IMPACT

Orthopaedic Research and Education Foundation

OREF

Volume VI | Spring 2004 | No. 3

David L. Glaser, M.D.

Cell Heritage Research Could Lead to New Therapies to Benefit Patients

A team of researchers, led by **David L. Glaser, M.D.**, will study the heritage of cells involved in bone and tendon formation and healing, possibly leading to new treatments for orthopaedic patients.

Dr. Glaser was awarded one of OREF's newly created Clinician Scientist Awards. Through this award, funded by the **Dr. Zachary B. and Mrs. Kathleen Friedenberg Endowment Fund**, Dr. Glaser will receive $100,000 per year for the next three years. The award is meant to supplement his salary, allowing him to spend more time in the laboratory.

"There is such tremendous pressure to generate clinical revenue, that in 2004, an orthopaedic surgeon cannot spend a minute of his time doing anything that is not financially productive," Dr. Glaser said. "The OREF award will allow me to devote substantial time to this project. You need to be able to spend several days in the lab to be productive. An afternoon here or even a single day is not enough."

With the OREF Clinician Scientist Award protecting his time in the laboratory, Dr. Glaser, an assistant professor of orthopaedic surgery at the University of Pennsylvania, will be studying the stem cells — cells that morph, or differentiate into specific cell-types that in turn make up specific tissues — responsible for the formation and repair of musculoskeletal tissue, such as bone, tendon and cartilage.

In normal circumstances, stem cells within the body repair damaged tissue and synthesize new tissue. But very little is known about where those stem cells originate. Dr. Glaser's research will investigate the sources of these stem cells.

"The body has many stem cell sources, or niches," said Dr. Glaser. "Depending on what type of tissue you're making, the body will contribute various cell types from these niches."

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OREF Endowment

Insurance Policy Provides Large Donation to OREF

Thomas A. Einhorn, M.D.

When **Thomas A. Einhorn, M.D.** decided to make a large gift to OREF's Unrestricted Endowment Fund, he knew it would be a substantial investment.

But when **Tom Coffman**, OREF Senior Vice President, Endowments, suggested donating an insurance policy as a deferred gift, Dr. Einhorn realized he could give even more than he had originally anticipated.

"I never dreamed I could be this type of donor," he told Mr. Coffman.

Dr. Einhorn, who is a member of OREF's Board of Trustees and is also a member of the Shands Circle recognition society, purchased a $250,000 insurance policy and designated OREF as both the owner and beneficiary.

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INSIDE

David L. Glaser, M.D. (continued)

Using what he terms an "elegant transgenic mouse model," Dr. Glaser will trace the lineage of these cells. Transgenic mice have been engineered so that specific cell populations are labeled, or tagged. No matter what the cells become, the researchers will know where they came from.

"We'll be able to see the ancestry of the cells so that, as they differentiate into bone, tendon, or muscle, we'll know what type of cells they were before they became what they are now," Dr. Glaser said.

For example, Dr. Glaser would be able to tell that the cells active in repairing tendon tissue were derived from endothelial cells if the cells in the newly formed tendon are flagged with the endothelial cell label.

Dr. Glaser and his team will primarily use three tissue formation and repair models to test their hypothesis that muscle satellite cells, pericytes, endothelial cells and bone marrow cells participate in the formation of musculoskeletal tissue and are active in tendon healing and fracture repair.

One model will create heterotopic ossification — bone formation outside of the natural skeleton. In another model, Dr. Glaser will create a patellar tendon injury. Researchers will also use a tibia fracture model.

"My research is geared toward trying to define the normal or physiological cells responsible for the postnatal repair of either fractures or the formation of new bone," Dr. Glaser said.

Once these tissue formation and repair models have been created, Dr. Glaser and his team will use light microscopy and standard histology to study the tissue's structure and immunohistochemistry to analyze the cells involved in healing the injuries created in the models.

They will apply the information they collect from this analysis to tissue engineering therapies that heal, or help heal musculoskeletal injuries and anomalies.

"In orthopaedics, people are talking more and more about tissue engineering and trying to improve healing of tissue, and perhaps even de novo synthesis of tissue, meaning creating new tissue from its component pieces," Dr. Glaser said. "Once we've identified the sources for these stem cells and have identified what these stem cells are, we'll be able to specifically use them or target them in our tissue engineering programs to either stop formation of bone outside the natural skeleton, or augment formation of bone or augment tendon healing."

Although stem cell therapy is not a new concept, being selective about which stem cells are used is. Because stem cells may be derived from many sources, including bone marrow, muscle, fat, peripheral blood, and even teeth, selecting the correct stem cell source could make treatment more effective.

