#24 -TRANSLATIONAL MODEL OF NERVE INJURY-ON-CHIP

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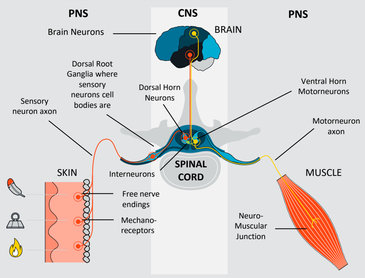
BACKGROUND



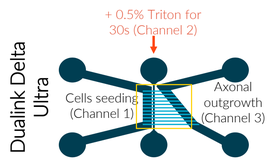
Nerve damage can lead to complete **loss of motor function** or chronic **neuropathic pain**. Peripheral nerves are made of motor and sensory nerves, two very distinct types of neurons that are linked but each have their specific function. **Organs-on-chip** (OoC) offer the advantage to **isolate** neuron **somas** from their **axons**, thus reproducing the human anatomical architecture and enabling injury or treatment paradigms aligned with real life situations. To tease apart each cell type and allow their study separately, we adapted the culture of **motorneurons** and **sensory neurons** onto our OoC platform. To bridge the gap between *in vivo* models and first-in-human studies, as well as increase relevance, we developed our models using **hiPSC**-derived neurons.

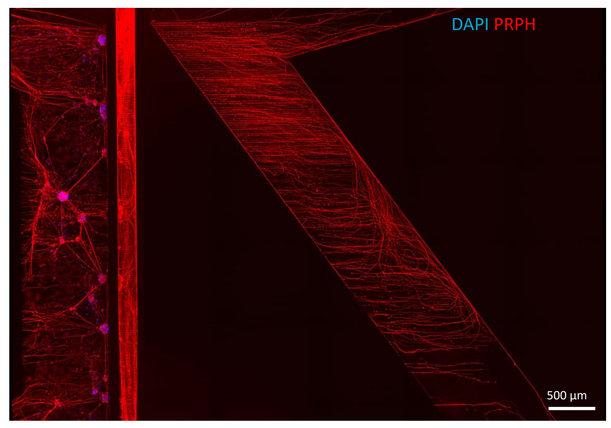
RESULTS

HUMAN NERVE INJURY-ON-CHIP VALIDATION

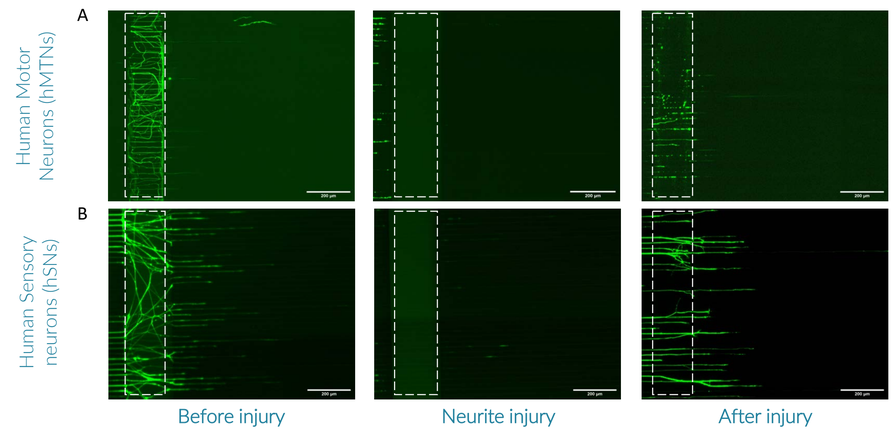
Neurite injury method in DuaLink Delta Ultra.

- Standardized culture protocols
- Localized neurite injury with a reproducible protocol
- Neurite regeneration post-injury





Human iPSCs-derived senrory neurons cultured 3-weeks in DuaLink Delta Ultra.
Peripherin, a marker of mature peripheral neurons is expressed by hSNs.

