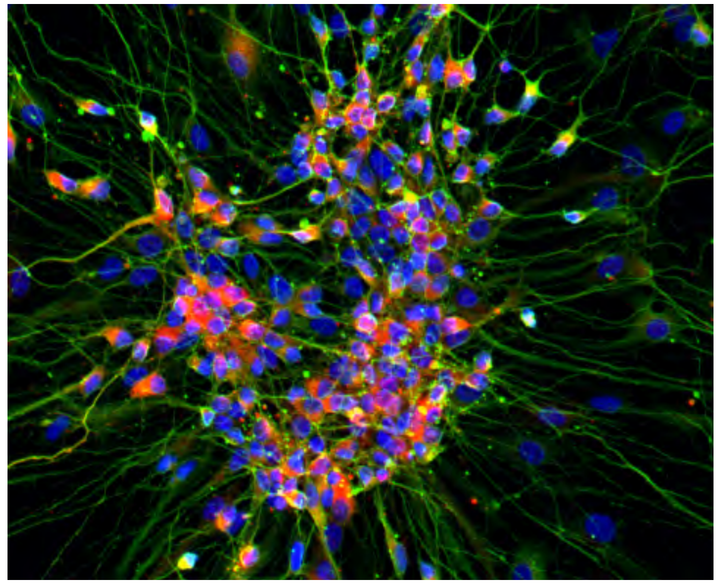
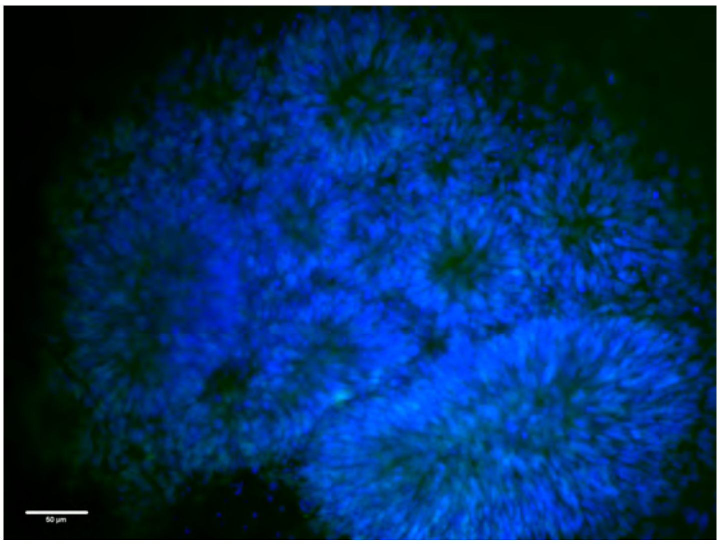
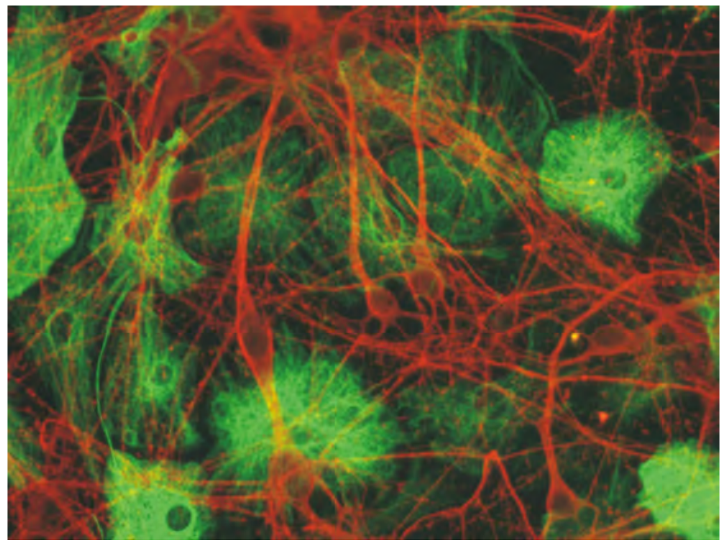
ANSARI ALS CENTER FOR CELL THERAPY AND REGENERATION RESEARCH AT JOHNS HOPKINS





