

FROM THE DIRECTOR

Powerful Progress

My talented colleagues at the UCSF Diabetes Center continue to make significant discoveries that are fueling our research pipeline – taking our promising scientific research into the pre-clinical and clinical setting.

This issue of our newsletter highlights our work in discovering the role of mesenchymal fetal tissue in the formation of insulin-producing beta cells. It also features our efforts to transform fat cells to help solve the world's societal challenges of obesity and cardiovascular disease, and to create a publicly available scientific resource that will help identify disease-causing genes.

In the clinical arena, you'll learn about two new prevention trials in type 1 diabetes and why it's so important to have your relatives screened for auto-antibodies through TrialNet. You'll also learn about one of our new studies that analyzes residual beta cell function in those living with type 1 diabetes for more than five years and with hemoglobin A1c less than 9.5 percent.

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Research Breakthrough **Mesenchyme in Pancreas Development** **Key to Generating Beta Cells**

Diabetes Center Director Matthias Hebrok, PhD, UCSF colleagues, and collaborators at Texas A&M University have discovered that mesenchymal fetal tissue plays a fundamental role in the formation of insulin-producing beta cells.

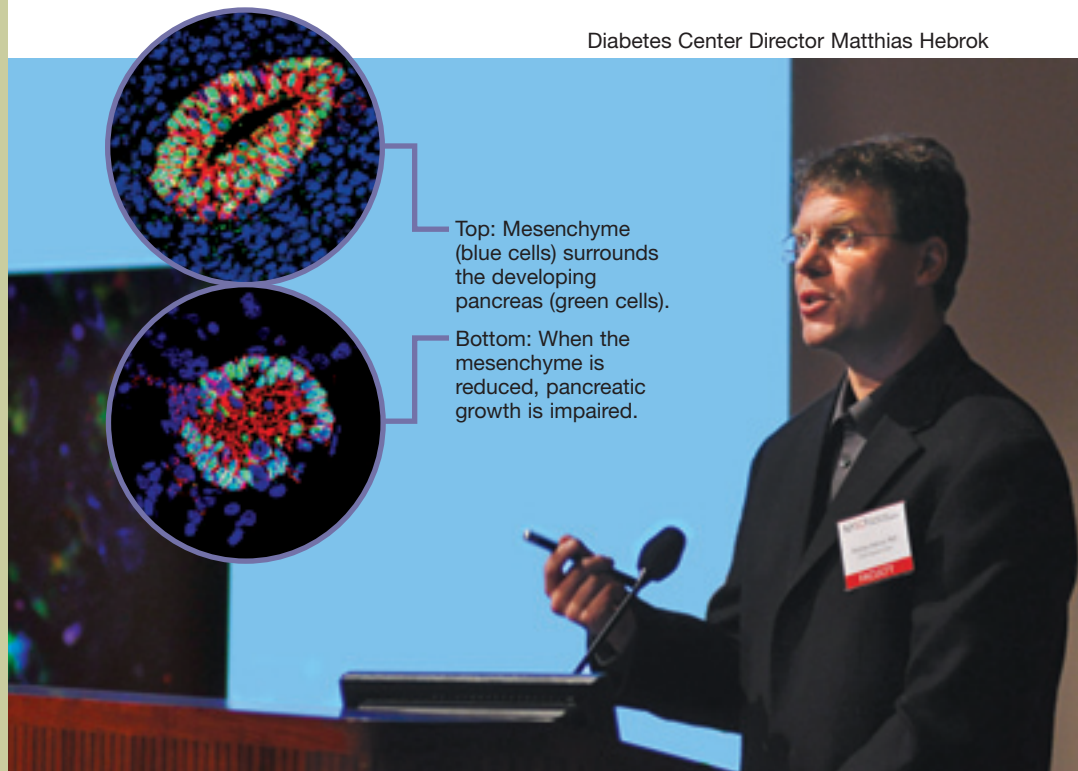
For a number of years, Hebrok and his colleagues have been studying the mesenchyme, a loose collection of cells in the embryo that surrounds the developing pancreas and eventually forms much of the body's connective tissue. To understand the role that the mesenchyme plays in pancreas development, they learned how to manipulate this tissue and make it

disappear at various stages. This allowed the team to take snapshots of the mesenchyme's role in development.

In lab animals, they found that the mesenchyme secretes chemicals that multiply and expand cells slated to become both hormone producing cells and beta cells. When this mesenchyme tissue is removed, even late in development, these embryos do not grow their full complement of beta cells.

This important discovery suggests that by identifying these mesenchymal signals, novel approaches may be created to help generate new, functional beta cells for replacement in the body. It may also lead to new ways to keep mature cells alive in adults.

Diabetes Center Director Matthias Hebrok



Top: Mesenchyme (blue cells) surrounds the developing pancreas (green cells).

Bottom: When the mesenchyme is reduced, pancreatic growth is impaired.

