Repairing the heart with silicon nanowires and stem cell cardiomyocytes

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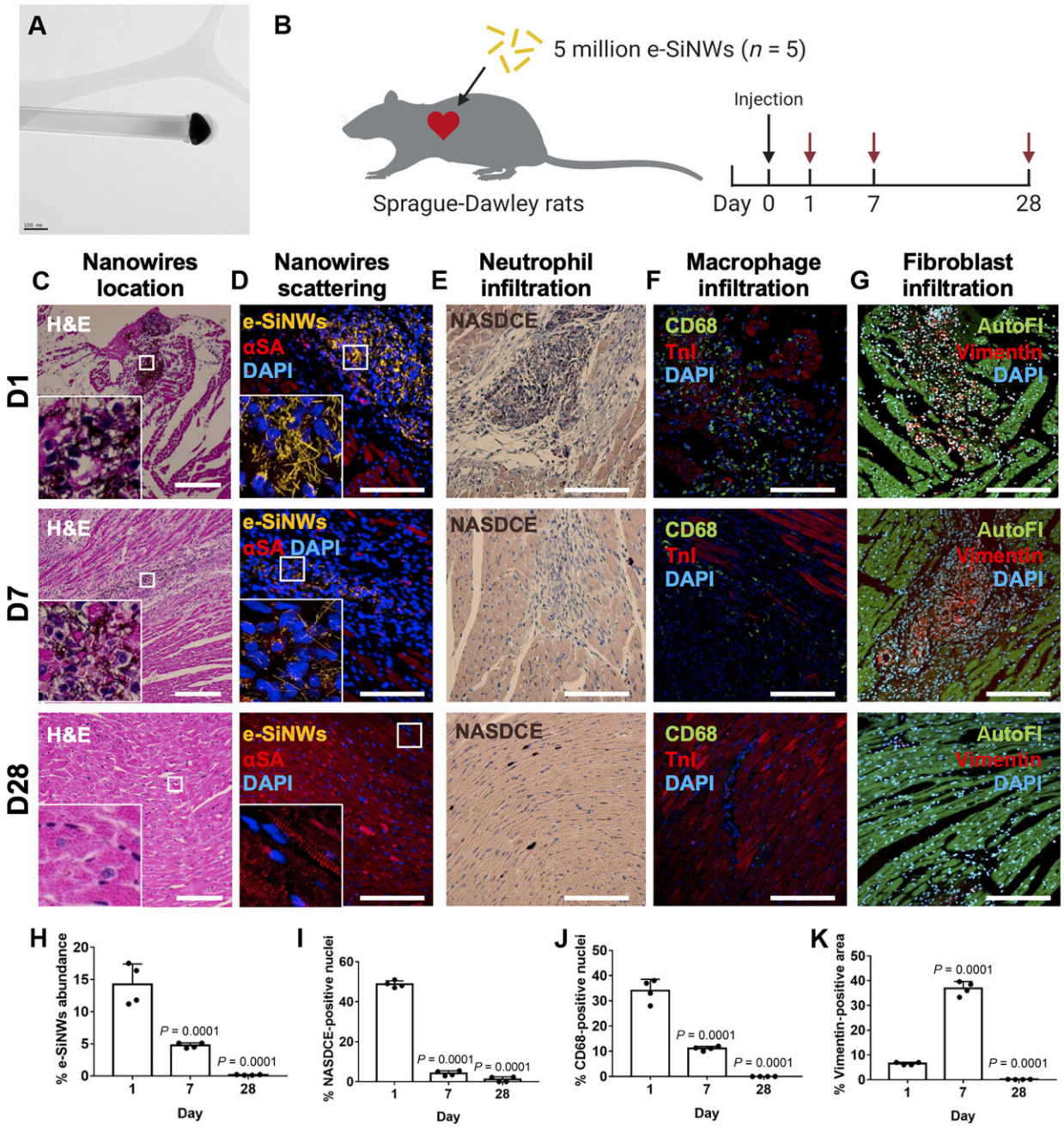

