# Tissue-engineered nerve graft

Surgical repair for severe peripheral nerve injury treatment represents not only a pressing medical need but also a great clinical challenge. Autologous nerve grafting remains a gold standard for bridging an extended gap in transected nerves. The formidable limitations related to this approach, however, have evoked the development of tissue-engineered nerve grafts as a promising alternative to autologous nerve grafts. A tissue-engineered nerve graft is typically constructed through a combination of a neural scaffold and a variety of cellular and molecular components. The initial and basic structure of the neural scaffold that serves to provide mechanical guidance and an optimal environment for nerve regeneration was a single hollow nerve guidance conduit. Later there have been several improvements to the basic structure, especially the introduction of physical fillers into the lumen of a hollow nerve guidance conduit. Up to now, a diverse array of biomaterials, either of natural or of synthetic origin, together with well-defined fabrication techniques, has been employed to prepare neural scaffolds with different structures and properties. Meanwhile different types of support cells and/or growth factors have been incorporated into the neural scaffold, producing unique biochemical effects on nerve regeneration and function restoration [1)].

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Functional restoration following major peripheral nerve injury (PNI) is challenging, given slow axon growth rates and eventual regenerative pathway degradation in the absence of axons. Smith et al. from the Center for Brain Injury and Repair, Department of Neurosurgery, Perelman School of Medicine, University of Pennsylvania, Philadelphia Axonova Medical are developing tissue-engineered nerve grafts (TENGs) to simultaneously “bridge” missing nerve segments and “babysit” regenerative capacity by providing living axons to guide host axons and maintain the distal pathway. TENGs were biofabricated using porcine neurons and “stretch-grown” axon tracts. TENG neurons survived and elicited axon-facilitated axon regeneration to accelerate regrowth across both short (1 cm) and long (5 cm) segmental nerve defects in pigs. TENG axons also closely interacted with host Schwann cells to maintain pro-regenerative capacity. TENGs drove regeneration across 5-cm defects in both motor and mixed motor-sensory nerves, resulting in dense axon regeneration and electrophysiological recovery at levels similar to autograft repairs. This approach of accelerating axon regeneration while maintaining the pathway for long-distance regeneration may achieve recovery after currently unrepairable PNIs [2)].

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Gu X, Ding F, Yang Y, Liu J. Construction of tissue-engineered nerve grafts and their application in peripheral nerve regeneration. Prog Neurobiol. 2011 Feb;93(2):204-30. doi: 10.1016/j.pneurobio.2010.11.002. Epub 2010 Dec 2. PMID: 21130136.
2)
Smith DH, Burrell JC, Browne KD, Katiyar KS, Ezra MI, Dutton JL, Morand JP, Struzyna LA, Laimo FA, Chen HI, Wolf JA, Kaplan HM, Rosen JM, Ledebur HC, Zager EL, Ali ZS, Cullen DK. Tissue-engineered grafts exploit axon-facilitated axon regeneration and pathway protection to enable recovery after 5-cm nerve defects in pigs. Sci Adv. 2022 Nov 4;8(44):eabm3291. doi: 10.1126/sciadv.abm3291. Epub 2022 Nov 4. PMID: 36332027.