Tree elements: Branching hopes after tissue injury in regenerative medicine

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Humans are poor model systems for studying tissue regeneration.[1] Unlike their amphibians or rodent counterparts, humans are deficient in this quality, making the repair process following a tissue injury infrequent and limited.[2] Most human tissues or organs, except the liver, lack in their regenerative potential. This tends to be a serious problem in organ damage until recently with the identification of enhancer regulatory elements that engage in regenerating tissue. Tissue regeneration enhancer elements (TREEs) trigger gene expression in injury sites and can be engineered to modulate the regenerative potential of vertebrate organs.[3] TREE orchestrates selective gene expression at the injury sites, thereby modulating the regenerative activities and potential of vertebrate organs.[4,5]

Using a genetic screen of a zebrafish-based tissue injury model, Kang et al.,[3] identified the gene expression signature associated with regeneration.

This concept is being tried and tested to see its possibility in regenerating injured myocardium following myocardium infraction leading to ischemia and tissue damage. TREEs displayed specificity and efficacy in a systemically delivered recombinant AAV vector system in mice and can be used as a gene-therapy module to repair damaged tissue. A team of researchers at the Duke School of Medicine, USA, headed by Ken Poss, reported their findings in cell stem cell, 2022.[6] These researchers further took a step ahead to actually orchestrate a damaged myocardium repair and the growth of new muscles to restore normal cardiac function. Even more spectacular is that tissue growth is selective only at injury sites and becomes quiescent once the damage is repaired.[7]

HOW THIS MAY IMPACT REGENERATIVE MEDICINE

Using a TREE-based system, one can attempt to use gene therapy with viral vectors to enhance heart tissue cell proliferation and growth, thus improving cardiac regeneration. This system will further strengthen by incorporating better gene payloads, thereby opening new possibilities to rescue scar tissue and restore function.

According to the World Health Organization, MI-related death in India accounts for one-fifth of deaths worldwide, which is alarmingly higher in the younger population.[8] The age-standardized cardiovascular disease (CVD) death rate of 272/100,000 in India is much higher than the global average of 235. Under these circumstances, these findings seem extremely relevant. Although we may not fix a broken heart, engineered TREE elements might at least fix a damaged myocardium branching hopes for numerous suffering from CVD.

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