Biocompatibility of e-SiNWs in rat myocardium. (A) Representative transmission electron microscopy image of an n-type e-SiNW used in this study on a carbon grid. (B) Experimental outline using 8- to 10-week-old male Sprague-Dawley rats for e-SiNW injection and biocompatibility analysis. Maroon arrows indicate days when analysis was performed. (C) Hematoxylin and eosin (H&E) staining of e-SiNW injection site at 1, 7, and 28 days after injection. (D) Confocal images of light scattering from injected e-SiNWs in myocardium. (E) Neutrophil infiltration identified by naphthol AS-D chloroacetate staining (NASDCE; dark brown). (F) Macrophage infiltration identified by CD68 staining. (G) Fibroblast infiltration identified by vimentin staining. (H to K) Quantification of (H) e-SiNWs, (I) neutrophils, (J) macrophages, and (K) fibroblasts at days 1, 7, and 28 after nanowire injection. Data represents means ± SD [n = 3 biologically independent regions from four hearts each, one-way analysis of variance (ANOVA) versus day 1]. Scale bars, 100 nm (A) and 200 μm [(C) to (G)]. Credit: *Science Advances* (2023). DOI: 10.1126/sciadv.adf2898

A research group led by Clemson University has developed a strategy to improve heart repair using human pluripotent stem cell–derived cardiomyocytes combined with biodegradable and biocompatible electroconductive silicon nanowires.

In the paper, "Nanowired human cardiac organoid transplantation enables highly efficient and effective recovery of infarcted hearts," published in *Science Advances*, the authors detail how cells self-assemble to form organoids that mimic fundamental cardiac tissue–level functions and contain vascular networks that reduce the risk of apoptosis during oxygen deprivation.

Nanowired cardiac organoids, tiny living and contracting orbs of heart tissue with microscopic wires embedded, were fabricated from human

pluripotent stem cell-derived cardiomyocytes (hPSC-CMs) and cultured along with electroconductive silicon nanowires (e-SiNWs) so that the wires were integrated into the tissues. The engineered spheres were then injected into damaged and dying tissues of rat hearts.

While the use of cardiac organoids for tissue repair is not new, there have been limitations of low cell retention at the repair site, leading to moderate functional improvements and scalability issues.

The addition of nanowires increased the conductivity of the tissues, allowing them to synchronize better, facilitating better communication among cells and integration with the existing heart tissue.

Nanowired organoids achieved double the functional recovery in the rats, with a lower number of engrafted cells (~0.5×10^6 hPSC-CMs per rat) compared to previous studies without nanowires in the hPSC-CMs (~10×10^6 hPSC-CMs per rat).

Integrating e-SiNWs did not exacerbate inflammatory responses in healthy or damage repair settings, as expected from the biocompatible nature of silicon.

Nanowired cardiac organoids also exhibited significantly less apoptosis than wireless cardiac spheroids. Though the reason was not explicitly apparent, the authors suggest that it could be attributed to the vascular network within the nanowire organoids providing a more cardioprotective microenvironment to support the survival of hPSC-CMs.

The new method appears to introduce a safe and effective solution to enhance the therapeutic potential of hPSC-CMs. In overcoming traditional limitations, resulting in improved cardiac function, engraftment, and vascularization, the method could become the

conventional clinical application of hPSC-CMs in treating heart injuries and potentially other conductive tissues like skeletal muscle and neuronal tissues.

Further study is needed with larger sample sizes and longer-term monitoring, and to investigate the gene expression of engrafted organoids and host myocardium for a mechanistic understanding of how the nanowire cardiac organoid-mediated cardiac repair functions as an assimilated tissue.

More information: Yu Tan et al, Nanowired human cardiac organoid transplantation enables highly efficient and effective recovery of infarcted hearts, *Science Advances* (2023). DOI: 10.1126/sciadv.adf2898