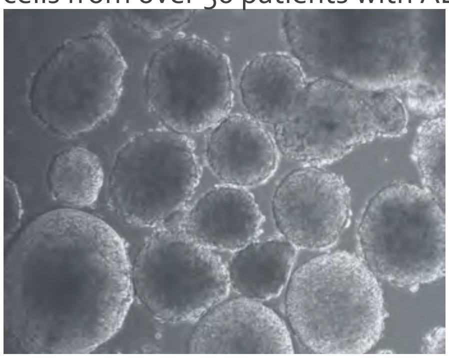


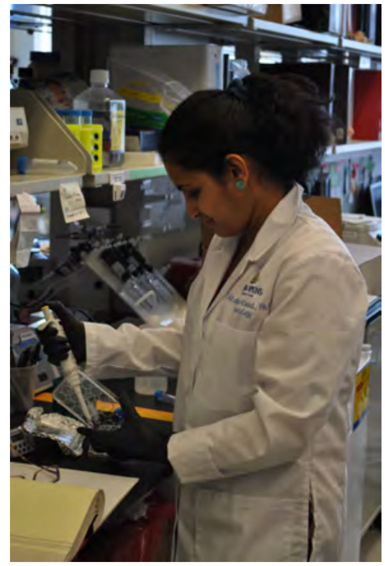
DIRECTIONS 2017

ALS Stem Cell Core

Creating induced pluripotent stem cells (iPSC) from ALS patients.

The ALS iPSC core at Johns Hopkins has utilized our large repository of iPS cells from over 50 patients with ALS.





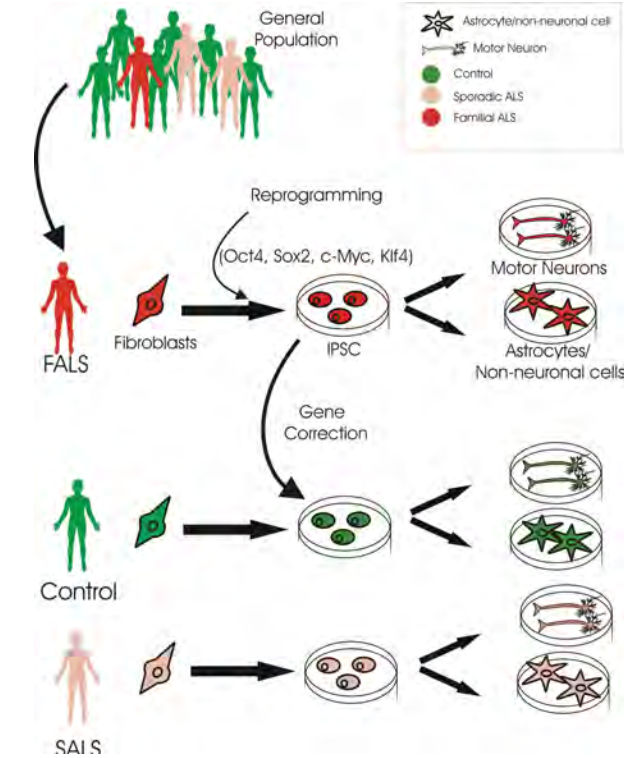
Supporting ALS investigators internationally

The Johns Hopkins ALS Stem Cell Core has sent iPSC, astrocytes, and motor neurons to investigators around the world. This work has helped accelerate the field of ALS research by supporting the efforts of ALS experts internationally.

