Case Study 11 : Regeneration : Dominic Giannangeli

To understand the effects of specific factors on a particular system, one must only alter one variable and observe the outcome. This is difficult to do with in vivo studies of nerve regeneration. Fabricating a standard environment to perform different nerve regeneration experiments will aid in the ability to alter one variable and extract its effects. A Lab on a Chip (LOC) for nerve regeneration would be beneficial.

To do this, one motor nerve organoid and one heart organoid, composed of ventricular cardiomyocytes, will be generated from human derived iPSCs [2]. The iPSCs will be stimulated with proper environmental factors so they differentiate into motor neurons. The motor neuron spheroid will then be implemented into a custom made microdevice that has compartments for the spheroids and bridging between these compartments will be a microchannel. This device will be composed of Poly(dimethylsiloxane) (PDMs) lined with Matrigel ECM proteins It will be formed to embody the required structure for axonal propagation from the motor nerve spheroid to the heart organoid. Axons will form a fascicle that transverses through the microchannel and will then innervate the heart organoid. The heart organoid is necessary to mimic the termination that occurs for axon fascicles in vivo[3]. There will be an accessible region along the axon specific microchannel. In this region, additional biological substance or signals (specific chemicals, mixtures, cells, etc.) can be implemented and cultured so that it is in direct contact with the axon. In this region, the axon fascicle will be damaged in some way [4]. Different biological variables can be integrated into this variable space and their specific effect on the ability of the axon to regrow and/or heal will be observed for each experiment. The specifics of what biological and chemical material, necessary for proper cell healing, can be evaluated by experimenting with the composition of material within this variable region. Although blood vessels and other essential mechanisms for nerve regrowth would not be present in this model currently, opportunity for experimentation within the variable region could lead to an explorer implementing a blood vessel mimic to observe its effect on nerve regeneration. The region makes available the potential for knowledge constituting nerve regeneration.

A researcher could create a medium within this variable region that consist of ECM proteins capable of housing macrophages. Macrophage behavior could then be observed at the onset of nerve injury. This would provide more insight on the signals the drive macrophage's purpose in nerve reconfiguration. In addition, concentrations of inhibitory factors (such as Myelin associated molecules) or neurite growth factors (such as neurotrophin 3, NT-3) can be evaluated [1]. Information can be collected about how specific concentration of inhibitory or growth elements effect nerve growth as all other variables can be controlled within the device.

References:

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