



PedsFocus

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DIABETES/ENDOCRINOLOGY

Enhancer-Based Beta-Cell Programming Strategies (EnhanceBeta)

A cell-based approach such as the generation of transplantable β -cells from pluripotent stem cells remains a major hope as a cure for diabetes mellitus. The Sander laboratory within the Pediatric Diabetes Research Center is focused on unraveling the mechanisms behind β -cell differentiation and subsequently translating these findings to the development of cell-based therapies for diabetes. One of the lab's studies seeks to integrate genome-wide next generation sequencing technologies with a highly efficient human embryonic stem cell differentiation platform to map enhancers as human embryonic stem cells (hESCs) differentiate towards the pancreatic lineage.

Enhancers are transcriptional regulatory elements within the human genome that drive lineage-specific gene expression programs as shown by their remarkable cell-type specific activity. Through in-depth analysis of the enhancers that become exclusively active during the commitment to the pancreatic lineage, Dr. Sander will define the mechanisms of how the pancreas and β -cells are specified during human development. Furthermore, Dr. Sander and her team will immediately take advantage of the cell-type specific activity of these newly identified regulatory elements to create much-needed pancreatic lineage and β -cell-specific reporter systems that will greatly accelerate the discovery of compounds that direct hESCs to differentiate into β -cells in vitro.

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GASTROENTEROLOGY

Basic and Translational Research in Obesity-Related Metabolic and Liver Disease

The Feldstein laboratory at Rady Children's Hospital San-Diego and the University of California, San Diego Department of Pediatrics studies the molecular and biochemical pathways leading to the metabolic complications of obesity. Dr. Feldstein is primarily interested in the mechanisms attracting phagocytes to obese adipose tissue, as well as the events that link excessive accumulation of lipids in the liver (hepatic steatosis) to liver injury, fibrosis and carcinogenesis.

Moreover, Dr. Feldstein is working to discover novel non-invasive biomarkers for early diagnosis and monitoring of metabolic dysregulation, hepatic steatosis and liver damage. His lab utilizes an array of mass spectrometry-based approaches (LC/ESI/MS/MS, proteomics) directed toward these translational studies. The goal is to use these discoveries to develop safe and efficacious diagnostic and therapeutic strategies for patients with these highly prevalent and potentially serious conditions. To this end, Dr. Feldstein is actively involved in the development of preclinical, translational and clinical research protocols for a number of non-invasive tests and therapeutic agents, including the cytokeratin-18 fragment test for NASH (nonalcoholic steatohepatitis) diagnosis, one of the most validated and promising markers for this disease.

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UROLOGY

Laparoendoscopic Single-Site Surgery for Bilateral Nephrectomies

Children with end-stage renal disease on dialysis may have multiple medical issues stemming from their native kidneys, precluding them from proceeding to renal transplantation. Recurrent pyelonephritis, renin-dependent hypertension, risk of malignancy in native kidneys, and nephrotic-range proteinuria often need to be addressed before transplantation. Bilateral nephrectomies had been performed in the past at the time of transplantation or prior to transplant via an open surgical approach.

At Rady Children's Hospital-San Diego, pediatric urologists have incorporated one of the latest minimally invasive surgical techniques — laparoendoscopic single-site (LESS) surgery — to perform bilateral nephrectomies. Rady Children's Pediatric Urology Program was one of the first sites on the West Coast to perform the procedure. The use of this technique has enabled chronic kidney disease patients to recover faster, to be more medically stable for transplantation, and to have excellent cosmesis.

The Program's success was published in *Pediatric Transplantation* (Laparoendoscopic single-site (LESS) bilateral nephrectomy in the pretransplant pediatric population, 2011 June 15(4): 396-399), and the overall experience was published in *Urology* (Comparison of laparoendoscopic single-site, conventional laparoscopic, and open nephrectomy in a pediatric population, 2011: July 78(1): 74-77). Rady Children's pediatric urologists continue to research other applications for LESS across the entire surgical discipline of the specialty.

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