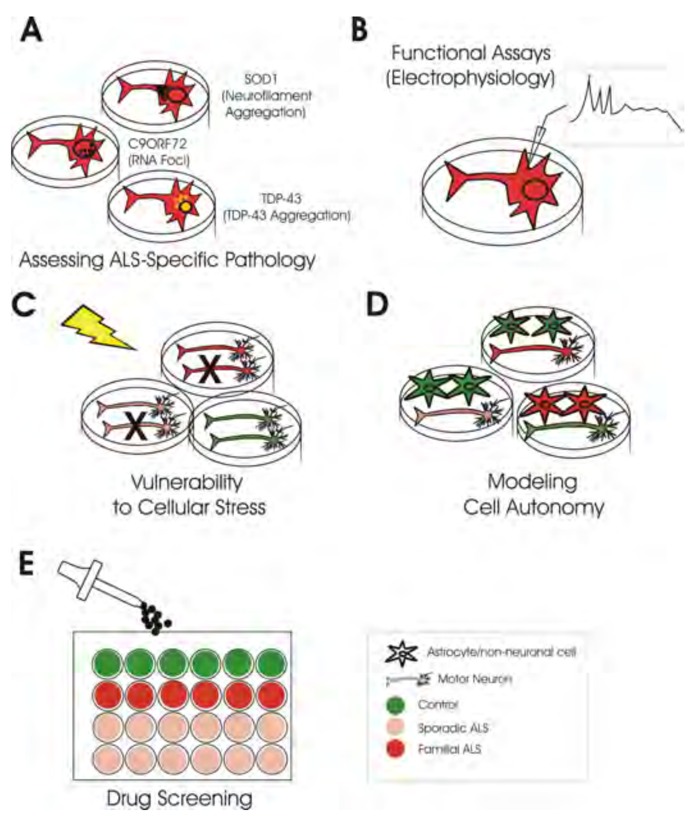
Induced Pluripotent Stem Cells (iPSC)

The Doorway to Personalized Medicine

Personalized medicine for ALS therapies begins with making stem cells from our ALS patients. These stem cells can then be made into all subtypes of brain and spinal cord cells.



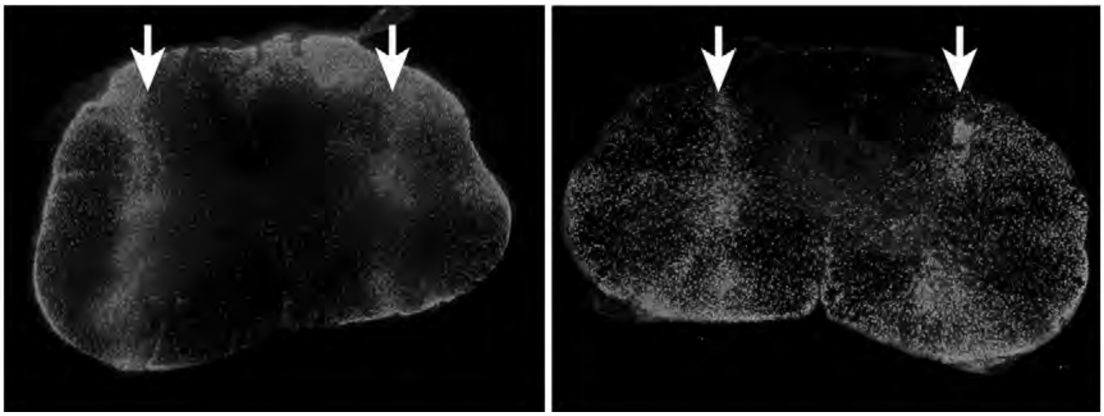
Making stem cells from individual patients provides unprecedented power to understand disease mechanisms in ALS and screen drugs for therapeutics.



Stem Cell Transplantation for ALS
The Future of Neuroprotection and Neuroregeneration

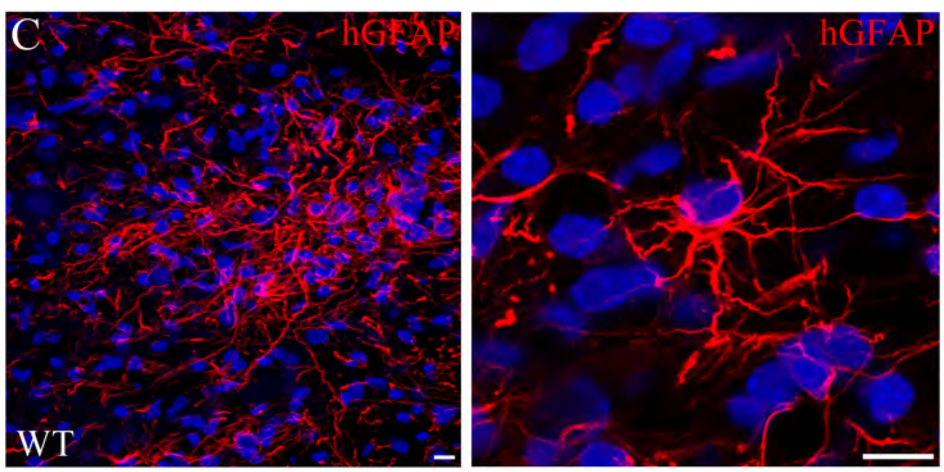
The future of stem cell transplantation in ALS is happening at Johns Hopkins.

