neuro

Institut et hôpital neurologiques de Montréal
Montreal Neurological Institute and Hospital

The Open Science iPSC/CRISPR Platform at the Montreal Neurological Institute

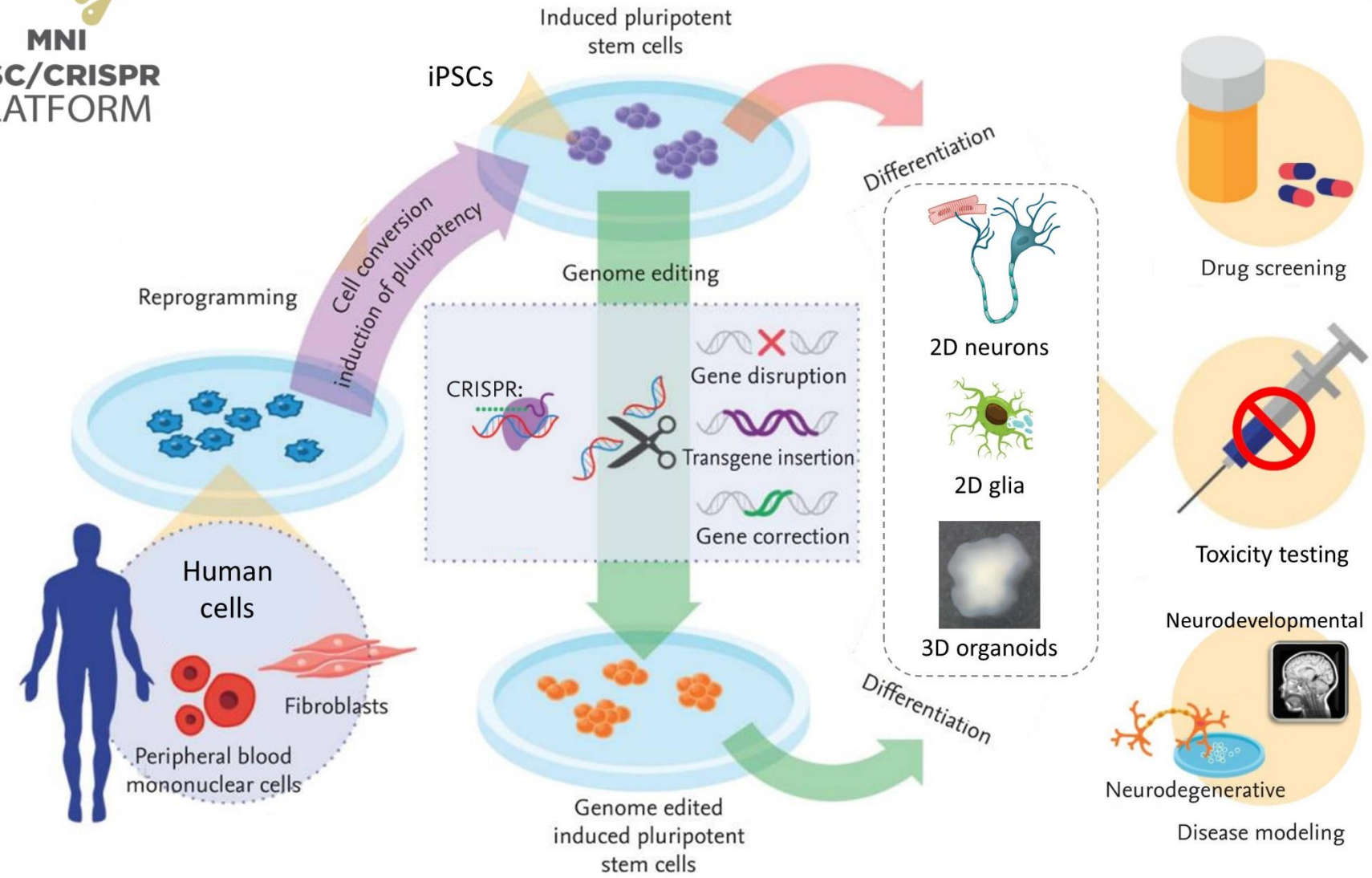
Lenore Beitel, PhD

McGill

Centre universitaire de santé McGill
McGill University Health Centre

MNI
IPSC/CRISPR
PLATFORM

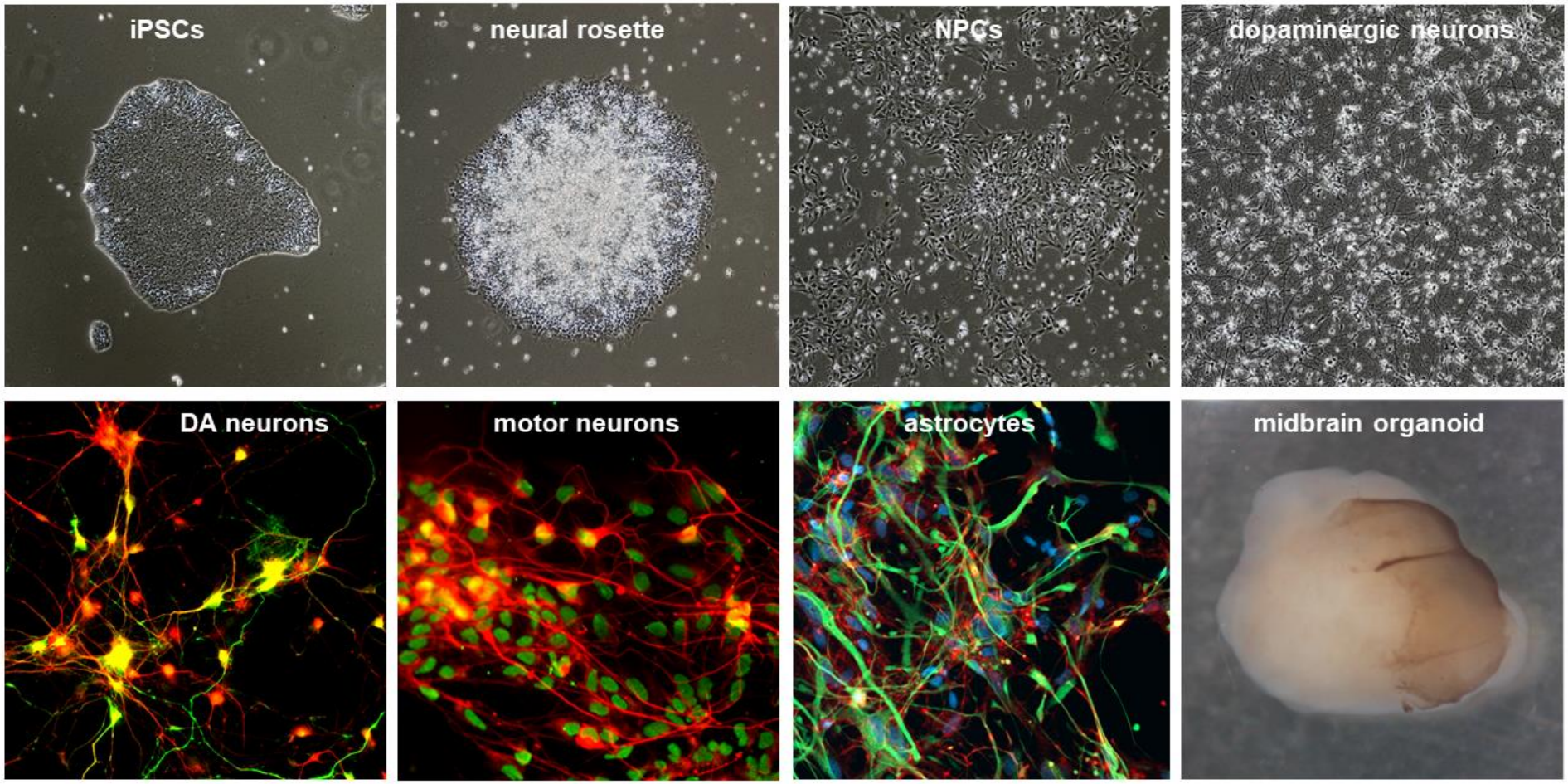
Induced pluripotent stem cells (iPSCs)



MNI
IPSC/CRISPR
PLATFORM

iPSCs to differentiated neurons

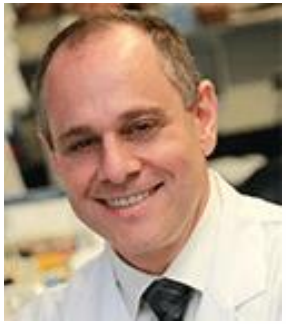
neuro



MNI iPSC/CRISPR Platform

- Established in 2015 - private donation, Brain Canada, MNI,Quebec Parkinson's Network
- Partner with iPSC reprogramming platform at Université of Laval
- Expertise in neuronal differentiation and CRISPR genome editing
- Work with academic and industry users
- Help design/execute assays using iPSC-derived neurons
- "In house" catalog of iPSC cell-lines
- Generate CRISPR knockout cell-lines
- Train users to make neurons from iPSCs
- All protocols openly available as part of the MNI Open-Science initiative

Brain Canada
UNIVERSITÉ LAVAL
cdrd The Centre for Drug Research and Development
cqdm Enabling Drug Discovery
RÉSEAU PARKINSON QUÉBEC
SGC



