An Engineered 3D Peripheral Human "Nerve-on-a-Chip": A Novel Assessment for Neurotoxicity *In Vitro*

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Overview

The development of human iPSC-derived neurons has vastly expanded the predictive potential of preclinical toxicity assays. Notably, such cell types have increased accessibility compared to neural stem cells for 3D tissue engineering and modeling purposes. The use of engineered 3D organoids have seen tremendous growth as a preclinical drug screening tool because they are more biomimetic than 2D assays. When modeling complicated tissues such as the human nervous system, 3D engineered cultures provide marked advantages by recapitulating cell-cell interactions. ***In this study, we have devised a novel method for engineering an in vitro human-iPSC based 3D nerve that supports axon growth analogous to PN anatomy. This in vitro nerve can provide clinically relevant metrics such as nerve conduction velocity (NCV) and histological ultrastructure.*** These read-outs represent the gold-standard in preclinical testing. Prior to the advent of iPSCs, such metrics were only obtainable through in vivo experimentation.

Methods

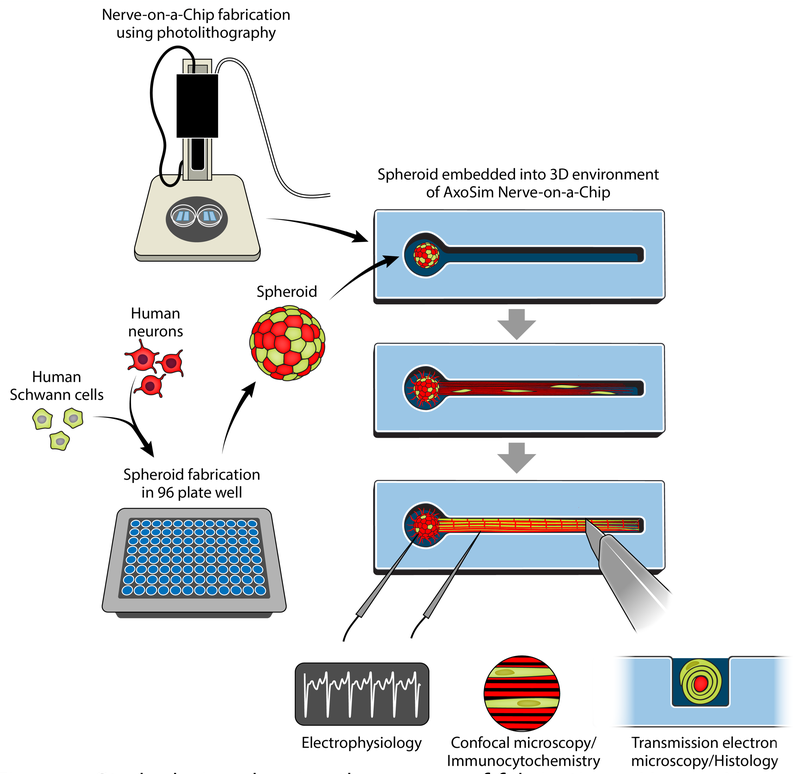
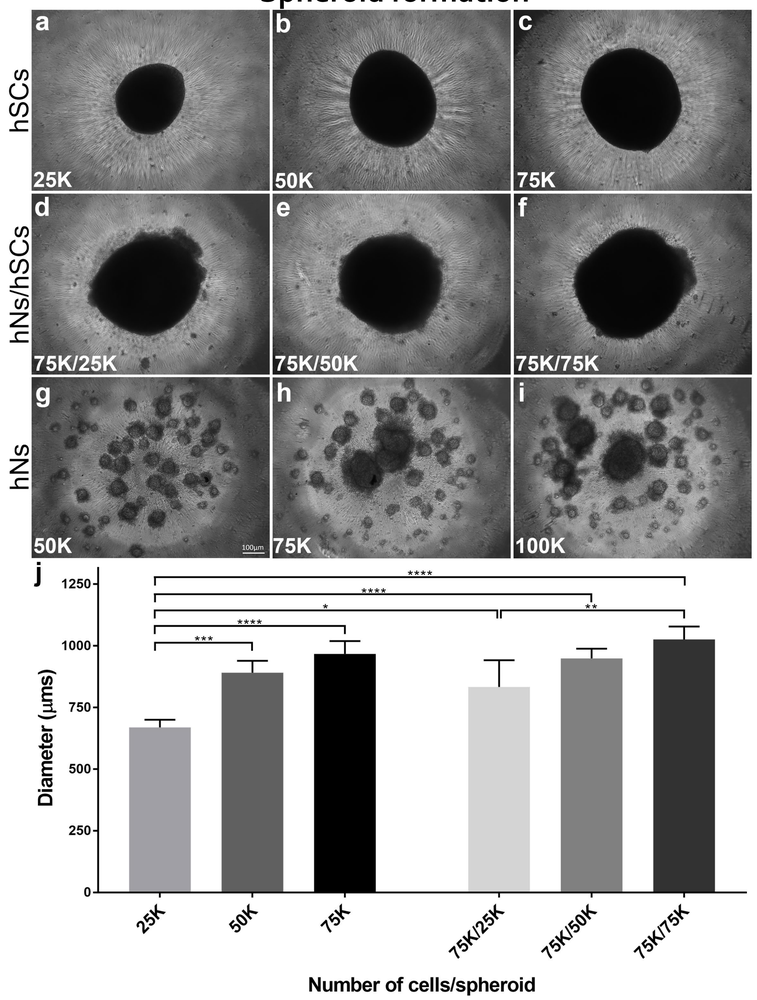


