focused research area. The purpose of these teams is to share information on individual research projects in order to initiate collaborations and to educate members regarding leading edge research through social events and presentations, external speakers, and incentives for pilot funding.

The ICMH has more than 100 members, many housed on the 5th floor of the Van Nuys Medical Sciences Building. The ICMH received 6,000 sq. ft. of newly renovated modern laboratory and administrative space in 2017. There are open laboratories for seven new faculty, which includes two tissue culture rooms, microscopy imaging, instrumentation/



EXECUTIVE SUMMARY

common equipment room, storage room, cold room, and animal surgery room. ICMH space also includes administrative space, graduate student office, small kitchen facility, collaboration work area, and an adjacent conference room. ICMH also provides space for ICMH investigators from the schools of Human and Health Sciences and the School of Dentistry and from two departments, Medical and Molecular Genetics, MMG, and Anatomy, Cell Biology & Physiology, ACBP. (See attachment for more details).

Pilot funding is provided for new collaborative projects, investigators partnering with industry, and to collaborations initiated with other center/institution members. Our committees include the Education Committee, the Equipment and Core Oversight Committee, the Industry Relations Committee, Pilot Applications Review Committee, Sustainability Committee, Bio and Medical Informatics Committee, and the ICMH DEI Committee. To date, the Center has a total of 117 members, who participate in our journal clubs, our research teams, our committees and attend presentations by renown researchers. The ICMH has made several landmark achievements since its establishment in 2017. One major landmark achievement by a team of ICMH investigators includes the generation of treatment for hypophosphatemic rickets, burosomab. Another landmark achievement is the creation and approval of a PhD in Musculoskeletal Health, the first of its kind. A third major achievement is the awarding of a clinical P30 application to fund ICMH clinical cores (outlined below). The total active external funding of our membership is \$61.9 Million as of 2022.

ICMH Members

The center includes outstanding, internationally known researchers in the areas of basic, translational, and clinical musculoskeletal research in multiple schools at Indiana University, Purdue University, and Marian University. These scientists are making important discoveries in the laboratory with the purpose of treating patients with metabolic and genetic musculoskeletal diseases, trauma, bone and muscle cancer, and aging. Several investigators are focused on how to harness the beneficial effects of exercise.

The Center for Musculoskeletal Health works to foster relationships with others in the field by hosting renowned speakers, providing leadership and collaboration within the five thematic research teams and by developing technology and services in the basic and clinical cores that enable our members to perform cutting edge, state of the art research.

The ICMH has currently **117 members** which includes **11 ICMH investigators** located within ICMH space on the 5th floor of the Van Nays Medical Building, 2 ICMH investigators not in ICMH space, with the rest of ICMH members located in 3 different institutions including Indiana University, Purdue University and Marian University.