FROM THE DIRECTOR

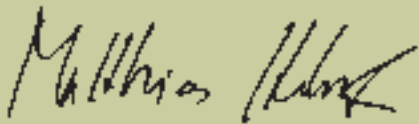
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As you know, our Diabetes Center team is considered a world leader in diabetes research. Focused on both type 1 and type 2 diabetes, our faculty and staff are experts in immunology, stem cells, genetics, inflammation and obesity, and we work together on multidisciplinary projects to develop novel therapeutics and cures. This often results in breakthrough discoveries, not likely to be achieved in silo-type research institutions.

To further encourage innovation, we have created an industry partnership with Sanofi, a respected pharmaceutical company headquartered in France. Together, our combined team of researchers will focus on beta cell drug targets for both type 1 and type 2 diabetes. We hope to launch similar industry partnerships in the near future.

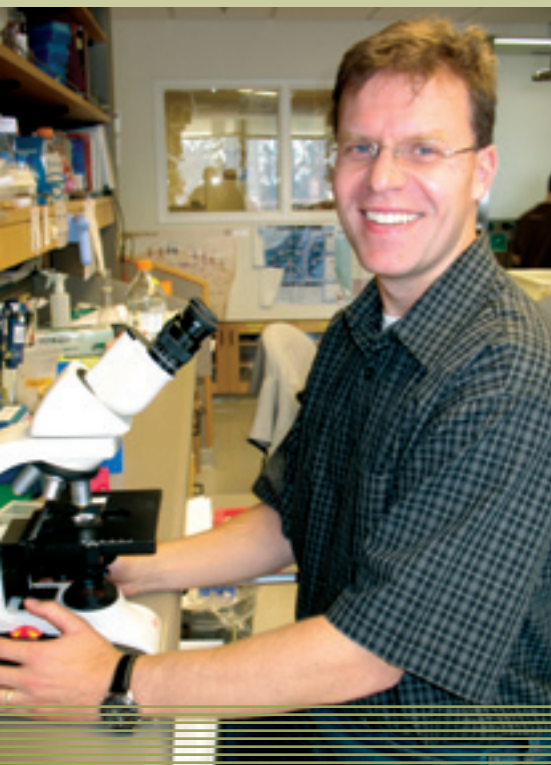
In closing, I wish you and your family great health and happiness this summer!

Sincerely,



Matthias Hebrok, PhD

Director, UCSF Diabetes Center
Hurlbut-Johnson Distinguished Professor
in Diabetes Research



Diabetes Center Launches New Industry Partnership with Sanofi

The Diabetes Center has created a new industry partnership with international pharmaceutical company Sanofi. The goal of this alliance is to identify novel therapeutic targets for the creation of new diabetes drugs that will improve the lives of those battling both type 1 and type 2 diabetes.

This pilot project will focus on beta cells and will operate under the oversight of an expert panel from UCSF and Sanofi. Three Diabetes Center faculty members are leading the effort: Director Matthias Hebrok, PhD, Michael McManus, PhD, and Michael German, MD. Together with Sanofi, the team will identify, assess and validate potential drug targets by using a UCSF library of roughly 100,000 small interference RNAs (siRNA) – molecules that play a crucial role in turning on and off genes, including the gene that produces insulin.



New Scientific Resource Created to Expedite Research Progress

Diabetes Center researcher Michael McManus, PhD, and his colleagues at UCSF, the Gladstone Institute for Cardiovascular Disease and Children's Hospital Oakland Research Institute have created a new, publicly available resource that will help researchers understand the importance of certain genes in causing diabetes and other diseases.

The resource consists of a library of gene-disrupting vectors that target and remove pieces of DNA, which encode for microRNAs – small bits of genetic material that regulate other genes. This resource also includes new stem cell lines and new strains of animal models that are missing microRNAs. These tiny genes are thought to be important regulators of human disease.



Michael McManus

UCSF Diabetes Center Leadership Council

Since the summer of 2001, the UCSF Diabetes Center Leadership Council has provided guidance, advocacy, and business and community expertise – in addition to critically important philanthropy – to support our multidisciplinary research, compassionate clinical care and cutting edge diabetes education.

In the past 11 years, research facilities have been created, patient clinics renovated, faculty members recruited, endowed chairs awarded, clinical care and education programs expanded – all of which created an environment where exciting scientific and clinical research discoveries have occurred.

We thank all of the members of the Leadership Council and all of our supporters and donors for your ongoing commitment to the Diabetes Center at UCSF.

Lisa Altman	J. George Hume	Thomas Parker
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New Clinical Trials



Two New Trials Underway as Part of TrialNet's "Pathway to Prevention" Campaign

The national research program called Type 1 Diabetes TrialNet recently screened their 100,000th family member for auto-antibodies as part of the Natural History Study, now known as the "Pathway to Prevention." UCSF is proud to have been selected as one of the first TrialNet Clinical Centers just over a decade ago.