Johns Hopkins investigators are using human glial restricted progenitor cells for preclinical study of the potential for stem cell transplantation into the spinal cords of ALS patients.



Human glial progenitor cells can be transplanted (white arrows) into both sides of the spinal cord into areas where motor neurons are located. These cells also migrate up and down the spinal cord even after a single local transplantation.

Human glial restricted progenitor cells (red) become astrocytes after transplantation and can help protect neurons.



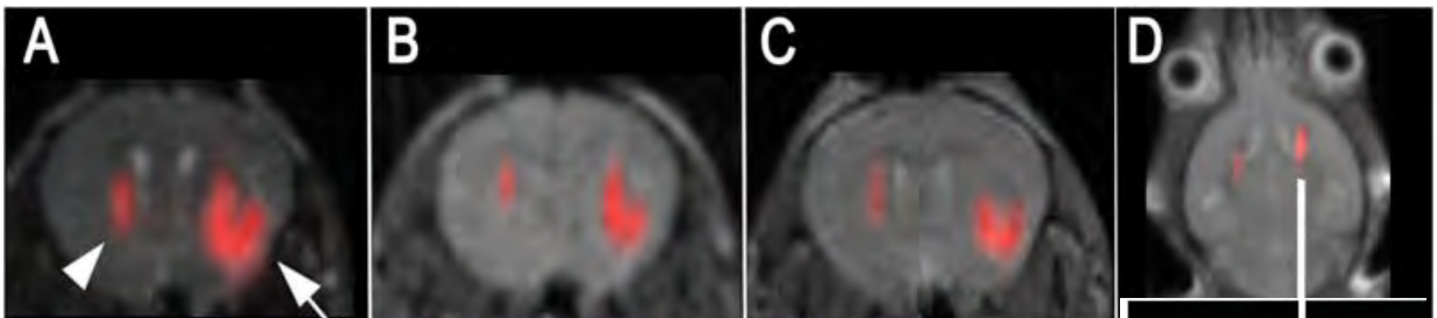
Stem Cell Transplantation for ALS

Imaging

Johns Hopkins investigators in the Institute for Cell Engineering are finding ways to non-invasively track cells after transplantation.

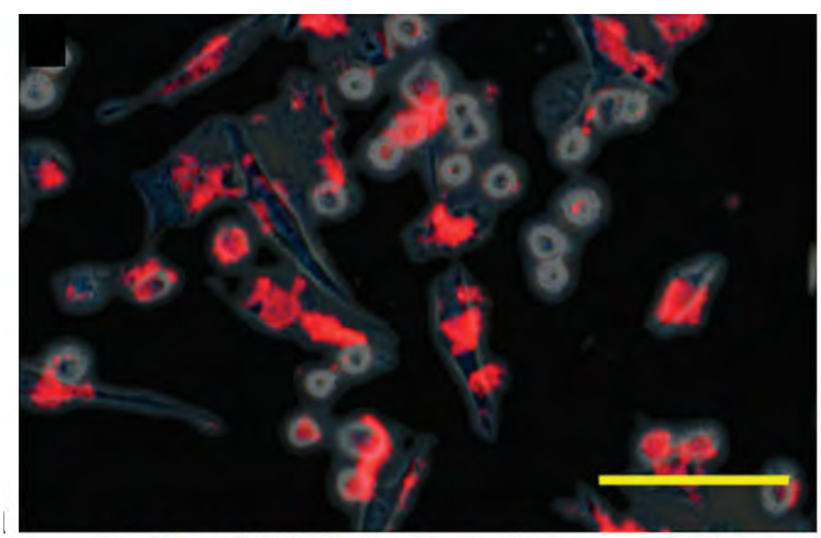
Using special cell tracking materials, investigators at Johns Hopkins are investigating the ability to track cells after transplantation using non-invasive MRI techniques. These methods would allow doctors to monitor cell survival and track the migration of stem cells in the brain and spinal cord over time.

