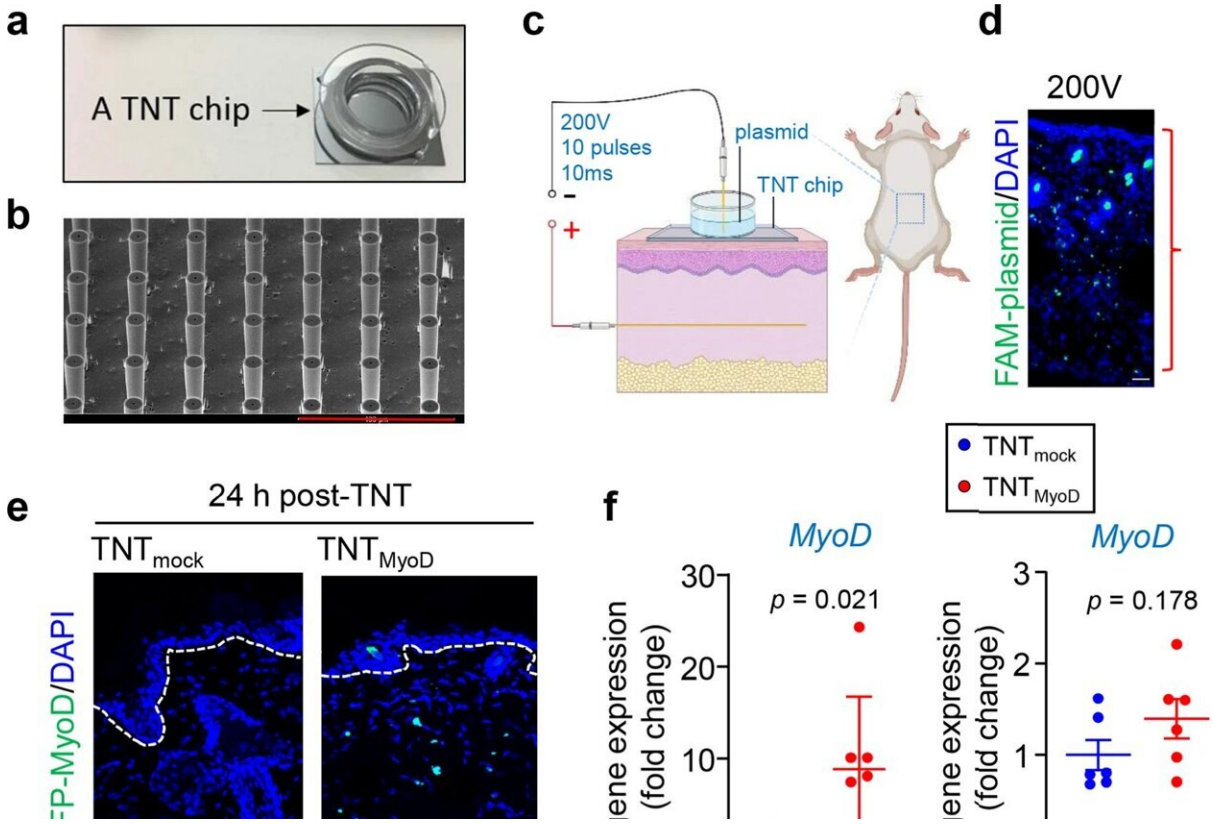
Silicon nanochip could treat traumatic muscle loss

November 9 2022



TNT_{MyoD} transfects deep into the dermis and causes myogenic reprogramming. **a** Image of $TNT_{2.0}$ device. **b** SEM images of TNT device showing needle array projections. Scale, 400 μm. **c** Schematic diagram showing TNT set up for skin. **d** Distribution of FAM-labeled plasmids immediately after TNT using various voltages on mouse dorsal skin. Scale bar = 40 μm. **e** Visualization of eGFP signal 24 h after TNT with the eGFP-MyoD plasmid, showing expression of eGFP in epidermis and dermis. No eGFP fluorescence was detected in skin transfected with mock plasmids. The white dashed line indicates the dermal-epidermal

junction. Scale, 50 μm. **f** *MyoD* expression in skin 24 h and day 10 post-TNT (*n* = 7,6). **g** Immunofluorescence staining of MF20 (myosin heavy chain) at 10 days post-TNT in the dermis. The white dashed line indicates the dermal-epidermal junction. The sections were co-stained with DAPI. Scale bar = 20 μm, 5 μm (**h**) transcript abundance of myogenic genes compared to mock-transfected skin (*n* = 9). All data are expressed as mean ± SD. Data analyzed by Student's *t*-test. Credit: *npj Regenerative Medicine* (2022). DOI: 10.1038/s41536-022-00259-y

Technology developed by researchers at the Indiana University School of Medicine that can change skin tissue into blood vessels and nerve cells has also shown promise as a treatment for traumatic muscle loss.

Tissue nanotransfection is a minimally invasive nanochip device that can reprogram tissue function by applying a harmless electric spark to deliver specific genes in a fraction of a second.

A new study, published in *npj Regenerative Medicine*, tested tissue nanotransfection-based gene therapy as a treatment, with the goal of delivering a gene known to be a major driver of muscle repair and regeneration. They found that muscle function improved when tissue nanotransfection was used as a therapy for seven days following volumetric muscle loss in rats. It is the first study to report that tissue nanotransfection technology can be used to generate muscle tissue and demonstrates its benefit in addressing volumetric muscle loss.

Volumetric muscle loss is the traumatic or surgical loss of skeletal muscle that results in compromised muscle strength and mobility. Incapable of regenerating the amount of lost tissue, the affected muscle undergoes substantial loss of function, thus compromising quality of life. A 20 percent loss in mass can result in an up to 90 percent loss in muscle function.

Current clinical treatments for volumetric muscle loss are physical therapy or autologous tissue transfer (using a person's own tissue), the outcomes of which are promising but call for improved treatment regimens.

IU researchers are using a minimally invasive nanochip device to reprogram tissue function. Credit: Liz Kaye, Indiana University

"We are encouraged that tissue nanotransfection is emerging as a versatile platform technology for gene delivery, gene editing and in vivo tissue reprogramming," said Chandan Sen, director of the Indiana Center for Regenerative Medicine and Engineering, associate vice president for research and Distinguished Professor at the IU School of Medicine.

"This work proves the potential of tissue nanotransfection in muscle tissue, opening up a new avenue of investigational pursuit that should help in addressing traumatic muscle loss. Importantly, it demonstrates the versatility of the tissue nanotransfection technology platform in regenerative medicine."

Sen also leads the regenerative medicine and engineering scientific pillar of the IU Precision Health Initiative and is lead author on the new publication.

The Indiana Center for Regenerative Medicine and Engineering is home to the tissue nanotransfection technology for in vivo tissue reprogramming, gene delivery and gene editing. So far, tissue nanotransfection has also been achieved in blood vessel and nerve tissue. In addition, recent work has shown that topical tissue nanotransfection can achieve cell-specific gene editing of skin wound tissue to improve wound closure.

More information: Andrew Clark et al, Myogenic tissue nanotransfection improves muscle torque recovery following volumetric muscle loss, *npj Regenerative Medicine* (2022). DOI: 10.1038/s41536-022-00259-y

Provided by Indiana University