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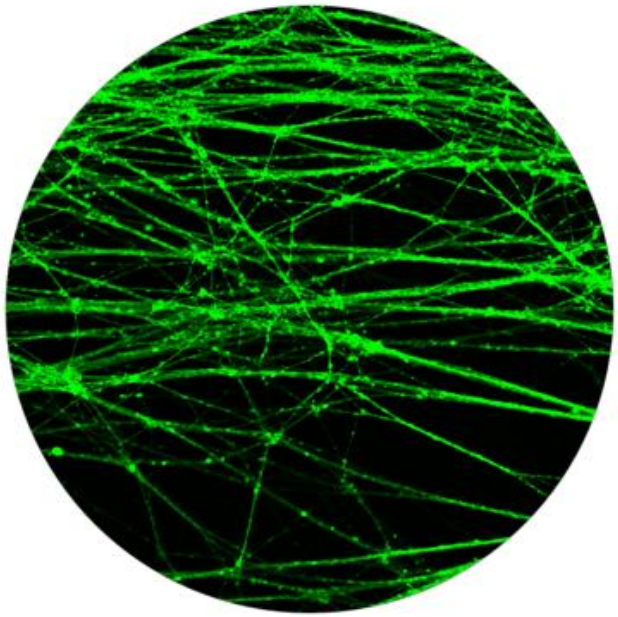
The use of induced stem cells and microfluidics for developing new assays to identify new therapies for Kennedy's disease

