Tissue engineering to model and repair the nervous system

Conference or Workshop Item

Tissue Engineering to Model and Repair the Nervous System

J B Phillips

Department of Life Sciences, The Open University, Walton Hall, Milton Keynes, MK7 6AA, UK

INTRODUCTION: Repairing the damaged nervous system is one of the greatest challenges facing regenerative medicine. Research into nervous system repair can be separated into two broad areas covering the central nervous system (CNS) and the peripheral nervous system (PNS). Damage to peripheral nerves can lead to loss of sensation, motor function and muscle weakness, but the PNS is capable of significant spontaneous regeneration and in many cases some function can be restored. In contrast, neuronal regeneration following damage to the CNS is generally unsuccessful and injuries can cause permanent paralysis and loss of sensation.

Tissue engineering approaches have been developed to tackle both PNS and CNS repair. For the PNS, a wide range of conduits have been explored, many of which aim to function as an alternative to an autograft. They provide an environment in which regenerating neurites can grow from the proximal stump across a gap in a damaged nerve, allowing them to penetrate the distal stump and eventually re-innervate target tissues. These conduits are engineered therefore to provide guidance and support as well as physical protection at the repair site. For the CNS, particularly the spinal cord, tissue engineered devices have been developed that provide a permissive environment for neuronal growth. However, having traversed the repair site, neurons generally fail to re-enter the surrounding CNS tissue due largely to the formation of an inhibitory interface (the glial scar) at the boundary of the implant.

An exciting new area of neuroscience where tissue engineering is pivotal is the development of advanced 3-dimensional (3D) cell culture models. These are starting to fill the gulf that has traditionally existed between simple cell culture systems and whole animal or tissue slice approaches and are providing new insights into cellular neuroscience.

METHODS: A range of tissue engineered approaches to repairing spinal cord and peripheral nerve injury will be discussed, particularly the use of protein biomaterials and the key design features to be taken into account. Tissue engineered culture models will be described which enable CNS or PNS cells to be maintained in highly controllable 3D environments and manipulated to emulate key features of the nervous system, especially its response to damage. Type I collagen gels form the basis for these models, which can incorporate mixtures of distinct cell types, mimic tissue interfaces, and provide a robust system in which glial cell behaviour and neuronal growth can be monitored and quantified.

RESULTS: Peripheral nerve repair devices have been tested in culture models and in vivo, and studies are underway to develop these further. An effective 3D culture model has been developed which mimics the peripheral nerve repair environment and is being used for studies that previously would have relied on animal models. Astrocytes, the glial cells in the CNS which form the glial scar, have been successfully cultured in a model which allows their response to spinal cord injury to be studied. Furthermore, controlling their alignment in 3D alters the extent to which neurons can regenerate, offering a potential therapeutic approach for overcoming the glial scar.

DISCUSSION & CONCLUSIONS: Tissue engineering is increasingly important in neuroscience, not just for the development of implantable repair devices, but increasingly in the provision of engineered cell culture models. Cells in traditional cultures often fail to adopt phenotypes and responses characteristic of their behaviour in vivo, whilst in animal models the dynamic environment and complex interactions between cells make it difficult to isolate a specific feature under investigation or to monitor cellular events continuously. Tissue engineered 3D models have the potential to exploit the advantages of traditional culture systems, facilitating detailed control and monitoring of cellular responses, whilst providing a spatial and mechanical environment in which cells more closely resemble their in vivo counterparts.

REFERENCES:

J. B. Phillips et al (2005) *Tissue Eng* **11**:1611-1617

E. East & J. B. Phillips (2008) Tissue engineered cell culture models for neuroscience research in *Tissue Engineering Research Trends* (ed G. N. Greco) Nova Science Publishers Inc, pp141-160.