



FROM THE DIRECTOR: A Message from Matthias Hebrok

As we launch our 11th year of the Diabetes Center at UCSF, I am proud of our significant progress toward preventing, treating and ultimately curing diabetes for you and your loved ones.

In the following pages you'll read that we are rapidly translating our scientific research discoveries into numerous clinical trials, moving us significantly closer to deliverable therapies. We're continuing our research emphasis on immune tolerance and autoimmunity, stem cells and islet cell regeneration, inflammation and diabetes, obesity and metabolism, and we're focusing on both type 1 and type 2 diabetes. We're pleased to welcome Suneil Koliwad, MD, PhD, to our faculty, an expert in inflammation and the role it plays in diabetes, and we're thankful for our new lab space in the recently

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Trailblazers in Stem Cell Research Have New Home on Parnassus Campus

While remaining key faculty members of the Diabetes Center, three of our renowned stem cell researchers, Mike German, MD, Eric Rulifson, PhD, and Miguel Ramalho-Santos, PhD, have moved their research labs into UCSF's new, state-of-the-art Ray and Dagmar Dolby Regeneration Medicine Building on the UCSF Parnassus campus.

This building serves as the new headquarters of the Eli and Edythe Broad Center of Regeneration Medicine and Stem Cell Research at UCSF. The \$123 million building, paid for with state and private funds, is an outgrowth of California's effort to advance stem cell research in the face of more than a decade of restrictive federal funding policies. The idea for the building was conceived in 2004 by leaders of the California Institute for Regenerative Medicine (CIRM), the state agency established to administer the \$3 billion fund for stem cell research made possible through California Proposition 71.

"We are pleased to have been able to help UCSF create this extraordinary building that is now home to 25 of the top stem cell laboratories in the United States," said Eli Broad, founder of The Eli and Edythe Broad Foundation, at the opening ceremony for the new building.

Designed by renowned architect Raphael Viñoly, the structure is a series of four split-level floors with terraced grass roofs. Open labs flow into each other, with office and lounge areas located on the routes between labs, promoting interaction throughout the building.

The opening of the building is a fitting metaphor for the advances that UCSF, and the field at large, have made in recent years, noted Arnold Kriegstein, MD, PhD, director of the Eli and Edythe Broad Center of Regeneration Medicine and Stem Cell Research at UCSF. In 1981, UCSF scientist Gail Martin, PhD, co-discovered embryonic stem cells in mice – and named them. Beginning in the late 1990s, UCSF was one of two

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Mike German, Miguel Ramalho-Santos and Eric Rulifson at their new home; the terraced green roof of the new Ray and Dagmar Dolby Regeneration Medicine Building.





Innovative Breakthrough Research Day

In April, members of the UCSF Diabetes Center's Investor Circle were invited to attend a special day of research presentations and lab tours featuring members of our basic and clinical research teams. Not only did Investor Circle members meet key members of our faculty, they were able to meet our team "behind the scenes" – our young and talented post-doctoral fellows and research staff. A highlight of the day was a tour of the new Ray and Dagmar Dolby Regeneration Medicine Building on the Parnassus campus.



If you'd like to hear how you can serve as a member of the Investor Circle and be invited to exclusive, upcoming programs, please contact Suzanne Ritchie: 415-476-6334; sritchie@support.ucsf.edu



At the new regeneration medicine building: Bruce Adams gives a tour of the diabetes stem cell lab (middle photo); Caroline Blanckenberg, Susan Gillfillan, Richard Wagner and Robin Marks on one of the terraced roofs (bottom photo)

UCSF Diabetes Center Leadership Council

Since the summer of 2001, this organization 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 10 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 basic 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 support of the Diabetes Center at UCSF.

Leadership Council Members

Lisa Altman	Robert N. Klein II
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New Home *Continued from front page*

U.S. universities, along with the University of Wisconsin, that pioneered the human embryonic stem cell field.