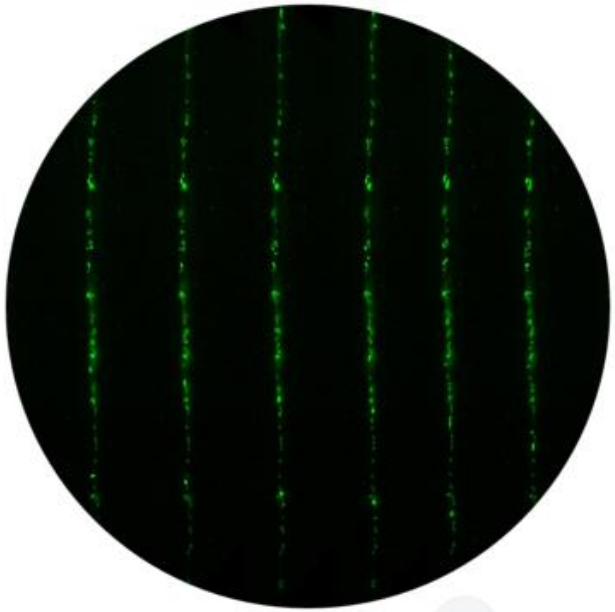
Thomas Durcan – KDA Grant 2017

biocompatible silicone insert
microchannels help direct axons



Without Ananda's device

Ambiguous analysis of axonal transport



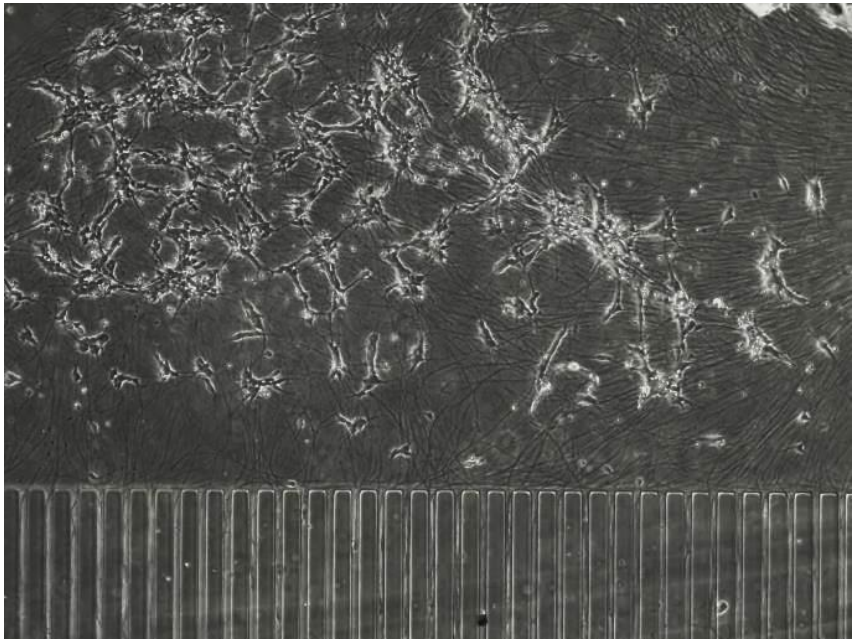
With Ananda's device

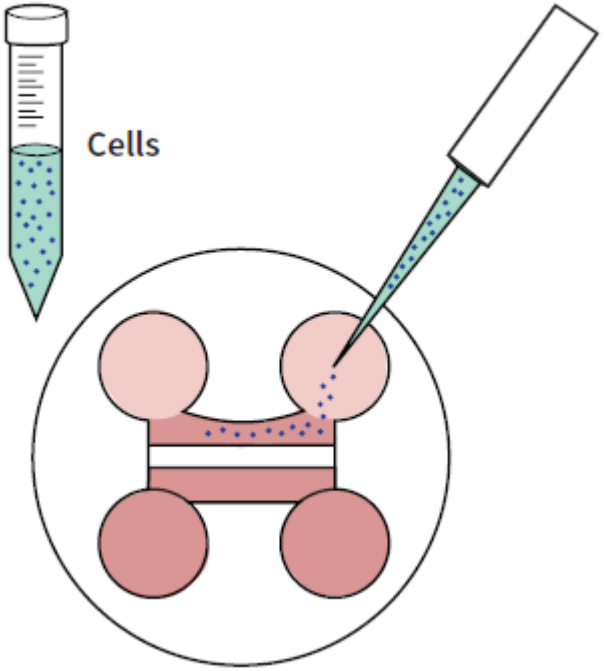
Fast and precise analysis of axonal transport

