NEWS from the Diabetes Center at UCSF

WINTER 2009/2010

Websites Created to Help Support Diabetes Community

This fall, the Diabetes Center launched a new website: **www.diabetes.ucsf.edu**. After conducting extensive market research, the faculty and staff have created a website that is much more informative and "user friendly" for patients, donors, the medical community and the public at large.

Features of the new website include a pediatric diabetes education section that provides downloadable documents on a variety of subjects, and an expanded clinical trials section for type 1, type 2 and non-diabetes clinical studies.

This website also serves as a companion site to the Diabetes Teaching Center's educational website Diabetes Education Online: **www.dtc.ucsf.edu**. This comprehensive diabetes self-management education program mirrors a successful teaching program given to thousands of patients at UCSF over the last 30 years. Not only is there a complete, separate curriculum for both type 1 and type 2 patients, there are also problem-solving sections including self-assessment quizzes and printable handouts of key tables, charts and illustrations.

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Efforts to Stop Beta Cell Destruction

New Trials Hope to Prevent or Delay Onset of Type 1 Diabetes

To cure type 1 diabetes, the insulin-producing beta cells must be protected from being attacked by the body's immune system. Fortunately, researchers and clinicians of the UCSF Diabetes Center have become national leaders in helping the body tolerate its own beta cells.

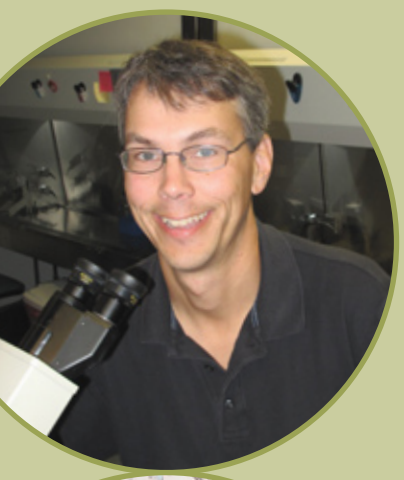
Nearly 20 years ago, Center Director Jeffrey A. Bluestone, PhD, created a drug called anti-CD3, a powerful monoclonal antibody that stops beta cell destruction. After years of human clinical research in newly diagnosed type 1 patients, plans are underway to administer this drug to "pre-diabetics" – those testing positive for antibodies but who still have beta cell function. It is hoped that this treatment may help prevent or delay the onset of type 1 diabetes.

Additionally, Pediatric Diabetes Program Director Stephen E. Gitelman, MD, has partnered with the National Institutes of Health (NIH)-funded Immune Tolerance Network to launch the START trial (Study of Thymoglobulin to Arrest Type 1 Diabetes). The national study involving ATG, or anti-thymocyte globulin, will see if this drug can halt the progression of new onset type 1 diabetes. Gitelman hopes to recruit 66 volunteers, 12 to 35 years old, within 100 days of diagnosis. Thymoglobulin, an FDA-approved drug used in organ transplantation, has been used to treat other autoimmune diseases. It is suspected that it may work in diabetes in at least one of two ways: by eliminating destructive immune cells from the blood stream or by changing how the remaining immune cells work. The START trial will test whether Thymoglobulin can "reset" the immune system so that immune cells accept the beta cells rather than continue to attack them.

Stephen E. Gitelman (left) and Jeffrey A. Bluestone; islet cells on a slide (inset)

ATG is also being used in the Diabetes Center's islet cell transplant trials involving people with long-established diabetes. *(See story inside.)*

For more information on the Diabetes Center's many type 1, type 2 and non-diabetes clinical trials, visit www.diabetes.ucsf.edu/clinical-care-education/clinical-trials, or call Kathleen Fraser, clinical trials recruitment coordinator, at 415/353-9084.



Congratulations Mark Anderson *(top photo)* for being awarded academic medicine's highest honor and thank you Bob and Michelle Friend *(above)* for your substantial investment to support an outstanding medical researcher and clinician.