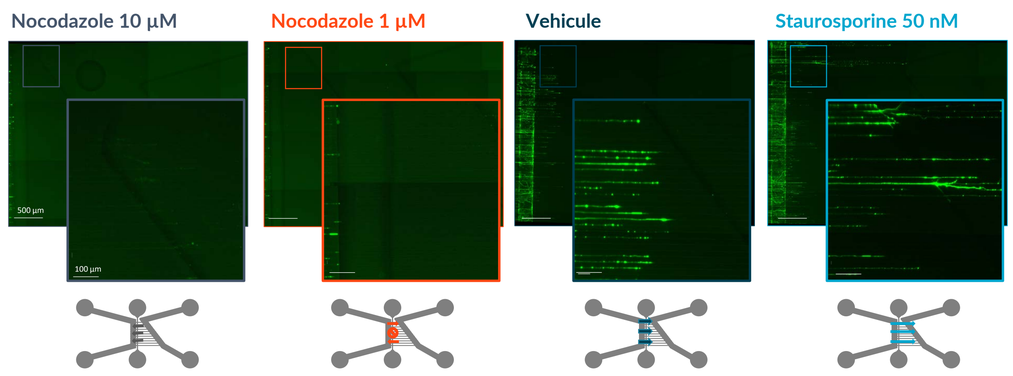


Human iPSCs-derived neurons cultured in DuaLink Delta Ultra.
A) Neurite visualization of hMTNs (01279, FCDI) ICC anti-βIII Tubulin, 3 days post-injury. B) Dynamic neurite outgrowth of hSNs (ax0555, Axol), before to 2 days post-injury with calcein live staining (0.1 µg/mL).

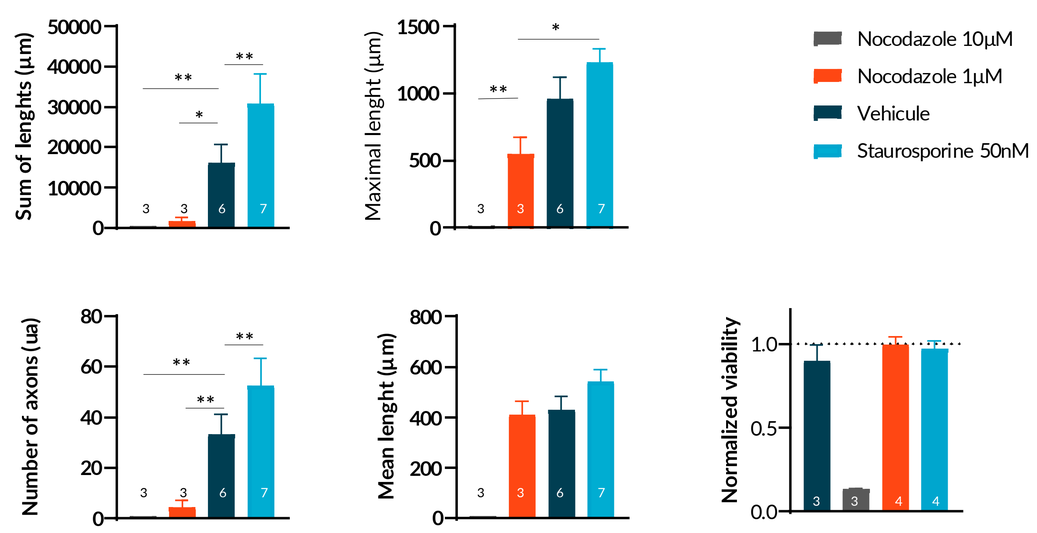
MOTOR NERVE REGROWTH POST-INJURY

Motor nerve injury model.

- Nocodazole destabilized microtubules and can be used as internal **neurodegenerative** control (Vasquez RJ *et al*., 1997).
- Staurosporine, a wide spectrum protein kinases inhibitor enhancing neurite outgrowth, is used as internal **neurotrophic** control (Wakita S *et al*., 2014).



Illustrative pictures of human motor neurons in DuaLink Delta Ultra stained with calcein live dye, 3 days of exposure post-injury.

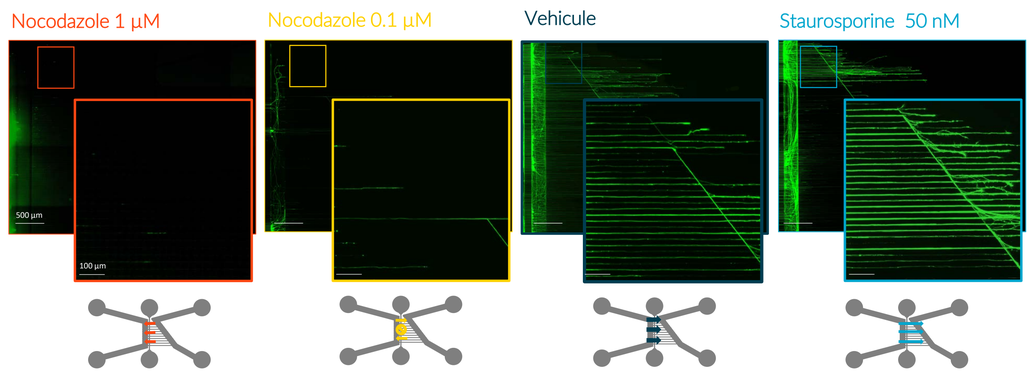


Human Motor Neurons regrowth quantification post-injury
Quantifications were performed using ImageJ and a homemade pre-processing algorithm.Graphs and statistical analysis were generated using GraphPad Prism. Independent t-test with Welch's correction (* p-value ≤ 0.05, ** ≤ 0.01).