www.anandadevices.com

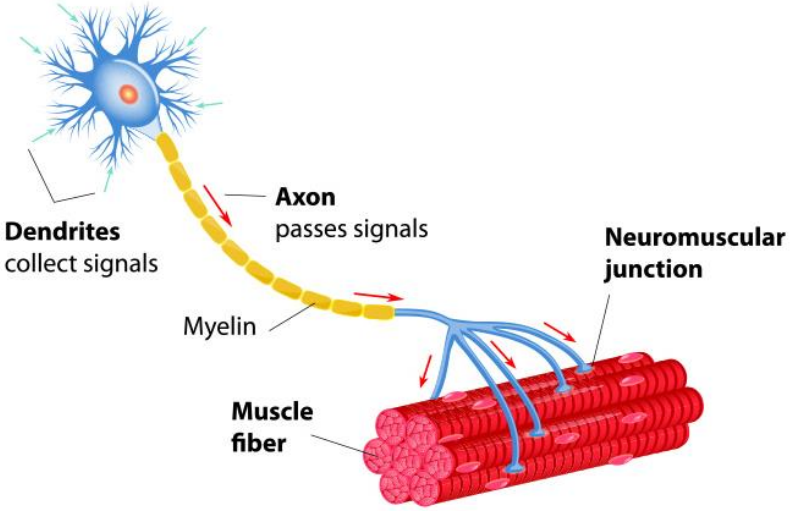

HOW TO USE
SILICONE
MOLDS


siliconfactory.en.alibaba.com

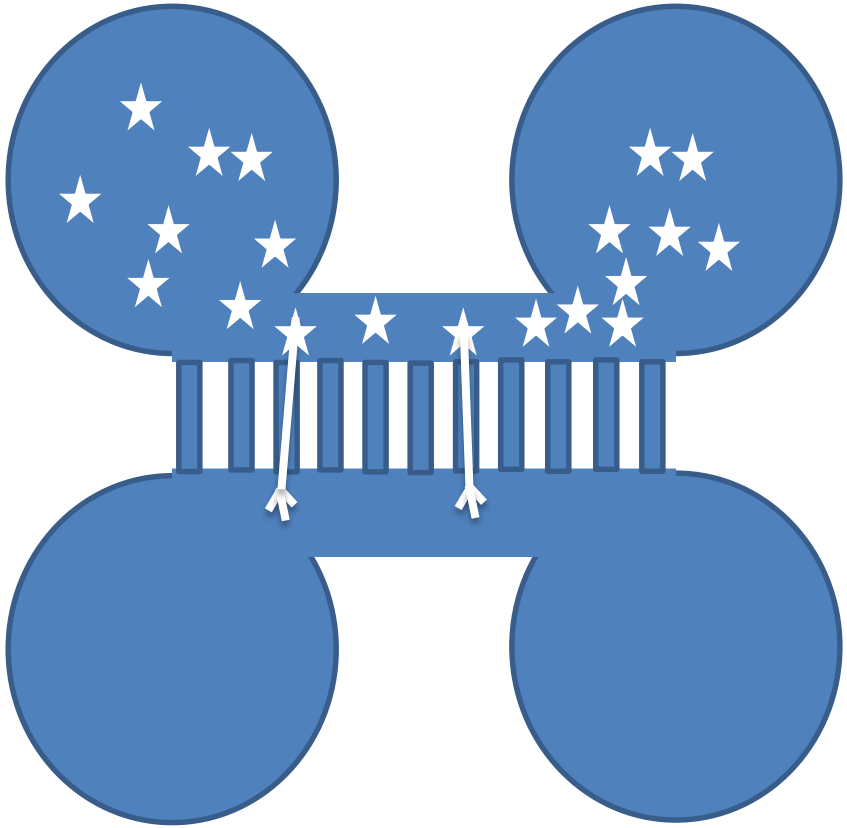




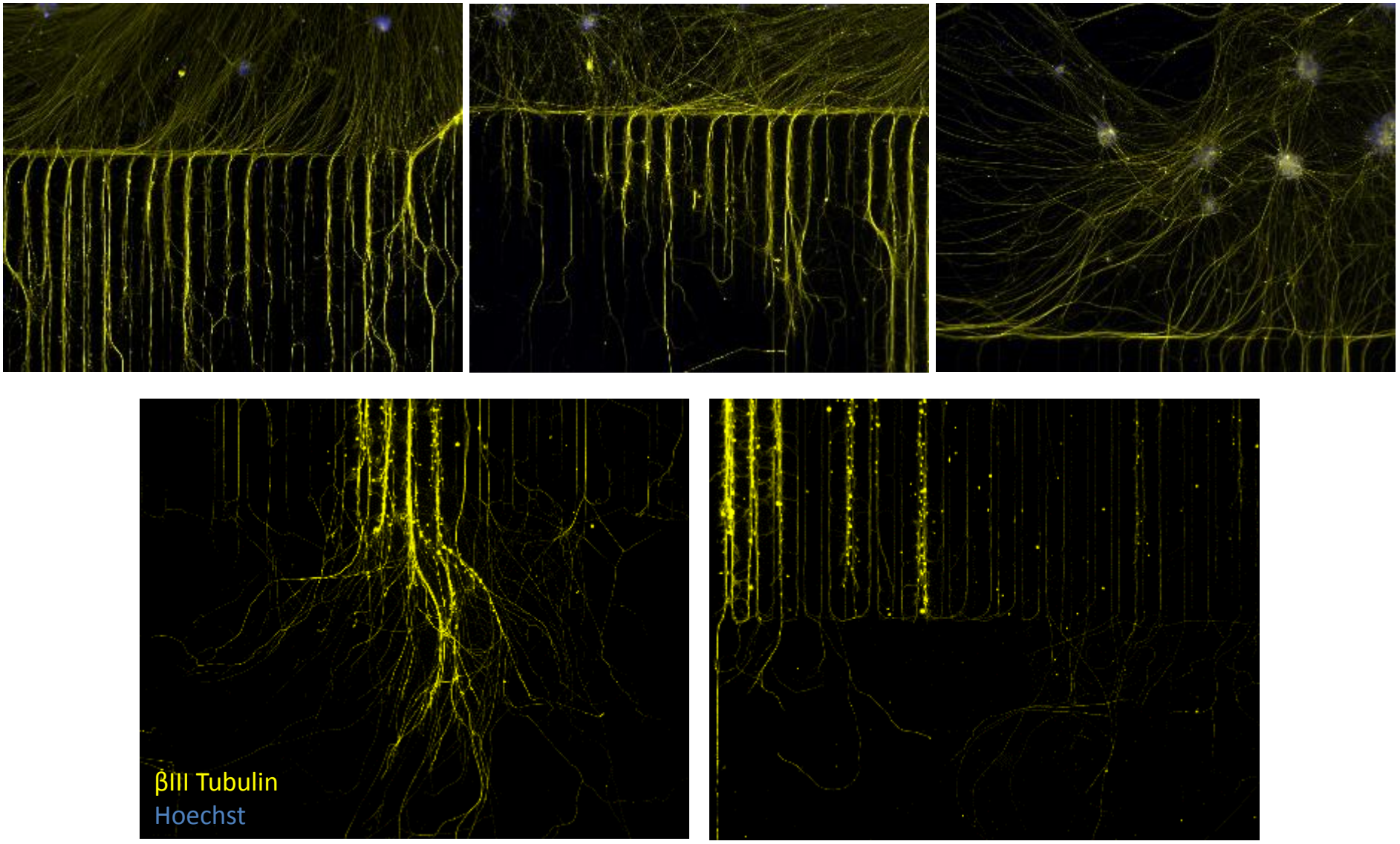