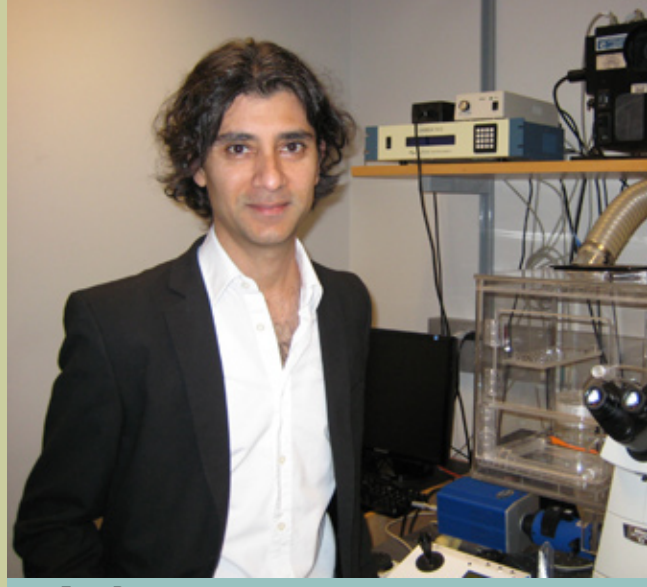
New Endowed Chair Awarded to Physician Researcher

Mark S. Anderson, MD, PhD, is the recipient of the newly established Robert B. Friend and Michelle M. Friend Endowed Chair in Diabetes Research. This chair was made possible by a generous gift from longtime Diabetes Center supporters Bob and Michelle Friend. Anderson is one of only a handful of researchers around the world making significant progress in solving the problem of autoimmunity by exploring the genetic determinants of autoimmune disorders.

A Phi Beta Kappa biology major from Northwestern University, Anderson received his PhD in immunology and his medical degree from the University of Chicago. He continued his studies as both a clinical fellow and a research fellow in endocrinology at Harvard University. He is board certified in internal medicine and endocrinology.

In less than 10 years, Anderson has become a respected leader in type 1 diabetes research. This early success prompted his election to the American Society for Clinical Investigation, one of the nation's oldest and most respected medical honor societies that pay tribute to young physician-scientists. Because members must be 45 or younger at the time of their election, membership reflects accomplishments relatively early in one's career.

Not only will Anderson's research benefit millions with type 1 diabetes, it has the potential of helping millions more who are suffering from numerous other autoimmune diseases including rheumatoid arthritis, multiple sclerosis and lupus. Anderson also sees patients in the adult clinic where he helps to bring research from the laboratory "bench" to the patient's bedside through his translational and clinical research efforts.



Feroz Papa

Physician Researcher Studies Beta Cell Death in Type 2 Diabetes

Diabetes Center/QB3 researcher and San Francisco General Hospital endocrinologist Feroz Papa, MD, PhD, is fascinated with the emergency care that is provided by a cell's endoplasmic reticulum, or ER – coincidentally the same abbreviation and even the same function as a hospital emergency room. The ER isolates sick proteins in the cell and attempts to revive them. Papa believes that during the gradual development of type 2 diabetes, the stress of processing large amounts of insulin will overwork the ER of a beta cell. Eventually the ER sends out death signals that result in beta cell destruction and ultimately type 2 diabetes.

An NIH New Innovator Award grantee, Papa has uncovered a new class of drugs that may prevent the death of stressed cells. In the August issue of *Cell,* Papa described how a cellular protein called IRE1 serves as a life-or-death switch for cells experiencing ER stress. He and his UCSF collaborator, Scott Oakes, MD, decided that the best way to reduce cell death due to ER stress is to create drugs that target IRE1. These drugs, called Kinase Inhibitory RNAse Attenuators, may protect cells by reducing the death signals being sent by IRE1.

Said acting NIH Director Raynard Kington, MD, PhD, "Dr. Papa's discovery opens up promising new approaches for saving crucial insulin-producing cells. This is exactly the type of research that the New Innovator Program was designed to foster."

