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Trigger found for autoimmune heart attacks

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People with type 1 diabetes, whose insulin-producing cells have been destroyed by the body's own immune system, are particularly vulnerable to a form of inflammatory heart disease (myocarditis) caused by a different autoimmune reaction. Scientists at Joslin Diabetes Center have revealed the exact target of this other onslaught, taking a large step toward potential diagnostic and therapeutic tools for the heart condition.

Researchers in the lab of Myra Lipes, M.D., have shown in both mice and people that myocarditis can be triggered by a protein called alpha-myosin heavy chain, which is found only in heart muscle and in especially low quantities in human heart tissue.

While myocarditis often follows viral attacks or other infections, Dr. Lipes and her colleagues previously demonstrated that mice genetically modified to model type 1 diabetes could generate myocarditis spontaneously.

In their latest work, reported online in the Journal of Clinical Investigation, the scientists analyzed blood from such mice and identified two types of autoimmune response directed specifically against the protein, with the first response directed by a specialized kind of immune system cells called T cells and the second by antibodies.

In both mice and people, T cells are "trained" by specialized cells in the thymus, a small organ in front of the heart, to recognize the body's own cells and refrain from attacking them. The researchers found, however, that in mice these specialized training cells couldn't train on the alpha-

myosin heavy chain protein because none of that protein was being produced in those cells.

Next, the scientists showed that the disease didn't develop in similar mice that were genetically engineered to produce the protein in the specialized training cells. "You can totally protect those mice from mortality, which is really extraordinary," says Dr. Lipes, an Investigator in Joslin's Section on Islet Cell & Regenerative Biology and an Assistant Professor at Harvard Medical School.

Furthermore, the studies also indicated that alpha-myosin heavy chain was not present in human thymus and that the T cells that sought out the protein could be found in the blood of healthy people. In patients with myocarditis, levels of these cells soared.

The investigation, Dr. Lipes says, suggests that people who are otherwise vulnerable to autoimmune conditions, such as those with type 1 diabetes, may be particularly vulnerable to this risk to their hearts.

Myosin heavy chain proteins are found in two very similar forms in human hearts: alpha-myosin heavy chain, which supports fast muscle contraction and may be particularly prevalent in athlete's hearts, and beta-myosin heavy chain, which is much more common and functions in slower muscle contraction. "We're trying to figure ways to identify the fragment of alpha-myosin heavy chain that is different, because that could aid in developing diagnostic tools and therapies," says Dr. Lipes.

More information: www.jci.org/articles/view/4458 … ca730049533908ae28b8

Provided by Joslin Diabetes Center

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