MR imaging of fluorine labeled Neural Stem Cells into the rat brain



MRI images at 1 hour (**A**), 3 days (**B**), 7 days (**C**), and 14 days **(D)** after injection of neural stem cells demonstrating persistence of the fluorine signal. The fluorine label can be seen in real-time by MRI. The arrow shows a high powered view of transplanted fluorine-labeled cells.

Ruiz-Cabello 2008



Human stem cells can be labeled (red) in the dish and can undergo live cell imaging.

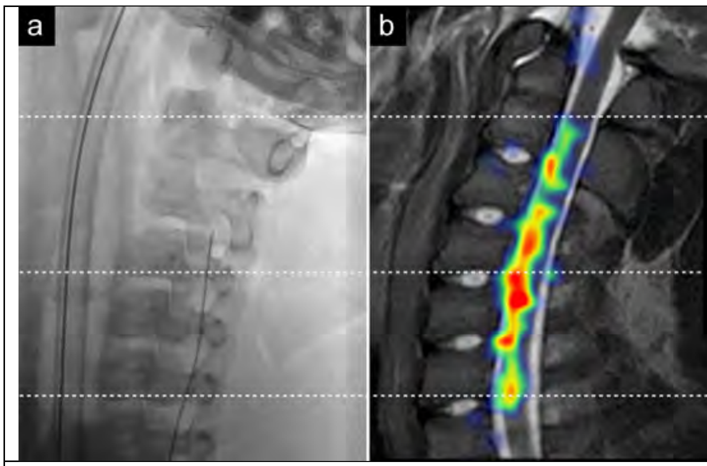
Stem Cell Transplantation for ALS

Special Delivery

Johns Hopkins investigators in Neurology and the Institute for Cell Engineering are finding new ways to deliver stem cells to the brain and spinal cord.

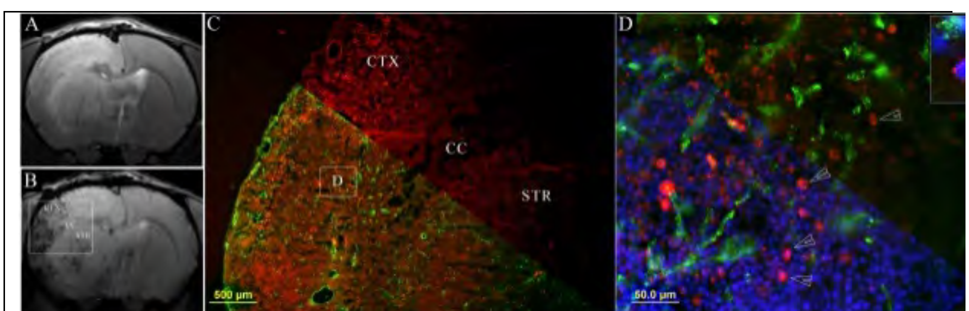
Current cell transplantation techniques involve spinal cord surgeries. Our investigators are working on strategies to deliver stem cells to ALS patients in the spinal fluid, arteries, and possibly veins. These would result in less invasive methods for treating the entire brain and spinal cord.

Utilizing hydrogels containing stem cells, Johns Hopkins investigators are able to use imaging tools to place cells into the cerebrospinal fluid surrounding the spinal cord. These cells will then stay in the region of interest and migrate into the spinal cord. This represents a relatively non-invasive method for delivering large numbers of stem cells to the spinal cord and to treat large regions of the spinal cord. All of these procedures can be done in the outpatient setting.



Real-time MRI of intrathecal cell transplantation in pigs. a) Fluoroscopy-guided placement of a lumbar drain within the cervical spine. b) T2 MRI of the cervical spine with an overlay of a dynamic GE-EPI scan, with color-coded pixels representing a reduction in signal intensity and corresponding to the cells injected intrathecally. The relatively symmetric and homogenous cell distribution on both sides of the catheter tip is prominently displayed.

Using MRI techniques, we can now actively visualize cells being transplanted into brains in real time. These cells were delivered by arterial injection of cells into the major blood vessels of the brain. This strategy would allow for a very rapid delivery of cells into large regions of the brain in a very short time frame.



