**Development of Engineered Neural Tissue Containing Elongated Neurons Supported by Aligned Glia**

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Much research focuses on developing biomaterial scaffolds that mimic the autograft and promote host neurite regeneration from proximal to distal stump, whereas here we aim to improve long gap repair by populating constructs with functional neurons. With a ready-to-implant construct populated with neurons exhibiting long neurite extensions supported by glial cells, the gap between proximal stump and muscle could potentially be reconnected promptly. Immediate muscle innervation would help reduce atrophy.

To test the concept, a method was developed for neurite extension in vitro using engineered neural tissue (EngNT) formed from simultaneous self-alignment of Schwann cells and collagen fibrils in a tethered gel resulting in an anisotropic tissue-like structure. Fluorescence microscopy and image analysis showed that neurites of NG108-15 cell line co-cultured with EngNT aligned parallel to Schwann cells, with 85% of neurites exhibiting less than 30° deviation from the alignment axis. The neurite length of NG108-15 cells in EngNT reached approximately 428 μm after 7 days which is considerably greater than reported previously using other culture conditions. These results indicate that EngNT may be an appropriate substrate for generating long neurites in vitro with a view to generating therapeutic constructs containing long functional neurons. Combining EngNT with techniques such as 3D-printed mould design and mechanical tension could further improve the potential of EngNT to support neurite elongation.