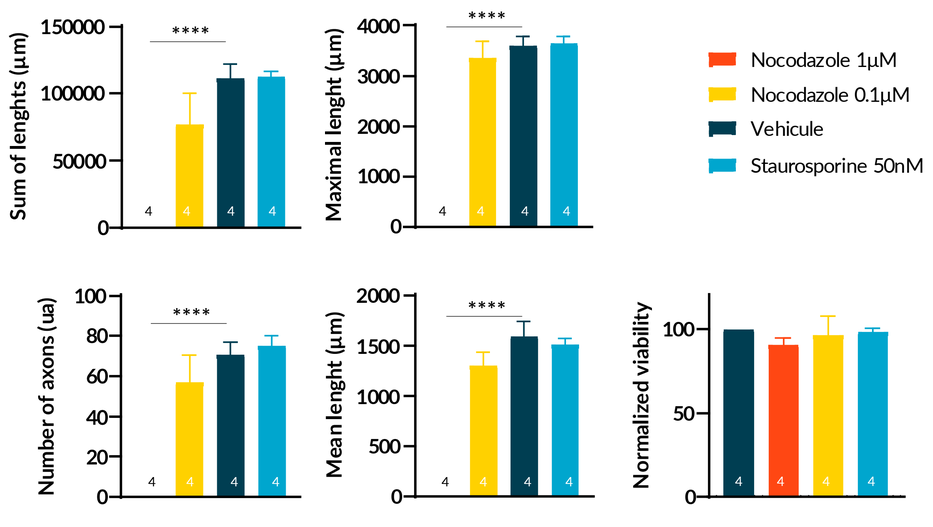
SENSORY NERVE REGROWTH POST-INJURY

Sensory nerve injury model.

- Nocodazole is more potent on hSNs compared from hMTNs.
- At the same concentration, staurosporine is less effective on hSNs. Dose should be adjusted to use it as internal neurotrophic control.



Illustrative pictures of human sensory neurons in DuaLink Delta Ultra with calcein live dye, 2 days of exposure post-injury.

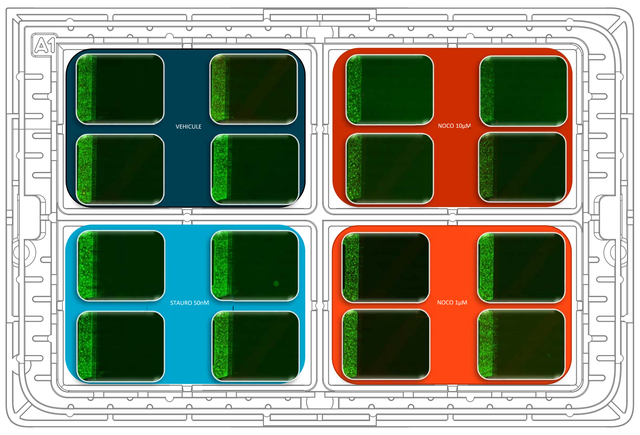


Human Sensory Neurons regrowth quantification post-injury
Quantifications were performed using ImageJ and a homemade pre-processing algorithm. Graphs and statistical analysis were generated using GraphPad Prism. Independent t-test with Welch's correction.

CONCLUSION & PERSPECTIVES

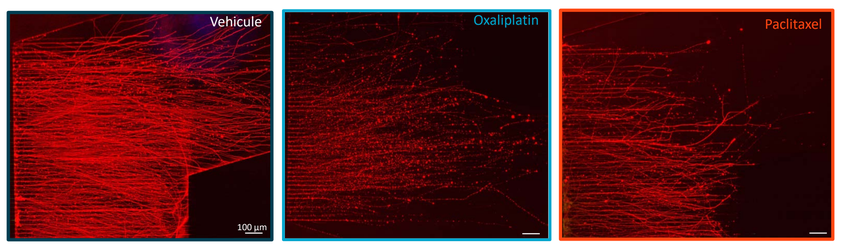
By **combining NETRI's engineering, biological & digital expertise**, we **validated our nerve injury model** by comparing axonal regeneration following treatment with a neurotrophic molecule or a drug inhibiting neurite outgrowth.

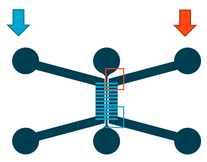
Our **Nerve Injury-on-chip platform** offers pharmaceutical companies and researchers a **new translational model** of traumatic nerve injury including digital analysis tools to study the efficacy and mode of action of novel therapeutic modalities.



After developing models to mimic traumatic nerve injury we are focusing on the potential of our technology to model neuropathic pain that can be translated further into neurodegenerative risk assessment.

Visit our booth to learn more about screening models for neuroprotective molecules.
Visit our website netri.com for the related information.





48h exposure to CIPN drugs

BOOTH #60

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