MOTOR NEURON



ANANDA Devices



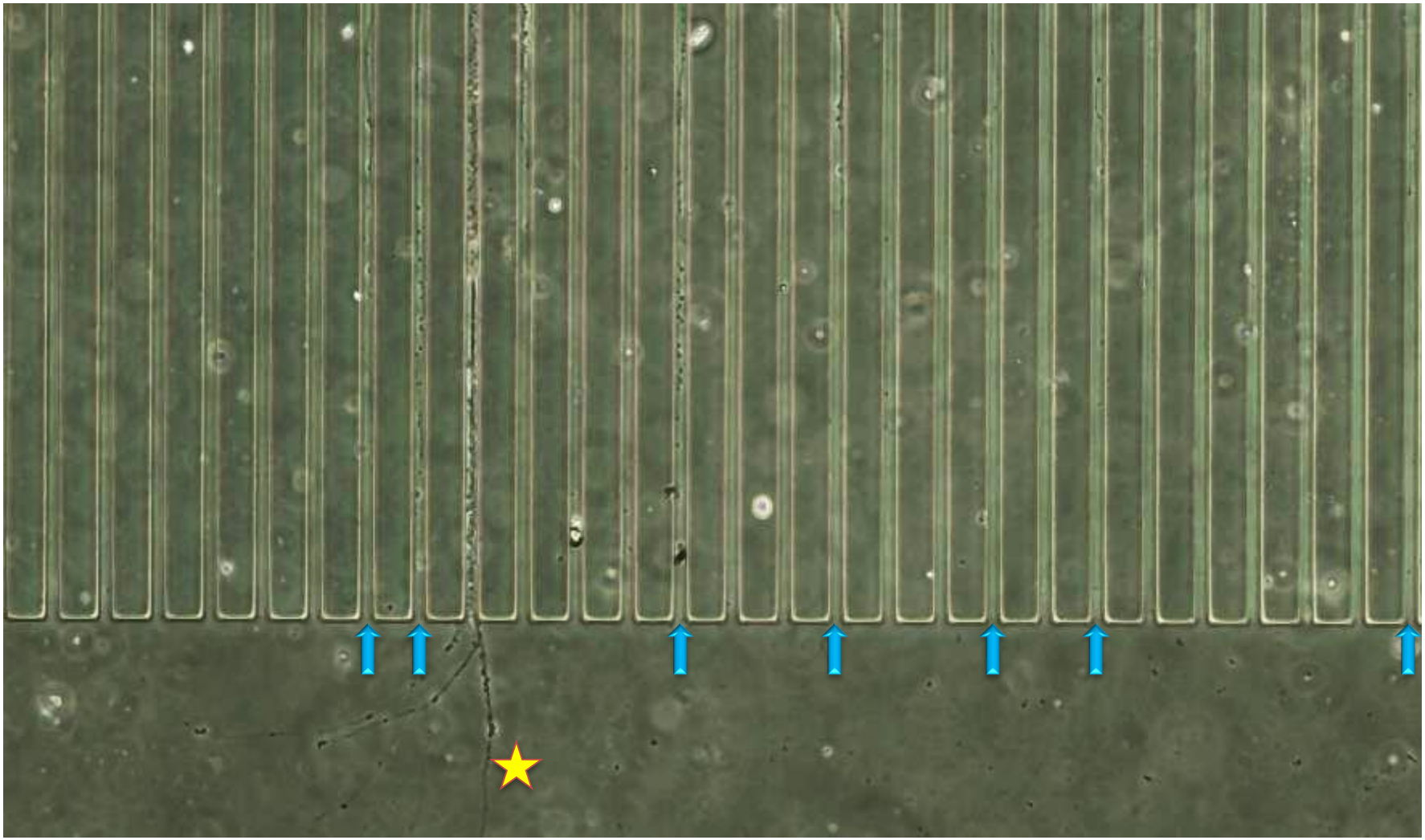
<u>Durcan Aim 1:</u> Investigate the survival and neurite outgrowth of motor neurons from controls and KD patients



