Orthopaedic research is best path to improved treatment

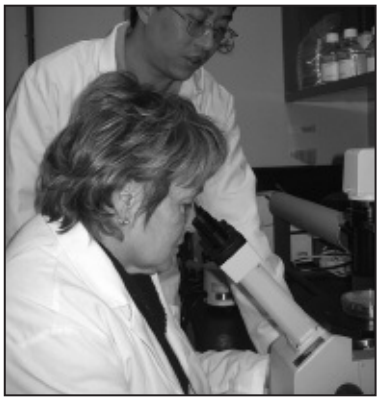
Musculoskeletal disorders and diseases are the leading cause of disability in the United States. More than one in four Americans has a musculoskeletal condition requiring medical attention. While the burden of musculoskeletal conditions is expected to escalate in the coming decades due to the aging population and sedentary lifestyles, research is currently less than two percent of the budget of the National Institutes of Health.

The American Academy of Orthopaedic Surgeons, participating in a collaborative project that seeks to raise awareness of the growing burden of musculoskeletal disorders on society, strongly advocates increased research:

"While musculoskeletal diseases are common, disabling and costly, they remain under-appreciated, under-recognized, and under-resourced by our national policy makers. The data (on disability and costs of musculoskeletal disorders to Americans) should stimulate increased investment in basic, translational, clinical, and health policy research to delineate the underlying mechanisms of these conditions and their response to treatment."*

The Campbell Foundation provides funding for research by Campbell Clinic residents at the University of Tennessee-Campbell Clinic Department of Orthopaedic Surgery.

Our research partners also include



UTHSC researchers in the Departments of Medicine and Biomedical Engineering, UTHSC Center of Integrative and Translational Genomics, InMotion Orthopaedic Research Center, and the Departments of Chemistry and Biomedical Engineering at the University of Memphis.

A broad array of projects

Basic research studies and projects currently underway at the University of Tennessee-Campbell Clinic Department of Orthopaedic Surgery include:

- Regenerative medicine, osteoarthritis, articular cartilage, and intervertebral disc studies that focus on identifying factors involved in cartilage repair
- Intervertebral disc disease tissue engineering studies that focus on stopping degeneration or degradation of discs
- Treatment of cartilage degeneration with bioactive peptides
- Antibody-targeted nanosome delivery system as a means to study damaged cartilage
- Study of herniated tissues from intervertebral discs treated with platelet-rich plasma
- Gender differences in the effect of Vitamin C on skeletal development
- Identification and analysis of candidate genes relevant to skeletal quantitative traits in order to study bone mineral density, bone size, bone strength, and bone quality
- Better integration of soft tissue and bone for ligament repair
- Development of a unique collagen scaffold for bone repair
- Biocompatibility of polymers and metals; factors affecting this response

Research's goal: better therapies

Dr. Karen Hasty, Wilhelm Professor of Orthopaedic Research at the UT-Campbell Clinic Department of Orthopaedic Surgery and a member of the Campbell Foundation Board of Trustees, is principal investigator in a study of genes relevant to arthritis and skeletal variation.

Dr. Hasty and her co-investigators will inject a male and female of defined inbred mouse strains with florescent

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Types of research

Basic Research

Laboratory studies at the cellular level conducted to increase understanding of fundamental life processes. The "bench" level of research. Findings from basic research are carried to pre-clinical studies before use with patients.

Clinical Research

Studies using human materials, patient records, etc. Includes studies on the mechanisms of human disease, therapeutic interventions, and clinical trials. The "bedside" level of research.

Translational Research

Applying discoveries generated during research in the laboratory and in pre-clinical studies to the development of trials and studies in humans.