We are pleased to report that this move has also allowed us to begin the renovation of our Diabetes Center's 10th floor lab space in the Health Sciences West (HSW) Building – a task that hasn't been pursued for over 30 years, since the days when recombinant DNA technology was employed to create human insulin.

From the Director *Continued from front page*

opened stem cell research building housing Diabetes Center researchers Mike German, MD, Eric Rulifson, PhD, and Miguel Ramalho-Santos, PhD.

All of our efforts in the Diabetes Center reflect our intense dedication to one mission: to advance the care and treatment of patients with type 1 and type 2 diabetes worldwide so that we may achieve the goal of bringing an end to the disease. Our team of more than 150 faculty and staff deliver expert clinical care, conduct groundbreaking research, and educate both the public and the next generation of health care practitioners about diabetes. Without your enthusiastic interest in our research and clinical activities – and your involvement and support – I'm convinced we would not be where we are today in achieving breakthroughs that will help to improve the quality of life of those living with this disease.

We in the Diabetes Center are fortunate to be working in a world class institution among renowned researchers and clinicians. As you may have heard, endocrinology and diabetes care at UCSF is ranked fourth in the nation by *U.S. News & World Report* in its recent 2011 America's Best Hospitals Survey. UCSF Medical Center ranks seventh among the nation's top 10 premier hospitals for the tenth consecutive year and is ranked first in Northern California. I'd like to take this opportunity to thank our accomplished clinicians and researchers for their tremendous dedication to our patients – both adults and children living with diabetes.

I am often asked by patient families what we need to expedite our research efforts to more rapidly take laboratory bench research to the clinic. The quick answer is additional financial support. As a public institution in this era of budget cutbacks and reduced government and private research grants, we are finding that we need to rely more and more on philanthropy to sustain our research program and to be able to respond quickly to emerging scientific opportunities.

On behalf of all of my colleagues, I'd like to thank each of you for your ongoing support of the Diabetes Center and for being our partner in our quest for more effective treatments and cures.

Sincerely,

Matthias Hebrok, PhD

Director, UCSF Diabetes Center

Hurlbut-Johnson Distinguished Professor in Diabetes Research

Diabetes Center Recruits Physician Researcher

Expert Studies Inflammation's Role in Diabetes

Suneil Koliwad, MD, PhD, formerly of the Gladstone Institute of Cardiovascular Disease, has joined our UCSF Diabetes Center faculty to continue his exciting research involving inflammation and the role it plays in diabetes.

Koliwad was appointed to the newly created Gerold Grodsky, PhD/JAB Chair in Diabetes Research by the dean of the UCSF School of Medicine, Sam Hawgood, MBBS. Thanks to a generous member of the Diabetes Center Leadership Council, this chair honors longtime diabetes researcher and emeritus faculty member,



Gerold Grodsky

Gerold Grodsky, PhD, who is well known for developing a way to measure insulin in the blood and determining the two phases of insulin release, among other discoveries.

A practicing endocrinologist, Koliwad is an expert in understanding how the cellular balance of fat cells – called adipocytes, and macrophages – the body's scavengers of dead cells, contributes to the development of inflammation in chronic obesity. When individuals become overweight, their adipocytes fill up with dietary fat and die. When the macrophages dispose of these dead cells, they become inflamed and secrete immune factors called cytokines. These cytokines over time help to cause insulin resistance, diabetes and heart disease.

CHRONIC INFLAMMATION: At right, a photo of a section of fat taken from a mouse fed a chronically high-fat diet, showing an adipocyte (fat cell) being surrounded and engulfed by a ring of macrophages, which have undergone inflammatory activation. These so-called crown-like structures are a hallmark sign of chronic inflammation within the fat tissue in the setting of diet-induced obesity in both mice and humans.



By increasing the amount of an enzyme called DGAT1 through bone marrow transplantation in mice, Koliwad and his colleagues are able to generate mice with macrophages that can store more fat. These altered macrophages are not only protected from the inflammatory response to a high fat diet, they protect obese mice from developing serious complications, including insulin resistance. Because humans possess DGAT1 in macrophages and adipocytes quite similar to that seen in mice, these results provide a new avenue in which to explore fresh ways to prevent type 2 diabetes in obese people.

