

THE J. DAVID GLADSTONE INSTITUTES

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GLADSTONE INSTITUTE OF CARDIOVASCULAR DISEASE NEWS

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GLADSTONE SCIENTISTS RECEIVE \$10 MILLION TO IDENTIFY GENETIC CAUSE OF CONGENITAL HEART DISEASE *National Heart, Lung, Blood Institute Funds Multi-Year Project*

SAN FRANCISCO, CA—October 28, 2009—Scientists at the Gladstone Institute of Cardiovascular Disease (GICD) will receive \$10 million over the next 6 years to find the genetic causes of congenital heart disease. Congenital heart disease affects 1 percent of all children and often leads to death or long-term illness. The team of investigators, led by Benoit Bruneau, PhD, will focus on the gene networks that underlie the disease and the regulatory factors that turn on and off genes related to congenital heart defects (CHDs). GICD was one of four national centers awarded this highly competitive grant to address CHD at a genome-wide level.

“We know that specific genes have to be turned on and off during a relatively narrow developmental window to correctly build a human heart,” said Dr. Bruneau, who is the William H. Younger, Jr. Investigator at Gladstone. “But so far we only understand how a handful of genes change during heart formation. Our study will look at all of the 25,000 genes in the genome to get a full picture of how the entire system is regulated. Understanding the all of the regulatory networks that control heart development will have important implications for preventing and curing congenital heart disease.”

According to Bruneau, the research team will use cutting-edge genome-mapping techniques to identify and define the function of transcription factors with known roles cardiac development and human disease, and so-called epigenetic regulators, the factors that open up chromosomes to allow the transcription factors to reach their targets.

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NHLBI Grant

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Transcription factors are the “master regulators” of a cell, acting to turn on or off other genes; they function by directly interacting with DNA, but it isn’t known how they function in concert with epigenetic regulators.

Dr. Deepak Srivastava, director of GICD and co-investigator, has identified the genetic causes of many CHDs and will use newly developed technology from Dr. Shinya Yamanaka, another co-investigator in GICD, to generate induced pluripotent stem (iPS) cells from patients with transcription factor mutations leading to CHD.

“Our studies will yield an important and transformative epigenetic atlas of heart development, which will link for, the first time, transcriptional and epigenetic regulators in a comprehensive network that will illuminate mechanisms underlying CHDs,” he said.

“Congenital heart defects are the most common and life-threatening problem for newborns in the United States,” said Elizabeth G. Nabel, MD, director of the National Heart, Lung and Blood Institutes, part of the National Institutes of Health. “Our Bench to Bassinet research efforts will offer new insights into how the human cardiovascular system develops and help speed transition of promising laboratory discoveries into treatments that can save young lives.”

Other team members include Katherine S. Pollard, PhD and Bruce Conklin, MD (from the Gladstone Institute of Cardiovascular Disease and UCSF), and Laurie Boyer, PhD (Massachusetts Institute of Technology).

Dr. Bruneau’s primary affiliation is with the Gladstone Institute of Cardiovascular Disease where he is the William H. Younger, Jr. Investigator, and where his laboratory is located and all of his research is conducted. He is also Associate Professor of Pediatrics at the University of California, San Francisco.

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About the Gladstone Institutes

The J. David Gladstone Institutes, an independent, nonprofit biomedical research organization, affiliated with the University of California, San Francisco, is dedicated to the health and welfare of humankind through research into the causes and prevention of some of the world's most devastating diseases. Gladstone is comprised of the Gladstone Institute of Cardiovascular Disease, the Gladstone Institute of Virology and Immunology and the Gladstone Institute of Neurological Disease. More information can be found at www.gladstone.ucsf.edu.

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