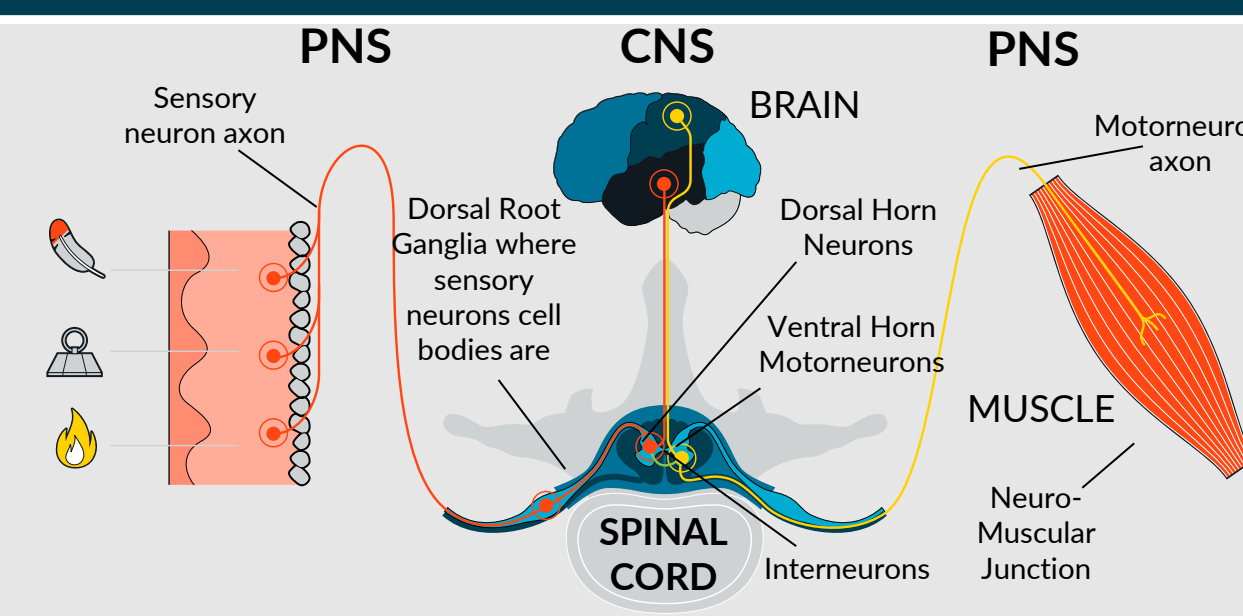


Hélène OB Gautier, Jessica Rontard, Camille Baquerre, Aurélie Batut, Louise Dubuisson, Louis Thibon, Damien Colas, Benoit Maisonneuve, Florian Larramendy and Thibault Honegger

