WINTER 2016 | 2017

# News from the Diabetes Center at UCSF

Diabetes Center
University of California San Francisco

*Alex Marson, MD, PhD, Assistant Professor, Diabetes Center and Department of Microbiology and Immunology*

> "We find that we're right at the intersection of two fields that are exploding: T cell-based immunotherapy… and genome modification. Putting them together has been really exciting."
>
> Alex Marson, MD, PhD

## New Faculty Highlight

This year we were delighted to offer a full-time faculty position to Alex Marson, MD, PhD. Dr. Marson has worked closely with our team since 2013, when he joined the UCSF Sandler Fellows Program, a donor-funded initiative that brings exceptionally promising young scientists to UCSF to establish independent research programs with the sole mandate to pursue their best science. We are thrilled that Dr. Marson is now a permanent member of the Diabetes Center family.

Dr. Marson attended medical school at Harvard University and earned a PhD in biology from the Massachusetts Institute of Technology. Recognized as a rising star in the field of immunology, he was selected for three prestigious awards in 2016: the American Society of Clinical Investigation Young Physician-Scientist Award, the Burroughs Wellcome Fund Career Award for Medical Scientists, and the National Institute on Drug Abuse/National Institutes of Health Avenir Award.

*(continued on page 3)*

> “Donors like you make it possible for us to pursue research projects and initiatives that are ineligible for funding from other sources.”
>
> Matthias Hebrok, PhD

## FROM THE DIRECTOR

People are at the heart of everything we do in the Diabetes Center.

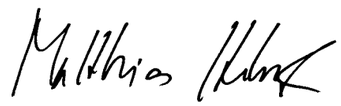
Patients and their families – like those we see in our clinics or who participate in our diabetes camps – inspire our work and instill in us a sense of urgency to convert our findings into better therapies.

Young scientists – such as new faculty member Alex Marson, MD, PhD – contribute novel perspectives and challenge us to develop fresh strategies for treating, and even preventing, diabetes.

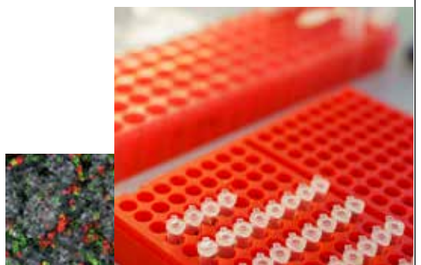
Donors like you make it possible for us to pursue research projects and initiatives that are ineligible for funding from other sources. Often, the pilot data we collect from these efforts ultimately enable us to launch clinical trials like the two highlighted here.

As we reflect on the past year, our team in the Diabetes Center has much to be grateful for, including all of the people who contribute to our successes. Thank you for your support and friendship.

With best wishes for a happy holiday season,



Matthias Hebrok, PhD
*Director, Diabetes Center at UCSF*
*Hurlbut-Johnson Distinguished Professor in Diabetes Research*





# New Faculty Highlight *(continued from front page)*

Dr. Marson recently sat down with us to discuss his research program and reasons for choosing to begin his career at UCSF.

**Q: What is your area of focus, and what do you hope to achieve with your research?**

A: My lab’s big-picture goal is to understand how genetics control the immune system and contribute to autoimmune diseases, including type 1 diabetes. We specifically focus on T cells and the underlying mechanisms that cause them to either attack the body’s own cells — as is the case in type 1 diabetes — or protect the cells from immune assault.

**Q: What are the implications of your work for improved treatments for diabetes?**

A: Our hope is that once we define the genetic causes of autoimmune diseases like type 1 diabetes, we will be better positioned to develop cell-based therapies to treat them. For instance, T cells circulate in the blood, so we envision the day when we can easily gather T cells from a patient with type 1 diabetes, edit the cells’ genomes to make them prevent attacks on beta cells, then return the cells to the body to exert therapeutic effects. Jeff Bluestone, PhD, Qizhi Tang, PhD, Stephen Gitelman, MD, and others in the Diabetes Center are already pursuing these possibilities, and my team is contributing to these efforts through our work with CRISPR-Cas9, which provides us with a powerful new tool to study and modify T cells.

**Q: What is CRISPR-Cas9?**

A: CRISPR-Cas9 is a genome-editing tool that makes it possible to easily modify genetic information in almost any organism. However, for many years, genome editing in human T cells proved to be a notable challenge, but one that I was eager to tackle when I arrived at UCSF. Supported by a philanthropic gift from Jake Aronov and working in collaboration with the Innovative Genomics Initiative — a joint UC Berkeley-UCSF program co-directed by UC Berkeley’s Jennifer Doudna, PhD, who pioneered the use of CRISPR-Cas9, and Jonathan Weissman, PhD, professor of cellular and molecular pharmacology at UCSF — my team and I devised a new strategy to precisely modify human T cells using CRISPR-Cas9. There are a lot of potential therapeutic applications, and we want to make sure we’re driving this as hard as we can.

