Medical Xpress

Gene knockout shows potential for diabetes-related heart failure

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Silencing the TLR4 gene can stop the process which may lead to cardiovascular disease in diabetic patients. Researchers writing in BioMed Central's open access *Journal of Translational Medicine* carried out a series of in vitro tests which demonstrated that TLR4 plays a critical role in hyperglycaemic cardiac apoptosis, and that silencing the gene using specific small interfering RNA (siRNA) can prevent it.

Wei-Ping Min, from the University of Western Ontario, Canada, worked with a team of researchers to perform the tests in cells taken from diabetic mice. He said, "We found that TLR4 was up-regulated in the myocardia of diabetic mice. Treatment with TLR4 siRNA attenuated the apoptosis seen in these cells, thus highlighting the potential clinical use of siRNA-based therapy".

Min and his colleagues induced hyperglycemia in adult mice by injecting them with streptozotocin, a toxin that poisons insulin-producing beta cells. They found that after 7 days of hyperglycemia, the level of TLR4 mRNA in myocardial tissue was significantly elevated, and signs of apoptosis were evident. Silencing TLR4 resulted in suppression of apoptotic cascades. According to Min, "This is the first demonstration of the prevention of cardiac apoptosis in diabetic mice through silencing of the TLR4 gene".

More information: Prevention of hyperglycemia-induced myocardial apoptosis by gene silencing of Toll-like receptor-4, Yuwei Zhang, Tianqing Peng, Huaqing Zhu, Xiufen Zheng, Xusheng Zhang, Nan Jiang,

Xiaoshu Cheng, Xiaoyan Lai, Aminah Shunnar, Manpreet Singh, Neil Riordan, Vladimir Bogin, Nanwei Tong and Wei-Ping Min, *Journal of Translational Medicine* (in press), www.translational-medicine.com/