For relatives of people with type 1 diabetes who are not yet diagnosed – but who are at risk for type 1 diabetes – there are now promising clinical trials available. For those found to be at intermediate risk of developing diabetes (25 percent chance of getting diabetes in the next five years), there is a trial introducing oral insulin. For those found to be at high risk (greater than 50 percent chance of diabetes in the next five years), there is a trial utilizing the anti-CD3 monoclonal antibody.

Clinical Study for Longstanding Type 1 Diabetes to Evaluate Residual Beta Cell Function

A new study has been launched that seeks to evaluate differences in the immune systems of those who have had type 1 diabetes for five or more years and who still make some insulin, versus those with type 1 diabetes who do not make insulin. It will also establish a blood bank for future studies of type 1 diabetes.

Led by Pediatric Diabetes Program Director Steve Gitelman, MD, and Endocrine Fellow Hilary Thomas, MD, the study seeks volunteers who are:

- eight years of age or older who have had type 1 diabetes for five or more years;
- and have a hemoglobin A1c less than 9.5 percent.



Steve Gitelman and Hilary Thomas

Thomas is excited to be leading this clinical study since she knows what it is like to have longstanding type 1 diabetes – her sister was diagnosed at age two and has been living with the disease for 34 years. "The commitment that my sister has had to make to take care of herself on a daily basis never ceases to amaze me," she says. Thomas received her undergraduate degree from Dartmouth and her medical degree from Emory, and completed her medical internship and residency at Johns Hopkins. She joined UCSF in 2010.

More information on these studies may be found on the clinical trials section of our website, www.diabetes.ucsf.edu/clinicaltrials, or by contacting Kathleen Fraser, 415/353-9084, kfraser@diabetes.ucsf.edu.

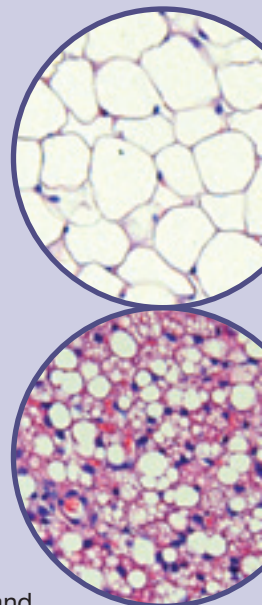
Increase Brown Fat, Burn More Calories?

Shingo Kajimura, PhD, has discovered how to re-engineer ordinary white fat into brown fat to help the body burn more calories and lose weight.

It is believed that brown fat evolved in man as a protection from the cold. Not only is the amount of brown fat in the body inversely proportional to the likelihood of obesity, we now know that the human body is capable of creating new brown fat cells throughout life.

In lab animals, Kajimura and his colleagues have discovered that a common class of drugs given to people with diabetes called PPAR-gamma ligands interacts with the protein PDRM16, enabling the conversion of white fat cells to brown fat cells. This discovery could lead to the creation of new weight loss drugs in the future.

Kajimura, a new faculty member of the Diabetes Center, is an accomplished researcher in the regulation of fat cell development and the molecular networks involved in the development of obesity-linked diseases such as type 2 diabetes and cardiovascular disease.



Above: White and brown fat cells
Below: Shingo Kajimura



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NEWS

from the
Diabetes Center
at UCSF



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Diabetes Teaching Center Launches Mobile App to Complement Successful Education Website – www.deo.ucsf.edu

“Education is a fundamental part of diabetes therapy,” says Martha Nolte Kennedy, MD, medical director of the Diabetes Teaching Center. In this country alone, more than 26 million people have diabetes and 79 million more have pre-diabetes, yet only 4,000 US endocrinologists

specialize in treating the disease.

Unfortunately, very few individuals with diabetes can expect to see a diabetes specialist – but everyone with internet access

may now receive education about diabetes – thanks to the innovations of the Diabetes Teaching Center. Kennedy and her team have launched a FREE mobile application, DiabetesIQ, that helps patients explore their knowledge of diabetes. Users take quizzes that provide extensive feedback, solve visual puzzles, progress through multiple game levels and compare results with other contestants. DiabetesIQ was just awarded Outstanding Mobile Application in the 2012 MobileWebAward Competition. It works with iPhone, iPad or iPod touch devices running iOS 4.0 or later, or Google Android 1.6 and higher – and is available on the Apple iTunes store and Google Android market.



Martha Nolte
Kennedy

DiabetesIQ was created using the robust educational content found on Diabetes Education Online, www.deo.ucsf.edu. Diabetes Education

Online is a comprehensive diabetes self-management education program that covers the American Diabetes Association’s recommended topics and more. The website mirrors the successful teaching program presented to thousands of patients at

UCSF over the last 30 years.

In recognition of their educational innovations, the Diabetes Teaching Center was named a Technical Innovation Finalist in the *San Francisco Business Times* Health Care Heroes Awards. Congratulations to Kennedy and her team for this well-deserved recognition.



DiabetesIQ is a FREE mobile app for you to explore your diabetes knowledge and track progress. Download DiabetesIQ by visiting diabetesiq.quantiacare.com with your mobile browser.