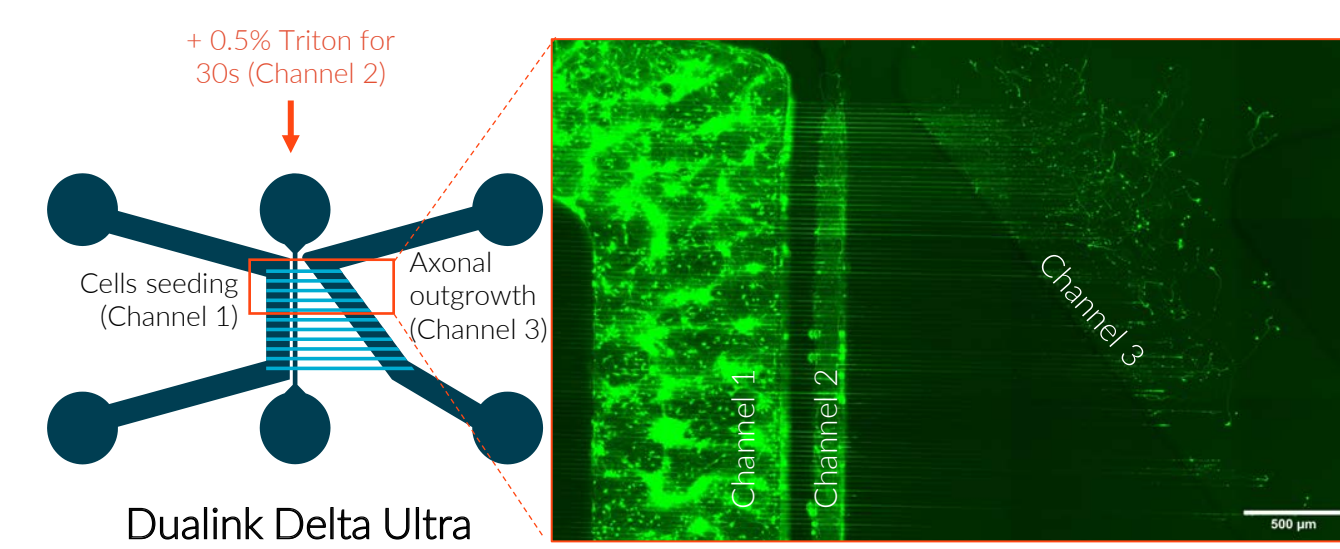
BACKGROUND



Day to day life can lead to traffic accidents, injuries at the workplace, incidents at home or during hobbies. Consequences can be devastating and include complete loss of motor function or chronic neuropathic pain due to nerve damage. 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 motoneurons 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.