"We are entering an age where personalized medicine will relate to the individual with respect to diagnosis of disease as well as optimized treatment protocols." —Dr. Karen Hasty

Dr. Karen Hasty (center) and the research team working on a current project involving soft tissue integration into bone for ligament reconstructions. Pictured from left are Dr. Tyler Cannon, Campbell Clinic resident; UTHSC medical student Tushar Jha; Dr. Jack Conoley, Campbell Clinic Fellow in sports medicine; Dr. Hasty; Dr. Jinsong Huang, instructor in the UT-Campbell Clinic Department of Orthopaedic Surgery; Dr. Scott Jackson, veternarian in the UT Dept. of Comparative Medicine, and Dr. Mark Gibbs, Campbell Clinic resident. Not pictured: Dr. Fred Azar of Campbell Clinic.

antibodies recognizing damaged cartilage in the joints to evaluate early arthritis. Identification of arthritis will be used to determine genes of interest in these mice.

The use of special inbred mouse strains developed and characterized by Dr. Rob Williams at UTHSC allows reproducible studies involving many genes that interact and influence cartilage and bone. This is one of a series of studies undertaken with the goal of developing therapeutic interventions for musculoskeletal problems.

Dr. Weikuan Gu, Associate Professor of Orthopaedic Surgery at UT-Campbell Clinic, is principal investigator for three research projects currently underway.

- Construction of a gene regulatory network (GRN) using a mouse model to study Bone Mineral Density (BMD), a critical factor in determining an individual's risk for bone fracture. Dr. Gu expects to learn about genetic controls of BMD and the significance of genetic background in one's risk for bone fracture.
- Comparison of gene expression levels in muscle from patients with bone fractures, comparing the tissues from aged persons to that from young persons. Dr. Gu will collect small samples of muscle tissue from young and aged volunteers with bone fractures, extracting RNA from the samples to identify differently expressed genes. Dr. Gu hopes to obtain information relevant to post-operative therapies.
- Comparison of levels of gene expressions in male and female mice, with and without bone fractures, to better understand genetic elements that regulate bone fractures. After extracting RNA, he will conduct a gene microarray and analyze resulting data in order to collect important data for sex-specific genetic control of bone fractures.

Dr. Hasty has served as principal investigator on numerous projects spanning a 25-year career in orthopaedic research.

She said, "We are entering an age when personalized medicine will relate to the individual with respect to diagnosis of disease as well as optimized treatment protocols. In order to provide the best healthcare for a particular patient, we need to know what genes are relevant for each musculoskeletal disease or condition and what genetic variations are present in this individual that would influence his treatment or outcome. Tomorrow's treatments begin with today's research."

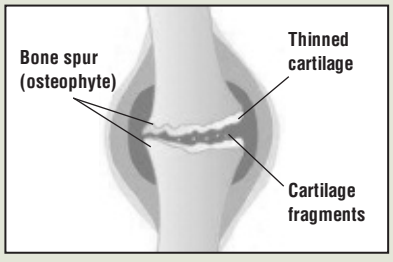
Osteoarthritis Studies Continue

Arthritis affects almost every American age 70 and older. Although there are many treatments, there are no cures. UT-Campbell Clinic researchers are working to change that.

Dr. Karen Hasty is leading a research effort using nanotechnology to develop a method for early detection and monitoring of osteoarthritis. Her colleagues on the project are Drs. Eugene Pinkhassik, Hongsik Cho, and John Stuart. A guinea pig model will be used; osteoarthritis in guinea pigs shares many features of human osteoarthritis.

This diverse team of researchers has developed detectable, fluorescent nanosomes (membrane-enclosed sacs that can be used to transport substances) specifically targeted to osteoarthritic joints with antibodies. The project's aim, Dr. Hasty said, is to show that such nanosomes can be valuable diagnostic tools capable of directing therapeutic agents to joints with early-stage lesions.

"There's a great deal of interest in earlier intervention for osteoarthritis when the cartilage damage is small and possibly more easily treated," Dr. Hasty said. "The major obstacle for developing disease-modifying treatments for arthritis is that we lack a method of detecting early lesions. Biomarkers to date for this disease are not sensitive or accurate enough, a fact that seriously impedes progress in the field."



Joint affected by osteoarthritis