Explaining heart failure as a cause of diabetes

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Either heart failure or diabetes alone is bad enough, but oftentimes the two conditions seem to go together. Now, researchers reporting in the January *Cell Metabolism* appear to have found the culprit that leads from heart failure to diabetes and perhaps a novel way to break that metabolic vicious cycle.

"Our findings clarify the reasons why the incidence of heart failure is high among diabetic patients, why the prevalence of insulin resistance is increased in heart failure patients, and why treatment of insulin resistance improves the prognosis of heart failure patients," says Tohru Minamino of Chiba University Graduate School of Medicine.

It's a domino effect, the new evidence shows: the stress of heart failure activates the sympathetic nervous system. That stress response activates p53, which Minamino calls a cellular aging signal. That p53 signal ultimately leads to inflammation in fat tissue, systemic insulin resistance, and worsening heart function.

Of course, the protein p53 is probably best known as a tumor suppressor. "It has been reported that p53-dependent cellular aging is a protective mechanism for cancer development," Minamino says. But, he adds, constant activation of the anticancer signal can promote inflammation, cancer, and other diseases of aging.

Minamino had earlier shown that age-associated or stress-induced accumulation of p53 in the heart promotes heart failure. Aging and extra

calories induce that same aging signal in fat tissue. Now it seems that activation of cardiac p53 also leads to activation of p53 in fat tissue. Those p53-dependent cellular aging signals in both tissues interact with each other, thereby accelerating the development of age-associated diseases, he says.

This suggests that an ideal treatment would block the inflammation that goes with p53's activation without compromising its tumor-fighting abilities. And for Minamino, that's the Holy Grail: an antiaging therapy without the cancer risk.

More information: Shimizu et al.: "p53-induced adipose tissue inflammation is critically involved in the development of insulin resistance in heart failure."

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