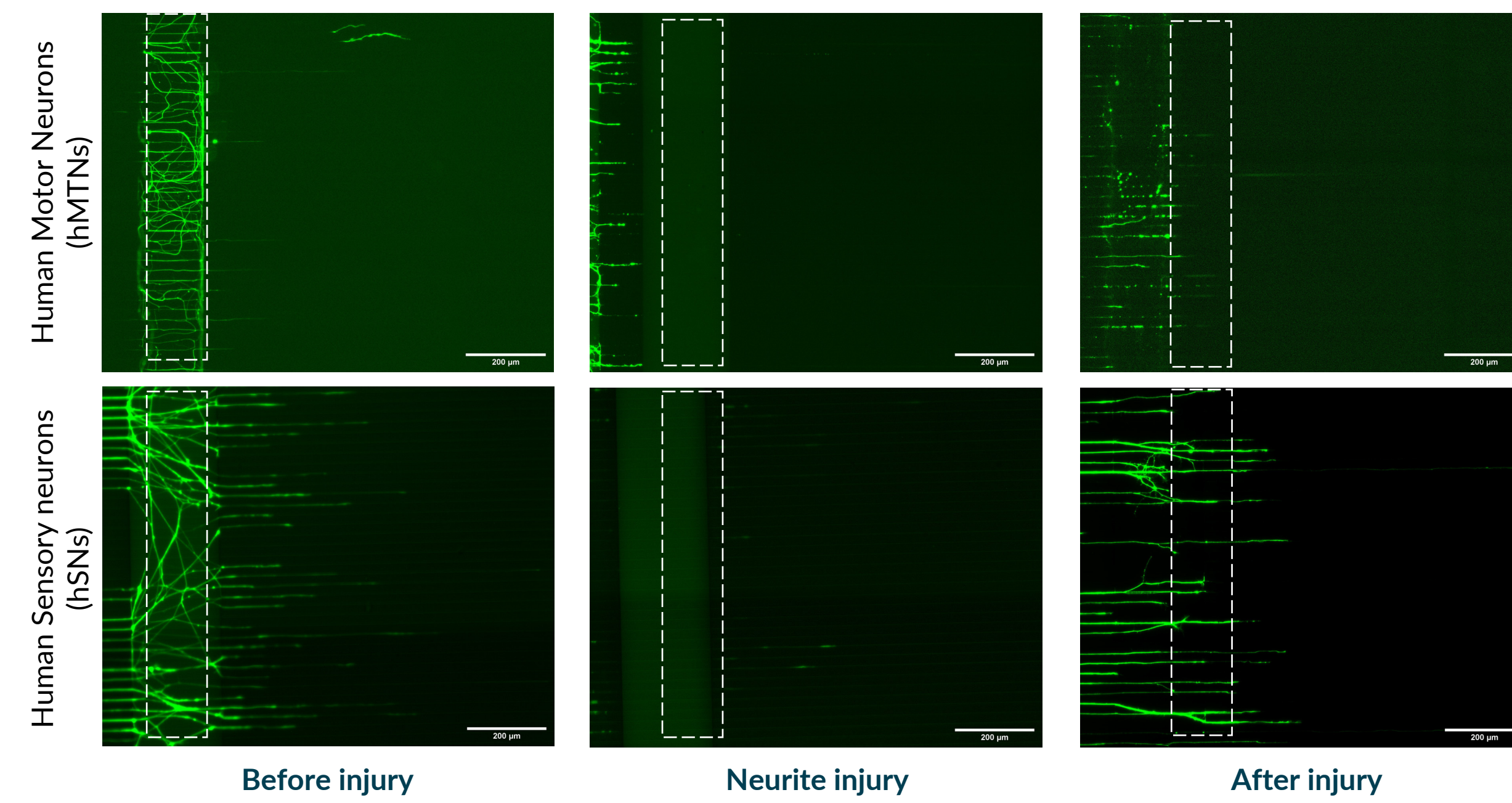
RESULTS

HUMAN NERVE INJURY-ON-CHIP VALIDATION



Neurite injury method in triangular microfluidic device

- Localized neurite injury with a reproducible protocol
- Neurite regeneration post-injury



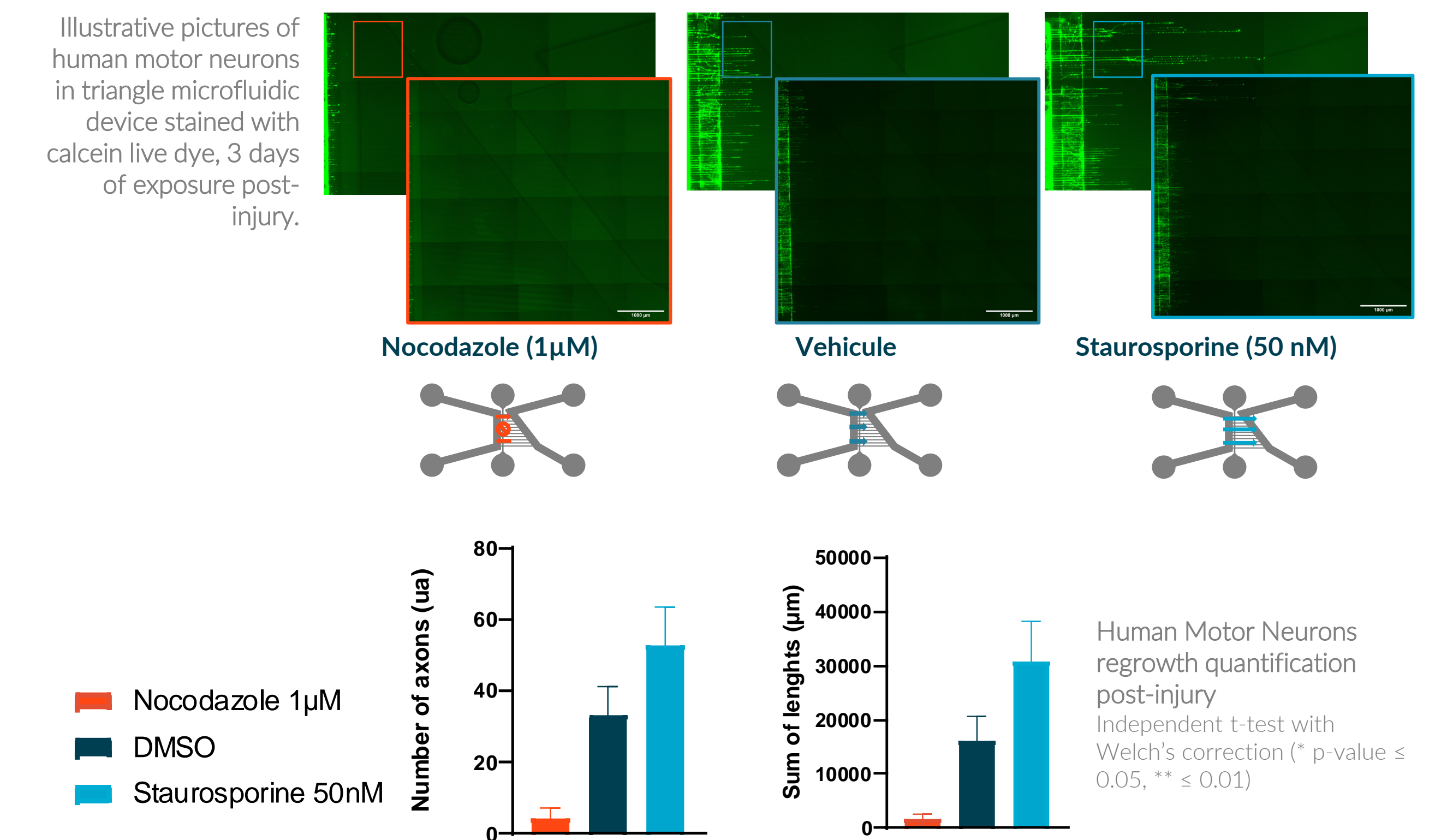
Human iPSCs-derived neurons cultured in triangle microfluidic device. A) Neurite visualization of hMTNs (01279, FCDI) ICC anti-βIII Tubulin, 3 days post-injury. B) Dynamic neurite outgrowth of hSNs (ax0555, Axol), before to 2 days post-injury with calcein live staining (0.1 μg/mL).