We find that we’re right at the intersection of two fields that are exploding: T cell-based immunotherapy for organ transplantation and diseases ranging from diabetes to cancer, and genome modification. Putting them together has been really exciting.

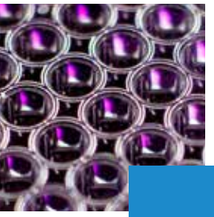
**Q: Why did you choose to start your career at UCSF?**

A: At other institutions, I was getting the message that young scientists had to pursue research that was considered “safe” in order to advance their careers. Here, I was told, “We’d like to bring you aboard to pursue your boldest ideas — the science that will have the biggest possible impact over the long run — and if it takes some time to build your program, that’s fine.” That was enough to really hook me, and I feel that it accurately describes my experience at UCSF thus far. UCSF and the Diabetes Center have invested a lot in me and have given me a long runway early in my career.

The other thing about UCSF — and this is almost a cliché at this point — is that it’s an incredibly collaborative environment. As soon as I arrived, people came into my office with ideas or had an open door when I had ideas. That has also made a big difference.

**Q: Beyond your research goals, what do you hope to accomplish now that you are a faculty member?**

A: I’m really looking forward to training the next generation of scientists. The graduate students UCSF attracts are unbelievably talented, and I’m fortunate to have four of them working on my team at the moment. It is a great honor to be in a position to be able to encourage and foster young people who have a shared desire to find answers to biological challenges, with an eye toward applications for therapies. These trainees are another reminder of how lucky I am to be in the UCSF environment. ■



*Stephen Gitelman, MD, leader of the Diabetes Center's clinical trials program and the Mary B. Olney, MD/ KAK Distinguished Professor in Pediatric Diabetes and Clinical Research, confers with a colleague.*

**Clinical Trials**

# Two New Studies of Immunotherapies Aim to Protect Beta Cells

Our investigators lead the field's efforts to develop cell-based therapies for type 1 diabetes. One promising approach created in our laboratories involves isolating and expanding patient-specific regulatory T cells, or Tregs – the immune cells that may ultimately defend beta cells against destruction – and reinfusing them back into the affected individual.

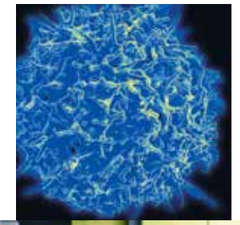


Late last year, in the first US safety trial of this novel form of immunotherapy for type 1 diabetes, the Bluestone Lab and our clinical trials team — led by Dr. Gitelman, the Mary B. Olney, MD/KAK Distinguished Professor in Pediatric Diabetes and Clinical Research — provided evidence of safety and tolerability of autologous expanded Treg cell therapy in study participants receiving infusions of as many as 2.6 billion Tregs. This small initial study was not designed to fully assess effectiveness of the therapy, but the clinical trials team did observe that many of the participants had no decline in beta-cell function during the two years of observation after the cell infusion.

The encouraging results from the study supported the development of two additional trials to test whether Tregs can stop further destruction of beta cells and preserve naturally occurring insulin production in people recently diagnosed with type 1 diabetes. The new trials, highlighted below, are currently underway and actively enrolling patients.

**TREX STUDY:** In this Phase II study, we are recruiting adolescents between the ages of 12 and 17 who have been diagnosed with type 1 diabetes within the previous three months. Our team will isolate and purify each participant's Tregs from his or her own blood sample, expand the Tregs approximately a thousandfold, and reinfuse the cells back into the same patient.

**TILT STUDY:** Open to adults between the ages of 18 and 45 who have been diagnosed with type 1 diabetes within the previous two years, this study will assess the safety of a combination therapy of Tregs and the protein interleukin-2 (IL-2). Part of the immune system's natural defense system, IL-2 is a protein that regulates the activities of cells responsible for immunity and has been found to be a crucial growth factor for Tregs. By combining Tregs and IL-2, investigators hope to create synergies that will help stabilize or boost the effectiveness of Tregs once they are given to the recipient. ■



If you or someone you know is interested in participating in one of these studies, please contact the Diabetes Center at 844-T1D-UCSF (844-813-8273) or clinicalresearch@diabetes.ucsf.edu.

# philanthropy

Our work would not be possible without the support of a community of dedicated individuals and families who share in our mission. We are grateful for every gift we received in support of our work this year and are honored to announce the following selection of gifts from longtime friends.

