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Engineered neural tissue with aligned Schwann cells supports neuronal regeneration in vivo and can be assembled using differentiated adipose-derived stem cells.

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INTRODUCTION: There are many limitations associated with the current gold standard treatment for peripheral nerve injury, the nerve autograft. Another option is to use nerve guidance conduits (NGCs) to bridge the gap in injured nerves. However these are limited to repairs up to ~3cm due to their lack of neurotrophic support in long gaps. We have developed Engineered Neural Tissue (ENT) - a living biomaterial with aligned neural cell architecture that can function as the ‘core’ of a repair device. In this study we aimed to optimise the assembly of this material in a nerve repair device, and then to produce a construct with clinically relevant cells (adipose-derived stem cells differentiated into Schwann cells (dADSCs)).

METHODS: The rat F7 Schwann cell line was used for device optimisation. For production of ENT, cells were mixed with neutralised type I rat tail collagen (2 mg/ml) and cast into the tethering/stabilisation system¹², Fig 1. ENT was assembled to form the nerve core of repair devices, Fig 2. Various column formats were tested in the rat sciatic nerve model (5mm gap). Regeneration was assessed by immunostaining with anti-neurofilament (axons) and anti-S100 (Schwann cells (SC)) antibodies, using confocal microscopy. To investigate neuronal growth on an ENT containing dADSCs, primary adult rat neurons were cultured on the ENT surface for 3 days. Deviation of neurite growth from the direction of cell alignment was quantified in confocal micrographs following immunostaining of cultures with anti-S100 and anti-βIII tubulin (neurites).

RESULTS: In vivo experiments suggested regenerating axons grew preferentially between layers of cellular ENT in close contact with the aligned SCs, compared to unaligned or acellular controls (Fig 3). dADSCs maintained their alignment during preparation of ENT & over 3 days in culture. Neurons growing on ENT-dADSC were guided by the aligned cells (Fig 4).

DISCUSSION & CONCLUSIONS: In vivo experiments showed that ENT supports axon regeneration and that this is greatest between the layers of ENT when aligned SCs are present. As a potential clinical source of SCs for development of ENT, we showed that dADSCs survive and maintain their alignment following the stabilisation process to form sheets of ENT. Neurons growing on the surface of ENT extended neurites that were guided by the orientation of the aligned dADSCs.