EXECUTIVE SUMMARY

Indiana University: Total- 102

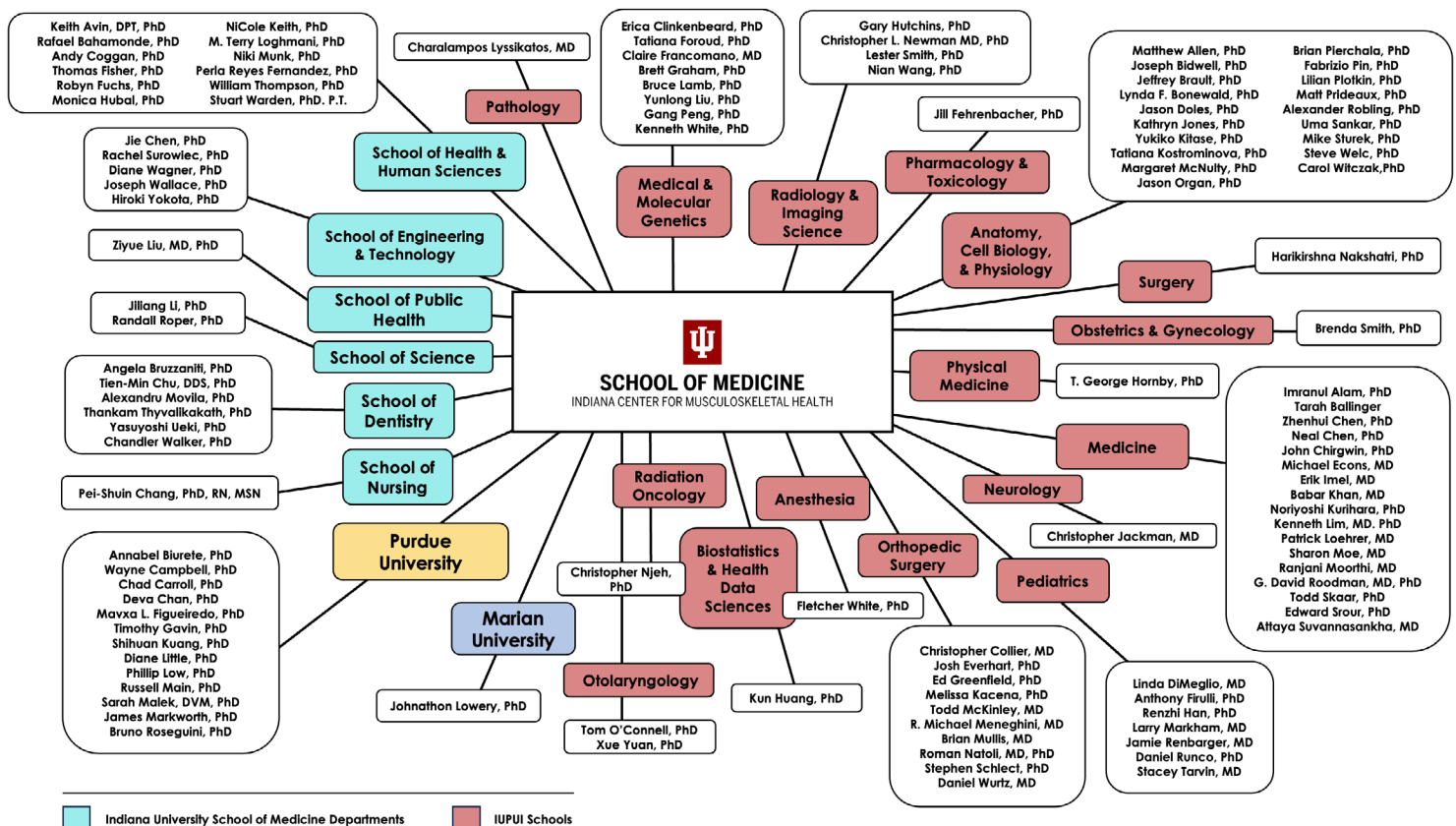
- School of Medicine- 75
- Dentistry- 6
- Engineering & Technology- 5
- Health & Human Sciences- 12
- Nursing- 1
- Public Health- 1
- Science- 2

Purdue University: Total- 13

- Engineering & Technology- 1
- Health & Human Sciences- 5
- Center of Aging and Life Course- 1
- Veterinary Medicine- 4
- Science- 2

Marian University: Total- 2

- Osteopathic Medicine- 2



ICMH CORE FACILITIES

The ICMH supports two clinical cores and six basic/translational cores.

Clinical Research Cores (ICMH-CRC)

A clinical P30, AR072581, was funded by NIH NIAMS in late 2017 and renewed in 2022 with the overarching theme to better define musculoskeletal diseases that have common pathogenesis and clinical presentations. The ICMH-CRC supports clinical research and trainees through two interconnected clinical cores the FIT and MIM cores. The ICMH-CRC oversees the Data Bank which contains blood samples from the FIT core and human bone and muscle samples discarded from surgery.

The Function-Imaging-Tissue, FIT, Core is located in University Hospital and performs a series of musculoskeletal tests including collection of blood and DNA stored in a musculoskeletal biobank, standardized physical function tests (gait speed, hand grip, timed up and go, and 6 minute walk), body composition and bone imaging (DXA and HRpQCT), and patient reported outcomes instruments. Goals are to perform functional phenotyping, provide controls for clinical studies (cancer, diabetes, etc) that lack or find it difficult to obtain normal controls, and generate reference datasets. Some individuals provide muscle and/or bone samples by biopsy or from orthopedic surgeries for basic and translational studies. The FIT core cohort is under a single IRB and includes a mix of healthy children and adults, as well as those with several chronic diseases. For research purposes, all these individuals have the results of the FIT Core testing and the blood/DNA samples (the majority will have whole exome sequencing by 2024) linked to their electronic medical records through the Regenstrief Institute that connects electronic medical records from multiple health care systems in the state (Indiana Network for Patient Care) through the Medical Informatics Methodological, MIM, core. This allows longitudinal assessment of FIT measures and facilitates the use of human samples with specific physical, medical, and functional characteristics for use in basic and translational research.

