

Discovery of cellular processes which regulate heart's energy supply

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The heart needs a steady supply of energy to function properly. MUHC researcher Dr. Vincent Gigue's and his colleagues recently identified several genetic programs which work together to ensure this energy is available. Dr. Gigue's findings, published in the May 2007 issue of *Cell Metabolism*, may suggest new approaches to the management of some forms of heart disease.

"The heart is a pump," says Dr. Gigue's. "It needs energy, and it gets this from different fuels found in the body "glucose or fatty acids" depending on availability. We've identified two new receptors that control the whole setup. This is very exciting."

Dr. Gigue's and his fellow researchers discovered that two closely related nuclear receptors known as ERRa and g play an essential role in coordinating the expression of a set of proteins that the heart requires to produce the energy it needs to pump effectively.

"Nuclear receptors receive signals from different parts of the body," explains Dr. Gigue's. "These signals "tell" the cell what action to take by controlling which genetic program will be turned on or off in the cell. Because the ERRa and g receptors are so important to heart function, drugs that influence their activity might offer a novel approach to managing diseases of the heart muscle."

The receptors identified by Dr. Gigue's and his colleagues had already been linked to the activity of cellular power plants called mitochondria.

However, their exact role in supplying energy to the heart muscle had not previously been understood.

Using powerful genomic tools, researchers discovered that the ERRα and β receptors play a key role in regulating the genes which guide the complex biological processes fuelling the heart. Because of this, the two receptors are essential to heart function.

"The receptors control some 400 genes, and probably more," Dr. Giguere's says. "These genes regulate well-defined energy pathways. Several have also been linked to disorders which affect the heart's pumping power. This discovery was "the cherry on the sundae" for us."

If it can be shown that the activity of these two ERR receptors can be safely modulated in the human heart, drugs targeting these receptors may hold promise for novel heart therapies. "There are not many ways to prevent heart failure, but molecules that act on these receptors might be one," says Dr. Giguere's.

Source: McGill University

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