Nanofibers may help treat heart attacks

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(Medical Xpress) -- Cardiovascular diseases kill over 17 million people a year globally, according to the World Health Organization, and many more suffer heart attacks but recover. Even those who do recover are more prone to suffer heart failure or future heart attacks because the heart tissue is damaged. Attempts to produce effective therapies to promote repair and regeneration of heart tissues and blood vessels have so far mostly been unpromising.

Now new research by scientists in Taiwan and the US has found a promising treatment involving vascular endothelial growth factor (VEGF), which promotes blood vessel re-growth. Previous attempts to develop a therapy based on VEGF were limited by the fact that the growth factor is rapidly washed out of the heart by the blood flow, but the new research solves this problem.

The team used a gel containing a lattice of self-assembling peptide nanofibers in combination with VEGF and found that the scaffold-like structure of the nanofibers held the VEGF in place, enabling it to be released slowly over a period of weeks.

The researchers, led by Assistant Professor Patrick C. H. Hsieh of the Institute of Biomedical Engineering, at the National Cheng Kung University, in Tainan, Taiwan, induced heart attacks in rats and then injected a combination of the nanofibers along with various doses of VEGF in the rats' hearts.

They found that the combination improved heart health and provided an

environment that promoted growth of new blood vessels, repair of damaged tissues and growth of new tissue. Dr. Hsieh, a cardiac surgeon, said the nanofibers provide an effective environment for attracting the stem cells that repair the damage and regenerate blood capillaries and even new arteries.

After 28 days the hearts of treated animals showed a much greater degree of repair and re-growth than the hearts of control animals. Arterial growth was five times greater in the treated animals, new heart muscle was being formed, and areas of weak, scarred tissue, were reduced. The controls received either VEGF alone or the nanofibers alone. The same beneficial effects were demonstrated in rats and pigs, and no harmful side effects were noted in either species.

The paper was published in the journal *Science Translational Medicine*. In an accompanying article in the journal, Karen Christman of the University of California San Diego, said the study could lead to therapies to help human heart attack patients to recover more quickly and have improved quality of life during the recovery period. More research is needed to study the long-term effects and to determine the "optimal time window," for administering the treatment, Dr Hsieh said.

More information: Y.-D. Lin, C.-Y. Luo, Y.-N. Hu, M.-L. Yeh, Y.-C. Hsueh, M.-Y. Chang, D.-C. Tsai, J.-N. Wang, M.-J. Tang, E. I. Wei, M. L. Springer, P. C. Hsieh, Instructive Nanofiber Scaffolds with VEGF Create a Microenvironment for Arteriogenesis and Cardiac Repair. *Sci. Transl. Med.* 4, 146ra109 (2012).

ABSTRACT
Angiogenic therapy is a promising approach for tissue repair and regeneration. However, recent clinical trials with protein delivery or gene therapy to promote angiogenesis have failed to provide therapeutic effects. A key factor for achieving effective revascularization is the

durability of the microvasculature and the formation of new arterial vessels. Accordingly, we carried out experiments to test whether intramyocardial injection of self-assembling peptide nanofibers (NFs) combined with vascular endothelial growth factor (VEGF) could create an intramyocardial microenvironment with prolonged VEGF release to improve post-infarct neovascularization in rats. Our data showed that when injected with NF, VEGF delivery was sustained within the myocardium for up to 14 days, and the side effects of systemic edema and proteinuria were significantly reduced to the same level as that of control. NF/VEGF injection significantly improved angiogenesis, arteriogenesis, and cardiac performance 28 days after myocardial infarction. NF/VEGF injection not only allowed controlled local delivery but also transformed the injected site into a favorable microenvironment that recruited endogenous myofibroblasts and helped achieve effective revascularization. The engineered vascular niche further attracted a new population of cardiomyocyte-like cells to home to the injected sites, suggesting cardiomyocyte regeneration. Follow-up studies in pigs also revealed healing benefits consistent with observations in rats. In summary, this study demonstrates a new strategy for cardiovascular repair with potential for future clinical translation.