F. Larroquette

F. Larroquette

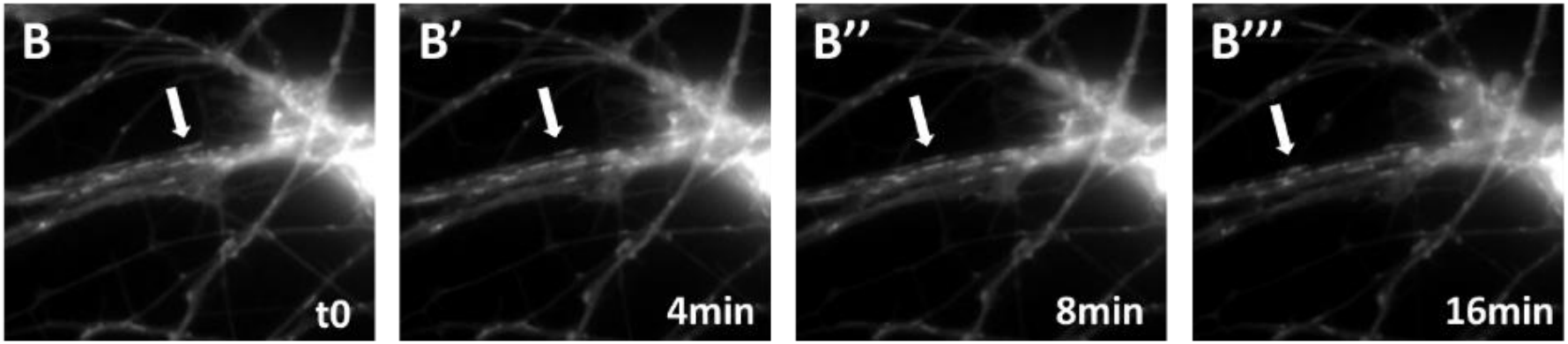
Motor neurons after 14 days growth



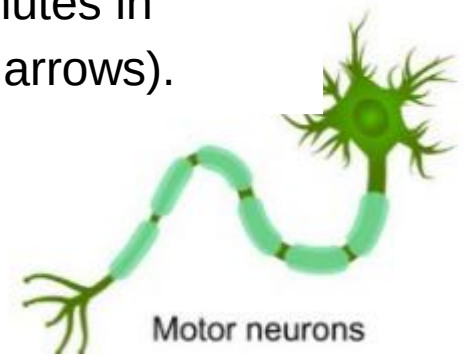
Axons coming out of channels

Axons not coming out of channels

<u>Durcan Aim 2:</u> Examine mitochondrial function in neurons derived from KD patients



Study mitochondrial properties in iPSC-derived motor neurons (MN). Above: Images of live cell Mitotracker recording over 16 minutes in control MN. Mitochondrial movement can be tracked (white arrows).



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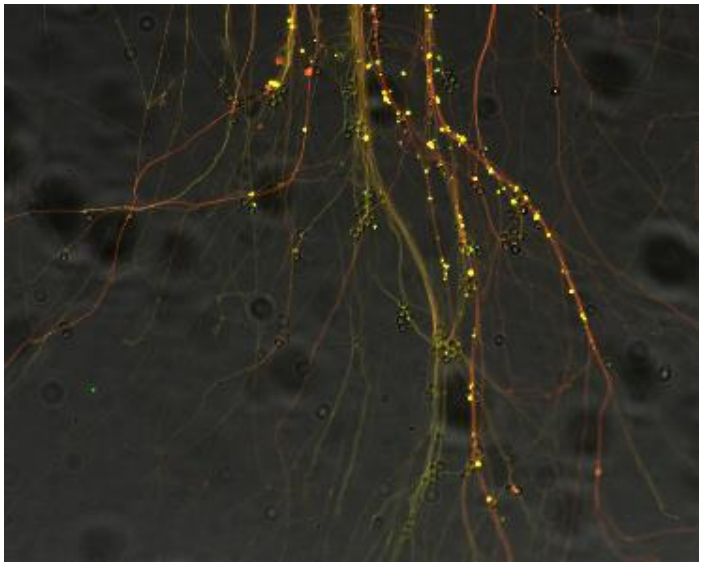
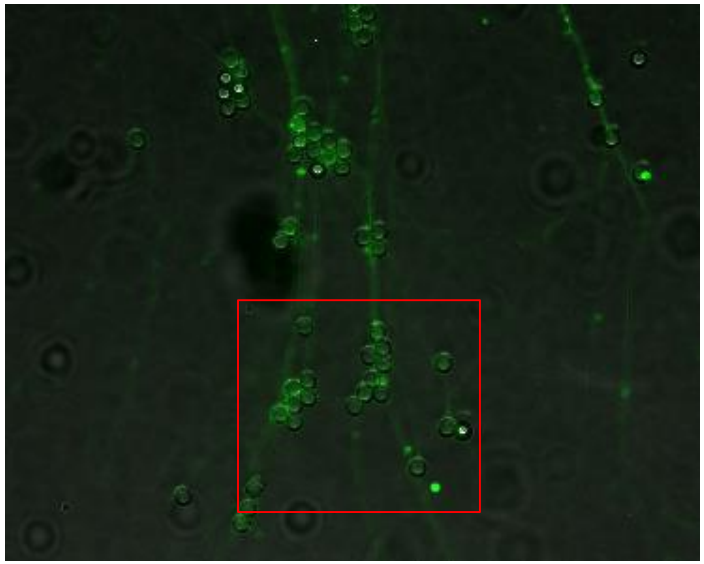
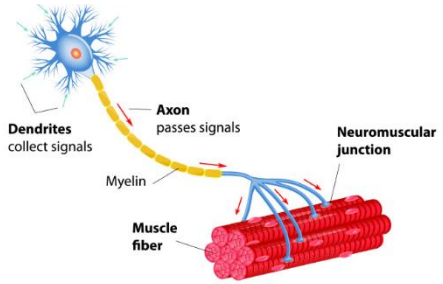
Durcan Aim 3: Characterize the formation and maintenance of synapses from mutant neurons