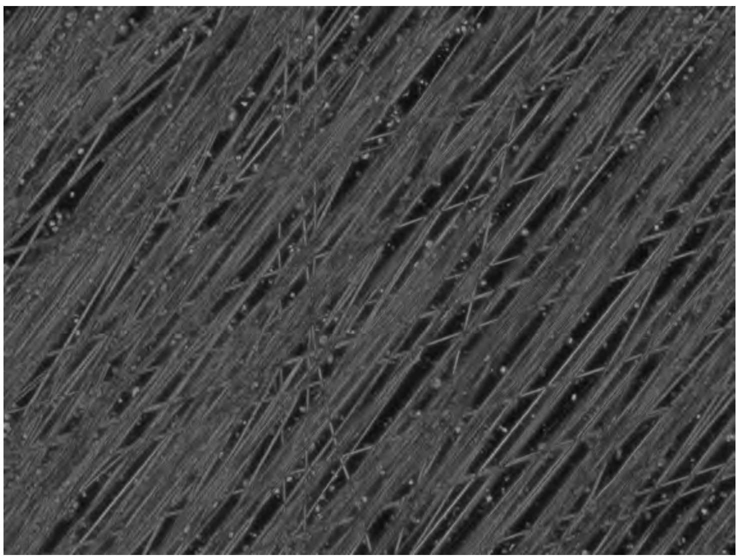
Human GRPs extravasate following stroke and intraarterial injection. (A) T2-w MRI of a rat brain three days after stroke; IA injection of SPIO-labeled GRPs. (B) T2-w MRI of the same rat with dark spots reflective of implanted cells. (C) immunostaining at low magnification, corresponding to boxed area in (B): red=GRPs in cortex (CTX) and striatum (STR), co-localizing with dark signal on MRI, and the partial green overlay corresponds to vascular von Willebrand Factor (vWF). (D) High magnification image from boxed area in (C) showing injected hGRPs (red) and vWF+ blood vessels (green). Notably, many hGRPs are outside the vasculature (arrowheads). Inset shows close-up of one iron-labeled cell. (from Walczak, P.)*

Using biomaterials to help motor neurons reach out

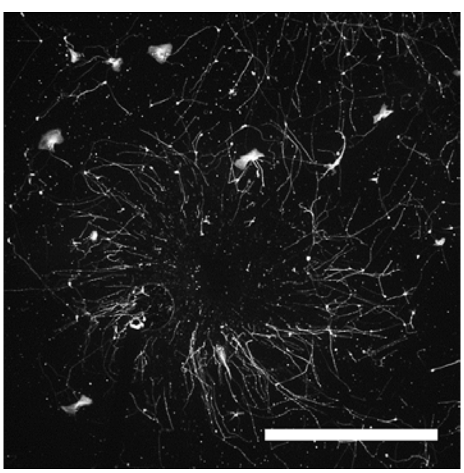
First Steps in Neuroregeneration

Collaborative efforts with the Johns Hopkins Department of Bioengineering reveals methods to help motor neurons to grow towards a target.

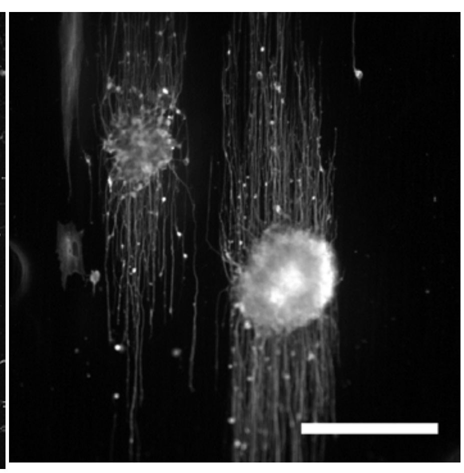
In collaboration with the world-class Department of Bioengineering, investigators are using nano-fibers and other biomaterials to help motor neurons grow in an organized fashion towards a specific target. These are the first steps in building pathways towards motor neuron regeneration.



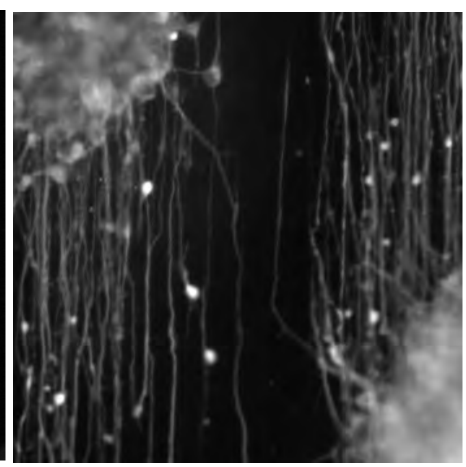
Nano-fibers seen under the microscope can be oriented in parallel to allow organized growth of nerve fibers.



