Telomerase limits damage after heart attack

The enzyme telomerase is known to repair various types of cell damage, and new results indicate that this activity can be exploited to prevent damage to heart tissue after acute injury such as a heart attack or myocardial infarction. The results were published in *Nature Communications* (doi:10.1038/ncomms6863; published online 18 December 2014). “Our work suggests telomerase activation could be a therapeutic strategy to prevent heart failure after MI [myocardial infarction],” write the authors of the report, led by Maria Blasco (Spanish National Cancer Research Centre, Madrid).

Telomerase is normally expressed during embryonic development but silenced after birth. The researchers used an adenovirus vector to activate telomerase expression specifically in the hearts of adult mice and then, 2–3 weeks later, when telomerase expression was maximal, induced myocardial infarction by ligation of the coronary artery. Telomerase expression improved mouse survival after infarction: more than 74% of mice expressing telomerase survived compared with only 57% of control mice. Telomerase expression also preserved the myocardium,

improved ventricular function and increased metabolic activity and tissue remodeling while minimizing infarct size and scar formation. Furthermore, mice expressing telomerase showed greater telomere length among cardiomyocytes and larger numbers of cycling cardiomyocytes. Activation of telomerase was also associated with changes in gene expression reflecting the activation of cardioprotective pathways. Gene expression profiles of adult mice with activated telomerase resembled those of neonatal mice, in which telomerase is normally active and cardiac regeneration can occur.

Taken together, the results suggest that telomerase expression might trigger heart muscle regeneration, a key therapeutic objective for myocardial infarction as well as chronic heart failure and other forms of cardiovascular disease. “Although efficient heart regeneration has been one of the goals of cardiology for the treatment of MI [myocardial infarction] and prevention of heart failure, no significant advances have been made in this regard,” the authors wrote.

The authors conclude that “telomerase activation in the adult heart is beneficial

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for survival in the murine model after acute MI [myocardial infarction], which is coincidental with longer telomeres and activation of several pathways associated with cardiac protection and regeneration. These findings serve as proof of concept for the development of innovative strategies based on telomerase activation to treat chronic and acute heart failure.”

According to a press release, Blasco and her collaborators next plan to test the effects of telomerase activation in pigs, a larger animal model whose cardiac anatomy and function more closely resemble those of humans.

Monica Harrington

TOWARD A BETTER UNDERSTANDING OF TAU

Results presented at Neuroscience 2014, the annual meeting of the Society for Neuroscience (15–19 November 2014; Washington, DC), highlighted the central role of tau protein in neurodegeneration associated with Alzheimer’s disease and with traumatic brain injury (TBI). Almost 36 million people worldwide suffer from Alzheimer’s disease, and 10 million or more sustain TBI each year. Clarifying how tau participates in neurodegeneration may enable medical researchers to formulate strategies to halt or even reverse the damage, improving the quality of life and prognosis for those affected by these conditions.

When functioning properly, tau facilitates neurogenesis and neural activity, but dysfunctional tau can trigger neuronal apoptosis, resulting in memory loss and other neurological symptoms. Now, Julia Gerson (University of Texas Medical Branch, Galveston) and colleagues report that a specific form of tau is over-represented in the brain in both Alzheimer’s disease and TBI: small aggregates of tau molecules, called tau oligomers. “Our findings add to the growing evidence that tau oligomers—not tau protein in general—are responsible for the development of neurodegenerative diseases such as Alzheimer’s and for damage associated with traumatic brain injury,” Gerson explained in a press release.

Tau oligomers formed in the brain in response to TBI in rats and mice, and these oligomers closely resembled those observed in Alzheimer’s disease. When injected into the brains of mice overexpressing human tau protein, the tau oligomers accelerated the onset of cognitive defects.

“Tau oligomers are likely the most toxic species of tau in neurodegenerative disease, and these results suggest that they play an important role in the toxicity underlying TBI as well. Together, these findings suggest that tau oligomers may be a viable therapeutic target in TBI and in preventing the increased acquisition of neurodegenerative disease,” concluded Gerson and her collaborators.

Another group of researchers, led by Tong Li (Johns Hopkins University, Baltimore, MD), approached the tau question from another angle, generating a new mouse model of Alzheimer’s disease that expresses a mutant form of tau protein. The genetically engineered mice develop neurological symptoms similar to those observed in Alzheimer’s disease, including progressive neuronal loss and memory deficits. “The new mouse model will help researchers clarify the mechanisms causing the loss of nerve cells in Alzheimer’s disease,” said Li in a press release. “It will also help researchers more effectively screen new drugs for treating Alzheimer’s before testing those drugs in clinical trials,” he added.

Monica Harrington