- A **$1.5 million pledge from Bruce Braden** will support the coordinated research of Drs. Mark Anderson, the Robert B. Friend and Michelle M. Friend Endowed Chair in Diabetes Research; Jeff Bluestone, the A.W. and Mary Margaret Clausen Distinguished Professor in Metabolism and Endocrinology; Michael German, the Justine K. Schreyer Endowed Chair in Diabetes Research; and Matthias Hebrok, the Hurlbut-Johnson Distinguished Professor in Diabetes Research, into the causes and treatment of type 1 diabetes. The investigators will use novel technologies and techniques to delve further into the cellular and molecular processes that lead to the development of diabetes, as well as identify and test new strategies for preventing and treating it.

- A **$300,000 gift from Dayton and Sheri Coles** created the Innovation Award to fund promising pilot research projects in the Diabetes Center. The 2016-2017 recipients are Julie Sneddon, PhD, and Gregory Ku, MD, PhD. Dr. Sneddon studies the cellular microenvironment and supporting tissues that guide the development of insulin-producing beta cells and sustain their functionality. Dr. Ku is interested in enhancing our understanding of how the secretion of insulin is regulated.

  Reflecting on their gift, Mr. and Mrs. Coles said, “Testing novel ideas and potentially paradigm-shifting hypotheses drives scientific progress forward. We are thrilled to support the innovative work of outstanding scientists in the UCSF Diabetes Center.”



Our donors are our partners, and we are grateful for every gift to our diabetes research, patient care, and educational programs.

- An investment of **$750,000 from Bob and Michelle Friend** will establish a dedicated bioinformatics program in the Diabetes Center. The program will enable our team to use vast amounts of valuable patient data and state-of-the-art computer technology to develop fresh approaches for better predicting, preventing, and treating diabetes.

  Describing their enthusiasm for the bioinformatics program, Mr. and Mrs. Friend said, “The advances the Diabetes Center has made in the last several years have been heartening and give us such hope for the future. We are proud to support the team’s efforts to further develop computational approaches to diabetes research.”

- A gift of **$225,000 from Michelle Griffin and Thomas Parker** will support the Cameron Fellowship in Pediatric Diabetes. The fellowship will facilitate the training of a pediatric endocrinology fellow in pediatric diabetes, providing the fellow with the tools needed to deliver the best care to current and future pediatric diabetes patients and laying the foundation for a successful academic career.

  This will be the second Cameron Fellow supported by Ms. Griffin and Mr. Parker. The first, Andrea Gerard Gonzalez, MD, is currently director of the Latino Care Program at the Barbara Davis Center for Diabetes in Colorado. Explaining the motivation behind their gift, they said, “We were so pleased with Dr. Gerard Gonzalez’s success that we jumped at the chance to offer another future pediatric endocrinologist the opportunity to learn from Saleh Adi, MD, director of the Madison Clinic for Pediatric Diabetes at UCSF, and model his high level of patient care for another type 1 diabetes community.”

- In late 2015, a portion of a **$5 million pledge from The Joseph & Vera Long Foundation** established the Joseph & Vera Long Foundation Endowed Professorship in Diabetes and Obesity. This year, the Diabetes Center’s Allison Xu, PhD, was named the inaugural beneficiary of the professorship. The crucial resources from the endowment will support Dr. Xu’s research on the neuronal circuits in the brain that regulate how much food we take in – an area of study that is key to developing strategies for combating obesity and type 2 diabetes. ■

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> "Volunteering at Campamento Familiar was a life-changing experience that I will always treasure. It taught me a lot and really opened my eyes. The families were amazing and so grateful."

Alondra Zambrano
Patient and volunteer

## Patient Care

# Campamento Familiar en Español

In partnership with Diabetes Youth Families (DYF) and the UCSF School of Nursing, the team in the Madison Clinic for Pediatric Diabetes at UCSF organized its first camp for monolingual Spanish-speaking families in October 2015. The camp at Redwood Glen in Loma Mar, Calif., was attended by 21 families — 51 children and 33 adults — and provided a much-needed supportive experience and crucial diabetes education for a largely underserved population. Please visit **vimeo.com/166852494** to hear firsthand about the wonderful impact of the camp on the families who participated.

Given the success of the camp and the long waiting list of interested families, the Madison Clinic and its partners hosted the second Spanish language camp October 28-30, 2016. More than 24 families — including 13 from the Madison Clinic — attended, and six patients served as staff members. The clinic team plans to make this camp an annual event.

For more information about the Diabetes Center at UCSF, contact Valerie Wingfield at (415) 502-8302 or Valerie.Wingfield@ucsf.edu.

Follow the Diabetes Center online at diabetes.ucsf.edu.

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