> *"I think it's a pivotal award. Without it I predict I would have been drawn into the clinical machine."*

"I hope our research opens up a new thought process in how people look at stem cells. Stem cell A and stem cell B might be able to be induced to form the same cell, however, they might have different potentials. If you want to use stem cells in therapies, it might make a difference in which stem cells you choose," Dr. Glaser stated.

Such stem cell therapies could be used in common surgeries, such as procedures that repair the rotator cuff — the group of tendons that stabilize the shoulder.

Preventing heterotopic ossification, either after joint replacement surgery, following an injury, or in rare diseases, such as such as fibrodysplasia ossificans progressive, may be another application for selective stem cell therapy.

"I hope to open the door to more productive stem cell therapies so that we can augment healing and repair of all musculoskeletal tissue," Dr. Glaser said.

Dr. Glaser is grateful for the Clinician Scientist Award. Without it, he fears that his research may not have been possible.

"I think it's a pivotal award. Without it I predict I would have been drawn into the clinical machine. There is significant pressure to do an extra few cases or see an extra 20 to 30 patients a day. This [award] will allow me to protect my time and really focus on the work."

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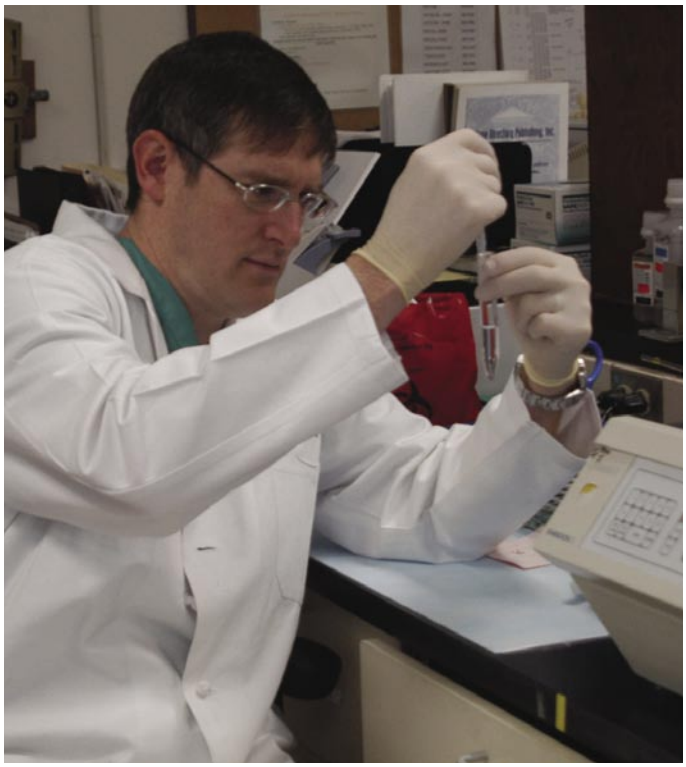
He also said that the Clinician Scientist Award provides a "tremendous opportunity for young clinician scientists" in that it could be the start of a full-fledged research program.

"Once that program starts to develop and expand, it will hopefully just continue to grow," Dr. Glaser said. "And hopefully it will lead to an NIH-funded award, which will lead to another, and another, and it might eventually lead to a program that would include many orthopaedic surgeons, grad students, and post doctoral fellows. It has far-reaching effects, far beyond what you would expect from just an initial few thousand dollars."

Dr. Glaser encourages others to fund research, observing that many major orthopaedic advances have come from individuals who have taken what they've observed in their clinics back to the lab to investigate.

"Many advancements in orthopaedics come from taking a clinical problem, bringing it to the laboratory, investigating it, and then going back to the clinic to apply what was learned. It leads to new breakthroughs and better care for patients. Everybody benefits."



Dr. David Glaser isolates cells using a density gradient. By studying the heritage of cells involved in bone and tendon formation and healing, Dr. Glaser's research could lead to new treatments for orthopaedic patients.

Dr. Zachary B. And Mrs. Kathleen Friedenberg established the Clinician Scientist Award category in 2002. Their donation to OREF's 2003 fund made **Dr. David L. Glaser**'s Clinician Scientist Award possible.

Dr. and Mrs. Friedenberg established an endowment fund that will award Dr. Glaser $100,000 per year for the next three years.

Because of the example set by Dr. and Mrs. Friedenberg, the ***Journal of Bone and Joint Surgery*** and **Dr. Dane and Mrs. Mary Louise Miller** have also established endowments that will fund two more Clinician Scientist Awards in 2004.

For information about making endowment gifts to OREF, or funding a Clinician Scientist Award, please contact **Tom Coffman**, OREF Senior Vice President, Endowments at (847) 384-4349 or coffman@oref.org.