Nerve-On-A-Chip for modelling motor neuron diseases and preclinical neurotoxicity testing

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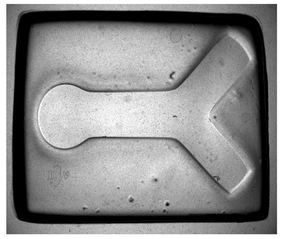
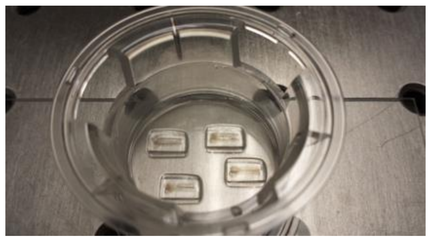
Objective

Develop an organotypic, micro-physiological model for mimicking motor neuron diseases and evaluating clinically analogous physiological measurements.

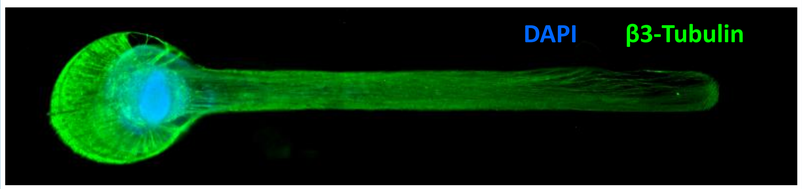
Nerve-on-a-Chip Design

Fabrication: Microengineered hydrogel scaffolding

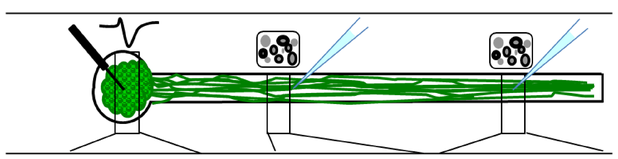




Biological Control: Direct and confine 3D axon growth and cellular positioning to mimic nerve fiber tract



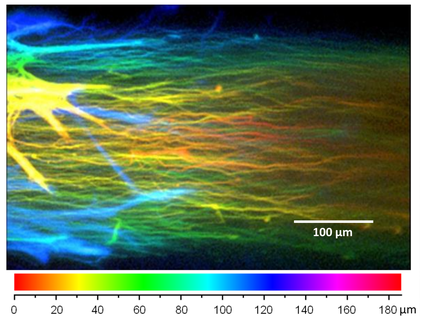
Test Metrics: Robust nerve growth, fasciculation, and glial interactions facilitates morphological and physiological outputs as a high-content screening assay for neurotoxicity and pharmacological manipulation



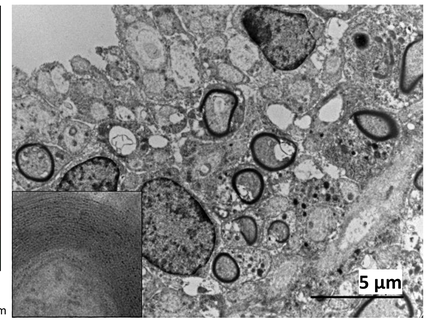
Morphology	MN density	Axon density
	MN diameter distr.	Axon diameter distribution
	Ultrastructure	Axonal fiber density
		Ultrastructure
Physiology	% Apoptotic cells	CAP amplitude
		CAP conduction velocity
		CAP integral