In addition, as an attending physician in the endocrinology and diabetes clinics at San Francisco General Hospital (SFGH), Koliwad sees diabetes patients, supervises rotating UCSF endocrinology fellows, residents and medical students, and has helped to develop outpatient treatment guidelines for types 1 and 2 diabetes for use at SFGH and its affiliated clinics.

We are delighted to have such an expert physician researcher join our team. Welcome, Suneil Koliwad!



Investing in Hope – Ensuring the Future

One way to continue supporting the fight against diabetes at UCSF is through a charitable bequest. A charitable bequest is made by including a provision in your will or revocable trust that describes your desire to provide a gift to the UCSF Diabetes Center once you are deceased. A bequest allows you to retain control and use of your property during your lifetime. Also, because a charitable bequest is a revocable commitment, you have the peace of mind of knowing that if your circumstances change, you can revise your plan. A bequest to support research would be as follows:

“I give to the University of California, San Francisco Foundation, a California non-profit public benefit corporation, [the sum of \$_____] or [the residue of my estate] or [___% of the residue of my estate] to be used for research into the causes, treatment and prevention of diabetes in such manner as the director of the University of California, San Francisco Diabetes Center shall determine.”

Bequests may be made for general, unrestricted support or may be directed to a specific type of research or program, such as stem cell research, the Diabetes Teaching Center or the Pediatric Diabetes Program.

For more information, contact Suzanne Ritchie: 415/476-6334; sritchie@support.ucsf.edu

ADDRESS SERVICE REQUESTED

Visit our Diabetes Teaching Center's highly acclaimed educational website, **Diabetes Education Online:**
www.deo.ucsf.edu

Learn more about our clinical trials in diabetes:
www.diabetes.ucsf.edu/clinicaltrials

Take advantage of our free educational program for Bay Area employers:
www.diabetes.ucsf.edu/community

NEWS from the Diabetes Center at UCSF



SUMMER 2011

For more information on any of these stories, contact
Suzanne Ritchie: 415/476-6334; sritchie@support.ucsf.edu

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New Type 1 Clinical Research Studies Launched

A number of new clinical studies using investigational drugs for type 1 diabetes have been launched by the UCSF Pediatric Diabetes Clinical Research Program under the leadership of Steve Gitelman, MD. Investigational drugs are those that are not approved for use in diabetes by the U.S. Food and Drug Administration (FDA).

One novel study involves the immune system's T cells. There are different types of T cells, including T cells that unnaturally attack and destroy the insulin-producing beta cells in type 1 diabetes, and T cells called regulatory T cells that help call off the attack. Gitelman's goal is to bolster the performance of the regulatory T cells, or "Tregs," and therefore end the misdirected immune system attack on insulin-producing beta cells. This study is open to adults ages 18 to 35 who are within two years of diagnosis.

A second study involving T cells aims to eliminate the T cells that attack insulin-producing beta cells, while increasing the number of Tregs, thereby resetting the balance of T cells. Gitelman and his colleagues are combining an antibody treatment anti-thymocyte globulin (brand name Thymoglobulin®), which is FDA approved to prevent organ rejection in kidney transplant patients, with granulocyte colony-stimulating (brand name Neulasta®), which is FDA approved to boost white blood cell counts in patients receiving chemotherapy. In mouse models of diabetes, this combination appears to be even more effective than Thymoglobulin alone. They hope the same will be true in people. This clinical trial is open to individuals ages 16 to 45 who are within two years of diagnosis.

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. Family members should take a simple blood test which screens for the presence of diabetes-related autoantibodies that may appear years before type 1 diabetes develops. This screening is part of a national research program called Type 1 Diabetes TrialNet and is being conducted to help understand more about the development of this disease and to look at ways to delay or prevent it. 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.

For more information on these studies or other clinical research being conducted at UCSF, contact Kathleen Fraser: 415/353-9084; kfraser@diabetes.ucsf.edu