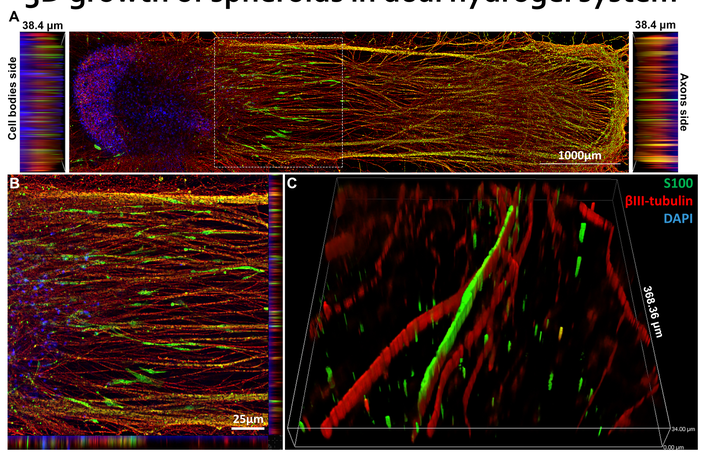
Figure 1. Study design showing the process of fabricating a Human Nerve-on-a-Chip system.

Results

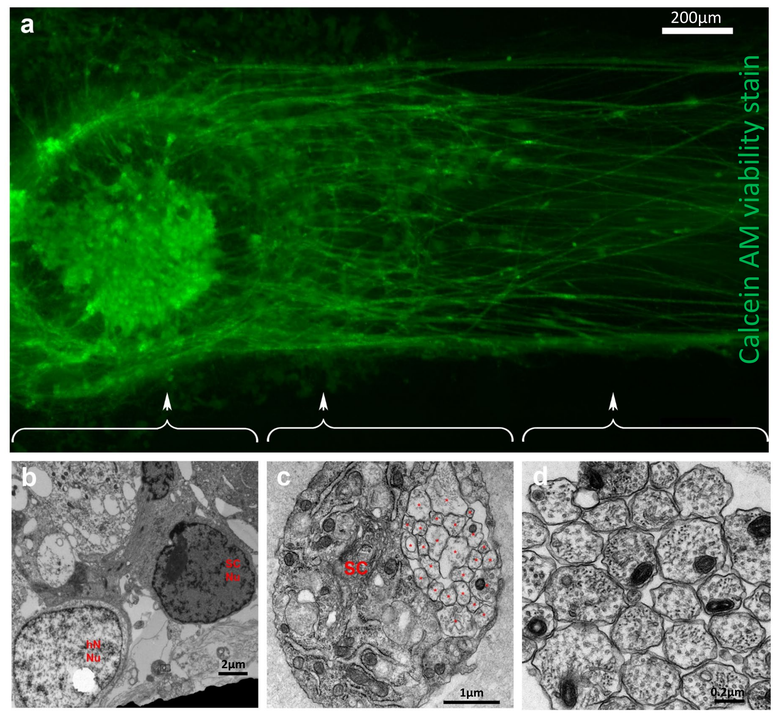
Spheroid formation



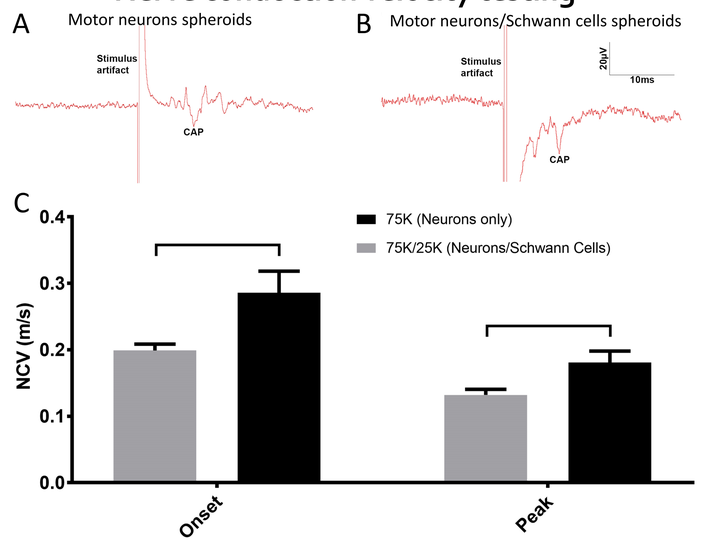
3D growth of spheroids in dual hydrogel system



Ultrastructure of *in vitro* human nerve



Nerve conduction velocity testing



Summary & Conclusion

- Schwann cells facilitated the spheroid fabrication process.
- Evidences of both Schwann cells migration & myelination was detected.
- Nerve conduction velocity was successfully evaluated for both mono and coculture spheroids.

Acknowledgements

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