Major Achievements in Islet and Cellular Transplantation

When Jeffrey A. Bluestone, PhD, and Gregory L. Szot arrived at UCSF nearly a decade ago from the University of Chicago, they were determined to accelerate the field of pancreatic islet transplantation. They succeeded in establishing one of the first, fully certified, state-of-the-art transplantation facilities of its kind, the UCSF Islet and Cellular Transplantation Facility. Szot is the facility's technical director.

In islet transplantation, healthy islets are taken from the pancreas of a deceased organ donor. Pancreatic islets – or islets of Langerhans – are found throughout the pancreas. They are made up of several types of cells, including insulin-producing beta cells, which are destroyed by the immune system in someone with type 1 diabetes. It's this insulin that helps the body convert glucose to energy. After the pancreas is removed from the donor, the islets are purified and transferred into a type 1 diabetic recipient. Once implanted, the beta cells in these new islets begin to make and release insulin.

Gregory L. Szot

Szot and his colleagues (J. Lang, M. Lee and V. Nguyen) significantly improved the islet isolation and preparation procedure in response to a possible bovine contamination of the enzyme once used by most islet transplantation centers. A new enzyme formulation optimized by Szot and his team is now being used by the international Clinical Islet Transplantation Consortium and other transplant centers around the country. For these significant accomplishments, the American Diabetes Association recently recognized Szot with a Scientific Achievement Award.

In its 2008 annual report, the Collaborative Islet Transplant Registry, which is funded by the National Institute of Diabetes and Digestive and Kidney Diseases, presented data from 33 islet transplant programs on 325 patients who received transplants between 1999 and 2007. According to the report, more than two-thirds of recipients achieved insulin independence – defined as being able to stop insulin injections for at least 14 days – during the year following transplantation. Other data showed that insulin independence typically decreases over time. However, one year after achieving insulin independence, 71 percent remained free of the need for insulin injections. At a two-year follow-up, the number dropped to about 52 percent. The report described other benefits of islet transplantation, including substantially reduced need for insulin among recipients who still required injections, improved blood glucose control, and greatly reduced risk of episodes of severe hypoglycemia.

Diabetics are more susceptible to episodes of severe hypoglycemia due to a condition known as hypoglycemia unawareness in which a person is unable to recognize that his or her blood glucose levels are too low. In a report on the Immune Tolerance Network's international islet transplantation study, researchers emphasized the value of transplantation in reversing hypoglycemia unawareness. The study showed that even partial islet function after a transplant can eliminate this condition.

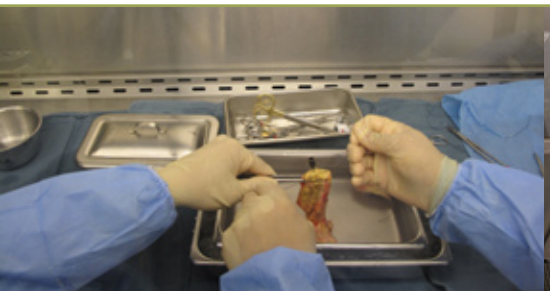
Center supporter Joanne Kagle (right), with (from left) her daughters Grace and Kelsey and their friend Nicole Gonzales at a recent visit to the UCSF Islet and Cellular Transplantation Facility

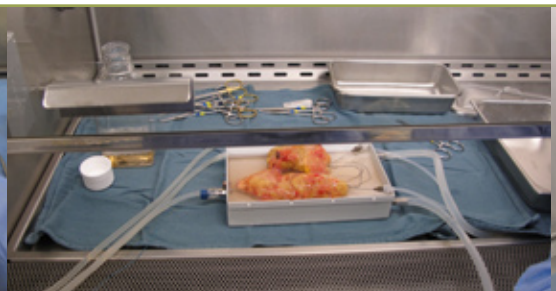
Thanks in part to Szot's efforts, UCSF islet cell transplant surgeons Peter G. Stock, MD, PhD, and Andrew M. Posselt, MD, PhD, are achieving remarkable successes. Transplant recipients have seen their hemoglobin A1c levels drop by more than 2.5 percent, and the majority have been insulin independent for greater than two years, some as much as three. The Diabetes Center is able to achieve these results without the need for steroids or calcineurin inhibitors. Additionally, Szot and his team are setting records in the numbers of islet cells they are able to isolate from a donor pancreas, reducing the need for additional pancreas organs and transplant procedures per patient.

