

Scientist discovers genetic factor implicated in heartbeat defect

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A scientist at the Gladstone Institutes has discovered how gene regulation can make hearts beat out of sync, offering new hope for the millions who suffer from a potentially fatal heart condition.

In a paper being published this week in the online Early Edition of the [Proceedings of the National Academy of Sciences](#), Gladstone Investigator Benoit G. Bruneau, PhD announces the identity of the molecular regulator that uses [electrical impulses](#) to synchronize each heartbeat.

Abnormalities in heartbeat synchronization, called heart arrhythmias, are a cause of death for the 5.7 million Americans who suffer from [heart failure](#), a condition in which the heart can't pump enough blood to meet the body's needs. At least 300,000 people die of heart failure each year in the United States alone.

"This is important progress for a better understanding of [heart arrhythmias](#), which when combined with heart failure can be fatal," said Deepak Srivastava, MD, who directs all [cardiovascular research](#) at Gladstone. "This is the first published research about a genetic regulator that coordinates the timing of the electrical impulses that make the heart beat properly."

In many animals, including humans, electrical impulses must spread rapidly and in a coordinated fashion along a dedicated network of [cardiac cells](#) in order for the heart to pump blood efficiently to the rest

of the body.

A genetic regulator, called *Irx3*, coordinates these impulses. When Dr. Bruneau and his team switched off the *Irx3* gene in mice, the heart's pumping fell out of sync. The electrical impulses-which normally follow a rapid path throughout the heart-diffused slowly and had trouble reaching their intended destinations. The mice developed arrhythmias as the heart's chambers lost the capacity to beat in time.

Dr. Bruneau, who is also a professor of pediatrics at the University of California San Francisco (UCSF), conducted the research in collaboration with two Canadian labs. Gladstone, which is affiliated with UCSF, is a leading and independent biomedical-research organization that focuses on cardiovascular disease, neurodegenerative disease and viral infections.

"These findings have potential implications for the prevention and treatment of human heart disease, once we better understand *Irx3*'s role in the human heart," said Dr. Bruneau. "An important avenue to explore could be whether humans with arrhythmias have mutations in the *Irx3* gene.

"Now that we know the importance of *Irx3*," Dr. Bruneau added, "We need to dig deeper to see if it's possible to use drug therapy to target any of the electrical-impulse pathways that *Irx3* regulates with drug therapy."

Provided by Gladstone Institutes

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