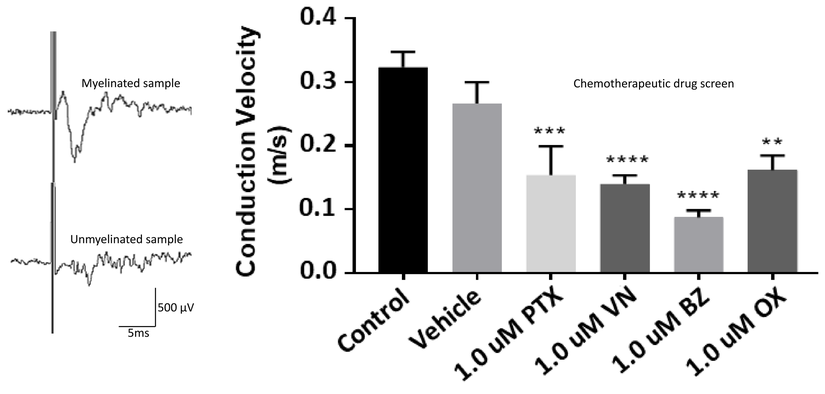
Morphology

Confocal Depth Color Map

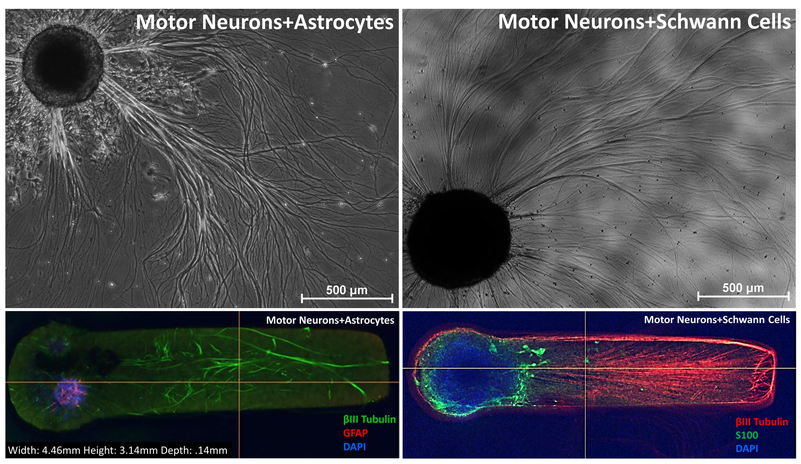


TEM Cross-Sections





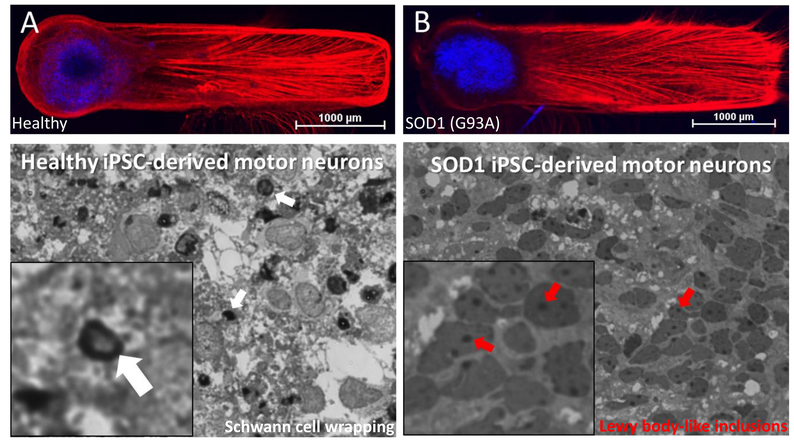
Human IPSC-derived spheroids growth in 2D and 3D



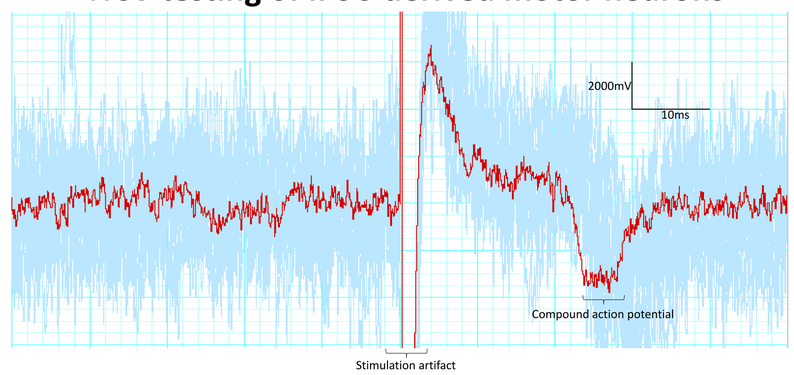
Result: Architecture resembles native peripheral nerve anatomy, allowing nerve density, fiber type and myelination tests, as well as studies of axon growth, cell migration, and glial differentiation.

Physiology

Healthy vs SOD1 (G93A) human motor neurons



NCV testing of iPSC-derived motor neurons



Result: Robust 3D neurite outgrowth (~5mm) was observed from both healthy and SOD1 motor neurons. Histological examination revealed ultrastructural changes in the two neuronal types. Healthy motor neurons were also found to be electrically active by recording compound action potentials extracellularly.

Conclusion: Successful incorporation of iPSCs derived healthy and SOD1 neurons to create the **first 3D *in vitro* Human-Motor-Nerve-On-A-Chip** showing robust neurite outgrowth, electrical activity and ultrastructural changes.

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