Human iPS neurons grow in different directions when put in a petri dish



Human iPS neurons grow in a very organized way when they are placed on nano-fibers

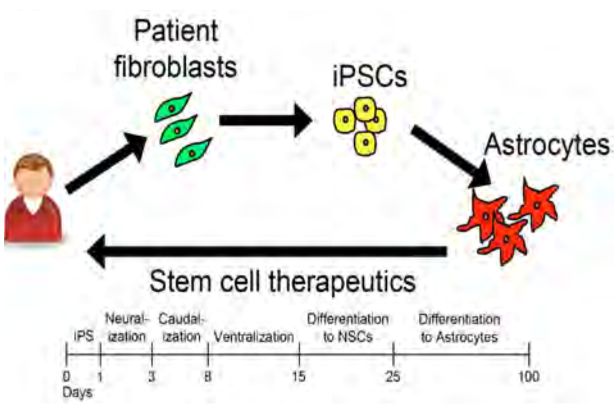


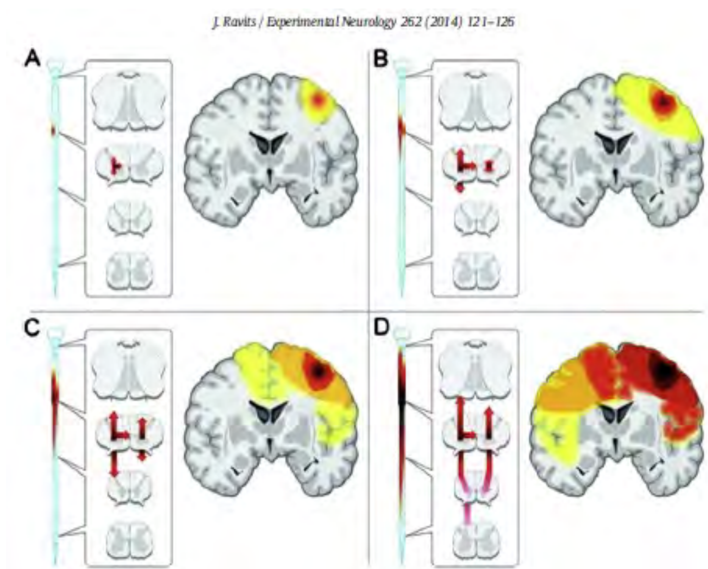
Close-up of Human iPS neurons grown on nano-fibers

Using iPS cells to understand how ALS progresses

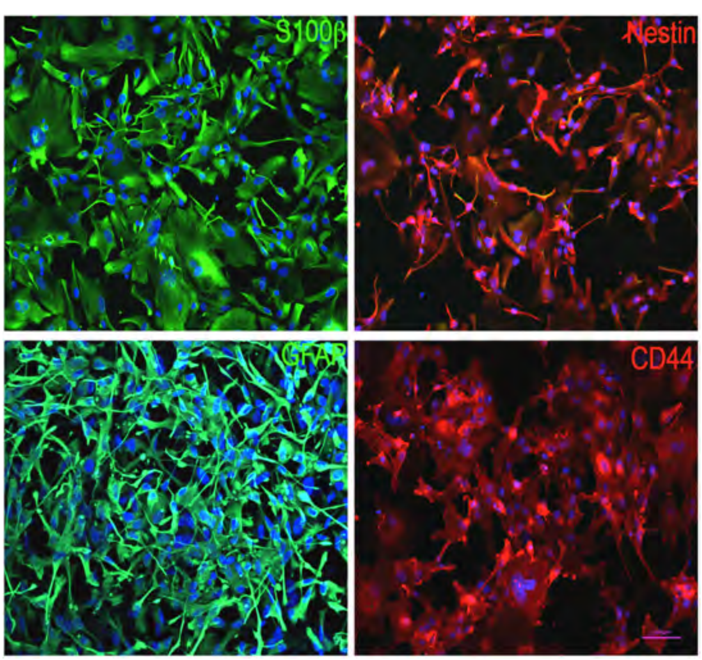
Astrocytes may be the “stars” of the show

We are using astrocytes (star-shaped cells) made from ALS patient iPS cells to understand how weakness in ALS spreads from region to region as well as to understand why progression is different amongst patients.