The Medical Informatics Methodological, MIM, Core supports the use of big data as it relates to clinical research including the electronic medical record with access to the entire Indiana Network for Patient Care. This facilitates answering questions from clinical databases that connect patient outcomes to medications, radiology reports and other clinical information. The Omics and Clinical Trial Service facilitates the conduct of clinical trials in musculoskeletal health by providing design service, biostatistical support, and guidance on sample collection to ensure that when the trial is done- specimens exist that

EXECUTIVE SUMMARY

can accommodate the latest of omics platforms. The MIM has developed a data mart that incorporates the FIT core participants and their collected appropriate specimens stored in the Indiana Biobank together with a larger cohort of individuals with musculoskeletal diseases ($n = > 150,000$) from the Indiana Network for Patient Care. Both cohorts are linked to social and structural determinants of health using geocoding. This will facilitate both epidemiologic studies around MSK health and studies from individuals who participated in the FIT Core.

ICMH BASIC CORE FACILITIES

Histology and Histomorphometry Core provides both human and animal bone and muscle histological phenotyping, including tissue preparation and staining, and bone histomorphometric analysis. This core provides consistency and comparability of measurement modalities across studies, provides protocols and quality control standards for technical procedures, coordinated guidance to investigators, and provides consultation on study design and post-study data interpretation. This core is located within Anatomy, Cell Biology, & Physiology, ACBP and supported by ICMH.

Animal Phenotyping Core coordinates expertise, techniques, and equipment to facilitate morphological, radiographic, and mechanical phenotyping of bone and muscle in whole animals and isolated tissues. The Animal Phenotyping Core offers a suite of essential services, established protocols, and scientific expertise to assess bone and muscle properties. This core focuses on (1) radiographic imaging, including dual energy x-ray absorptiometry, micro-computed tomography, peripheral CT, and planar radiographic imaging, and (2) mechanotransduction, including anabolic (ulnar loading, tibia loading, and catabolic (tail suspension, Botox paralysis) techniques as well as in vitro bone and muscle cell mechanotransduction services, such as parallel plate fluid flow and substrate strain techniques. Additionally, the Core provides consultation, training, and education in all techniques provided. This core is located in ACBP and supported by ICMH.

The ICMH Muscle Phenotype Core is a newly established core that offers services related to in vivo and ex vivo muscle contraction, muscle electrostimulation, and in vivo disuse experiments in collaboration with the ICMH Animal Phenotyping Core. This core proposes to advance the field in technical aspects while providing quality control and training/education for more standard techniques. This core also contains state of the art equipment for applying and measuring the effects of mechanical strain and shear stress on cultured cells. This core is located within the ICMH.



EXECUTIVE SUMMARY

Indiana Metabolomics Collaborative (IMC) is housed with the ICMH and works with investigators on the entire workflow of metabolomics experiment from study design and sample collection to data processing, analysis, and interpretation. The IMC has access to aSciex 5500 QTrap instrument for large, targeted metabolomics analyses, located in the Clinical Pharmacology Analysis core An Agilent 6546 QToF for high resolution analyses and isotope tracer studies is located in the Chemical Genomics Core. Both instruments are equipped with Agilent UPLC chromatography systems. The IMC operates a dedicated Agilent 6890N GC equipped with a 5973 mass spectrometer for the development of targeted assays which is located within the ICMH. The IMC has developed an extensive suite of data analysis and visualization software to aid in data interpretation.

Intra Vital And Dynamic Imaging Core Is being established and contains a Leica Stellaris 5 laser scanning inverted confocal microscope equipped with a White Light Laser (WLL). The WLL technology gives an extended near infra-red detection range enabling bone researchers to perform intravital imaging of live bone as well as ex vivo imaging of live cells. This capability to perform experiments on mineralized tissue is only available here on campus. The scope can also be used for multispectral imaging, fluorescence recovery after photobleaching (FRAP), optical sectioning, 3D imaging, and reflection imaging. The core will support diverse research studies focusing on trauma, craniofacial, musculoskeletal, and cancer bone health, development, aging, and drug delivery. This core is located within the ICMH.

Musculoskeletal Bioinformatics has been initiated with the recruitment of a new Director. This resource will provide education and collaboration in the analysis of data generated from sources such as RNAseq, Single cell seq, spatial transcriptomics, epigenetics, and other sources of bioinformatic data. This core is located within the ICMH.