As this facility approaches its eighth anniversary, it is timely to recognize the critically important role it is playing in diabetes research. Special thanks go to Tom and Polly Coleman, the Guzik Foundation, Joanne Kagle, Robert Kagle, the Vera M. Long Foundation, Pierluigi Zappacosta and Enrica D'Ettore, and the Juvenile Diabetes Research Foundation for their early commitments to this facility's development.

If you or a loved one has type 1 diabetes and has experienced poor glucose control despite intensive insulin therapy, please contact the UCSF Islet Transplantation Office at 415/353-8893 or islettransplant@ucsfmedctr.org to learn more about these exciting studies.

Islet cell isolation and preparation process at the UCSF Islet and Cellular Transplantation Facility





Diabetes Center Leadership Council

The Leadership Council was formed in the summer of 2001, one year after Jeffrey Bluestone arrived at UCSF to lead the Diabetes Center. Dedicated to supporting the mission of the UCSF Diabetes Center to prevent, treat and ultimately cure the disease through multidisciplinary research, compassionate clinical care and excellent diabetes education, council members provide guidance, advocacy, and business and community expertise.

2009-2010 Leadership Council Members

Lisa Altman
A.W. Clausen
Thomas M. Coleman
Robert B. Friend
Loren K. Gordon
Michael B. Gordon
J. George Hume
Joanne Kagle
Robert C. Kagle
Diane L. Klein
Robert N. Klein II
Alan B. Lefkof
Donald A. Lucas
Sarah S. Lucas
Connie C. Price
P. Anthony Price
Chara Schreyer
Will K. Weinstein
Michael W. Wilsey

Have You Considered an Insulin Pump?

If you have diabetes and require insulin, an insulin pump may be right for you. The pump is a device that is programmed to cover your basal insulin needs by continuously delivering droplets of rapid-acting insulin under the skin. A pump can provide better diabetes control with fewer highs and lows. There are options to match varying insulin needs during exercise, pregnancy or illness, and you can give yourself a bolus with the pump for food and high glucose corrections. It also offers increased flexibility to match your lifestyle and more precise insulin delivery.

However, it is important to have realistic goals for using a pump. Achieving successful glucose control with multiple daily injections is a lot of work. The same is true for a pump. The pump does not check your blood glucose or make decisions about the amount of insulin you need. While the pump lasts for years, some components must be changed every few days. There are also the drawbacks of cost, having to wear it all the time, and a higher risk of ketoacidosis and infection at the infusion site.

The UCSF Diabetes Center has programs and workshops for starting adults and children on pumps. Insulin pump starts are available to patients who have established their diabetes care with our physicians in the UCSF Diabetes Adult and Pediatric Clinics. Any existing pump users may attend the pump therapy workshops to review self-management skills and learn new pump concepts.

Using an insulin pump requires competence in carbohydrate counting, insulin action and blood glucose pattern interpretation. It also requires an understanding of the increased risk of ketones and infusion set infections; infusion set selection and placement; and pump programming. These skills are taught by certified diabetes educators, registered nurses, dieticians and the adult and pediatric endocrinologists of the UCSF Diabetes Center through classes, workshops and one-on-one meetings prior to and after starting on a pump.

For more information, please contact the UCSF Diabetes Teaching Center at 415/353-2266 or diabetesteachingcenter@ucsfmedctr.org, or visit www.dtc.ucsf.edu. For pediatric patients, please contact Jeanne Buchanan, RN, CDE, at 415/514-3932 or diabetes@peds.ucsf.edu.

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For more information on any of these stories or the UCSF Diabetes Center, contact Suzanne Ritchie at 415/476-6334 or sritchie@support.ucsf.edu.

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