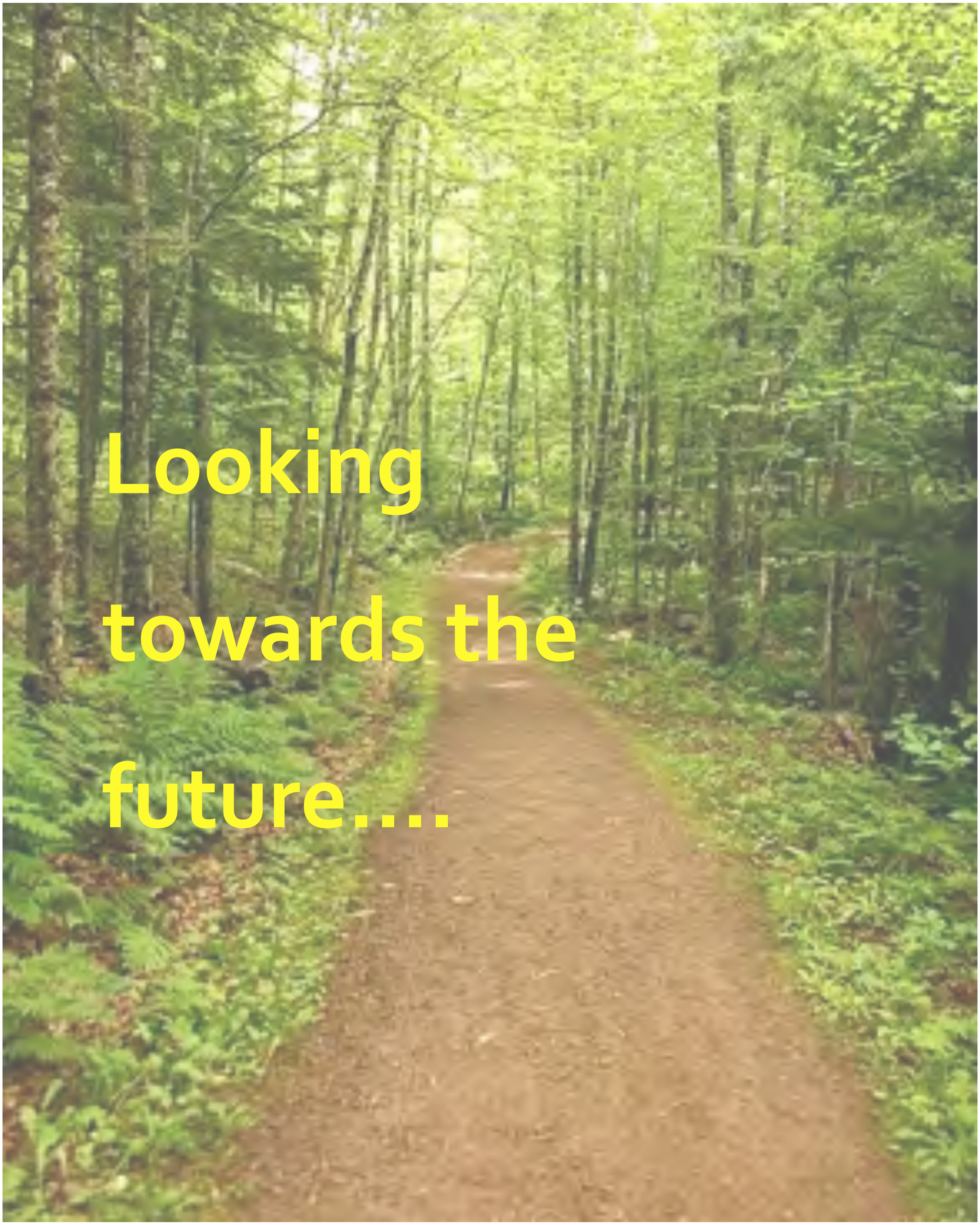




Investigators are trying to understand how ALS spreads from one region to another



Astrocytes from ALS patient iPS Cells


Looking
towards the
future....