MOTOR NERVE REGROWTH POST-INJURY

Motor nerve injury model

- Nocodazole¹ destabilized microtubules and can be used as internal neurodegenerative control
- Staurosporine², a wide spectrum protein kinases inhibitor enhancing neurite outgrowth, is used as internal neurotrophic control

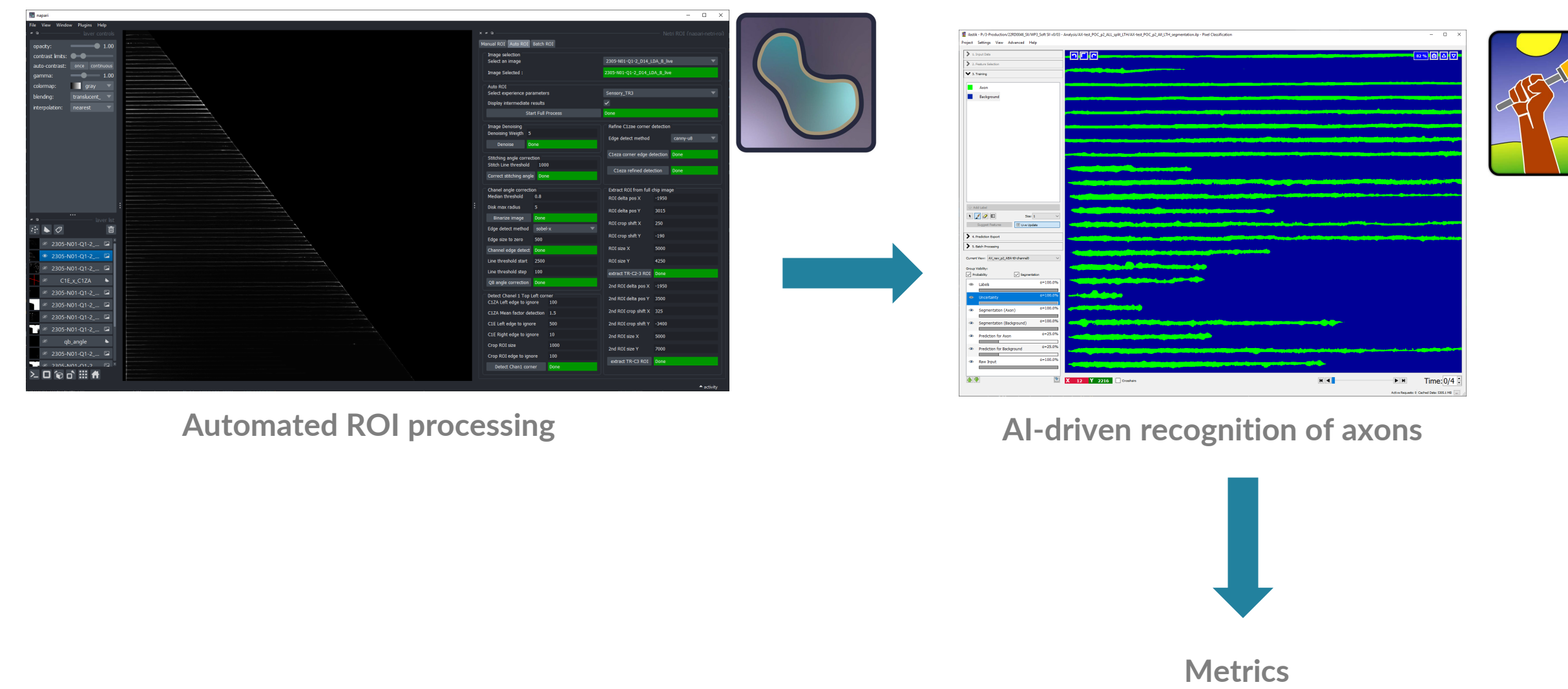


¹ Vasquez RJ et al., 1997
² Wakita S et al., 2014

DEVELOPMENT OF SEMI-AUTOMATED IMAGE ANALYSIS

Digital analysis

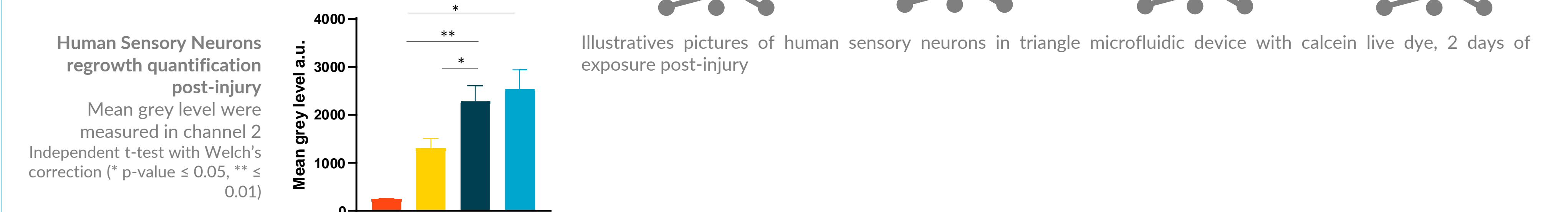
- Specific plugins were developed in Napari to pre-process by batch the images (contrast, luminosity and ROI determination)
- Preliminary manual analysis was done in Image J.
- Ilastik is used to automatically detect axons in microchannels



SENSORY NERVE REGROWTH POST-INJURY

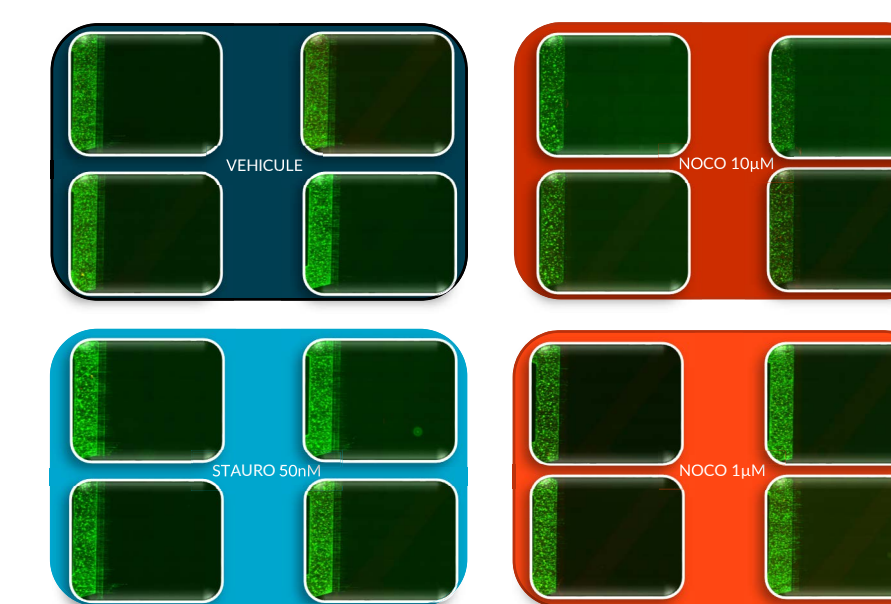
Sensory nerve injury model

- Nocodazole is more potent on hSNs compared from hMTNs.
- Large test window Neurodegenerative-Neurotrophic.



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 #36 for the related information.