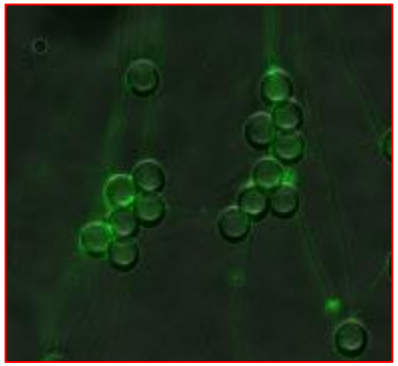
Hoecht/Tuj1/NFM/
Synaptophysin/Beads Brightfield



Synaptophysin/Beads Brightfield x40



netrin-1 bead



Synaptophysin
Beads Brightfield (zoom)

netrin-1 - involved in axonal guidance

Synaptophysin - a protein in neurons

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Acknowledgements

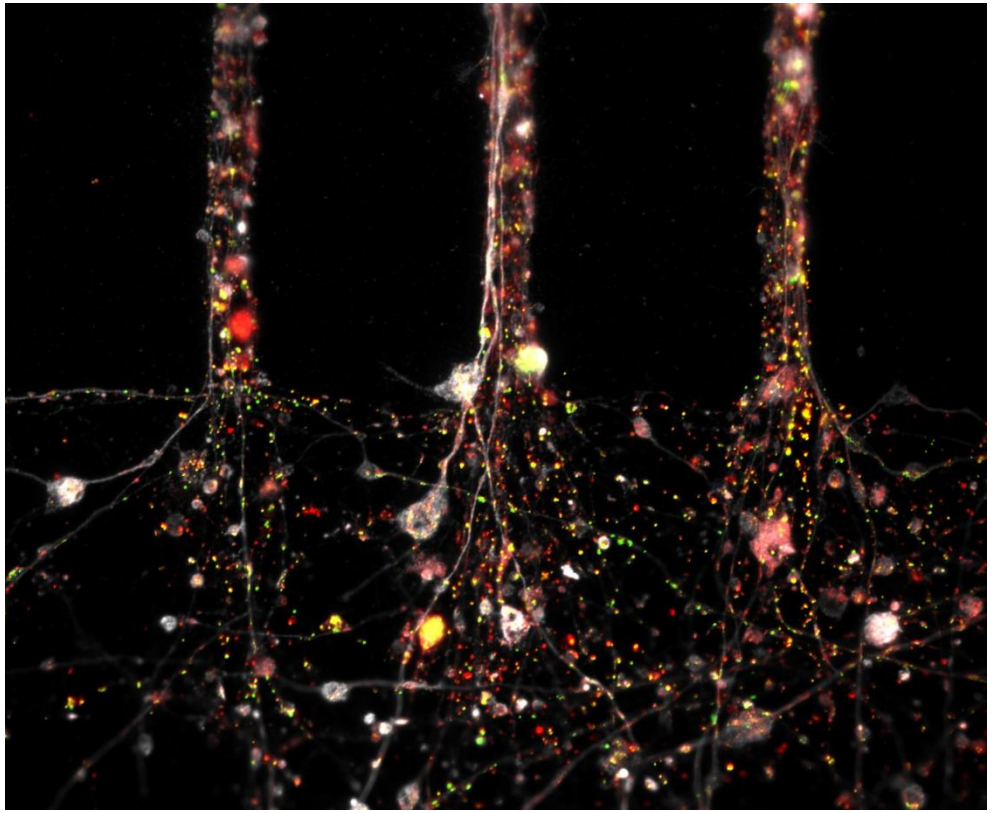
Thank you all...

Kennedy's Disease Association

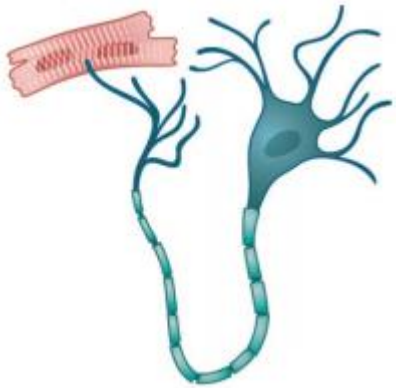
Tom Durcan

MNI IPSC/CRISPR PLATFORM

Frédérique Larroquette



The roots of life



The use of induced stem cells and microfluidics for developing new assays to identify new therapies for Kennedy's disease

Thus, our ***global aim*** for this project is to develop a suite of state of the art disease-relevant assays using human motor neurons (MNs) derived from induced pluripotent cells (iPSCs).

<u>Aim 1:</u> Investigate the survival and neurite outgrowth of motor neurons from control and KD patients

<u>Aim 2:</u> Examine mitochondrial function in neurons derived from patients

<u>Aim 3:</u> Characterize the formation and maintenance of synapses from mutant neurons

A drug screening in human neurons based on phenotypic defects specific to KD would be an effective way to identify such promising compounds for therapy