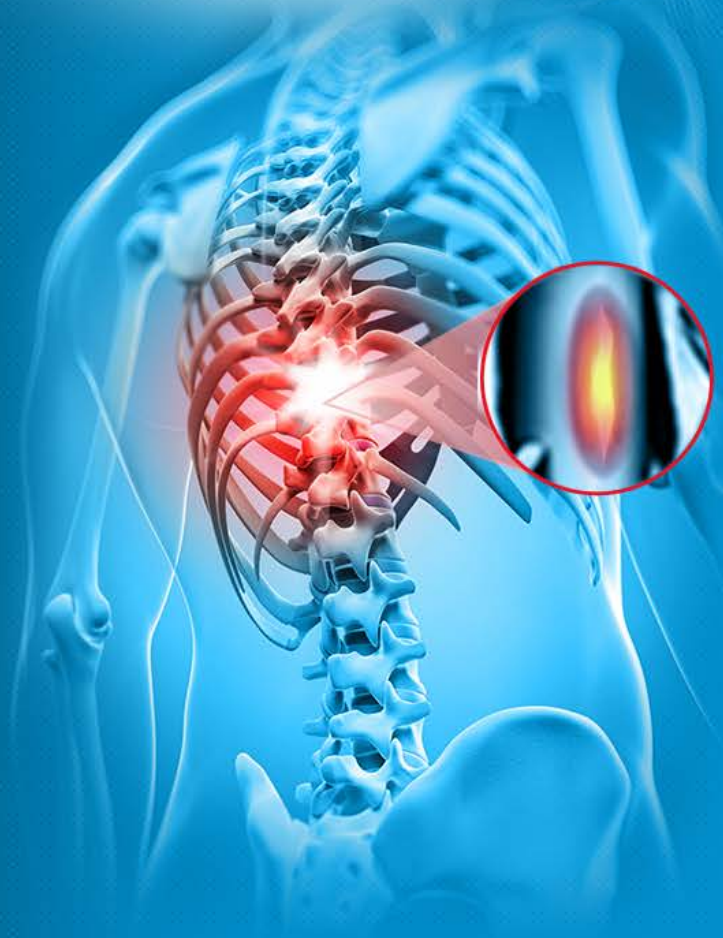
INVIVO THERAPEUTICS™



Translation of Biomaterial-based Therapies for the Treatment of Acute and Chronic Spinal Cord Injury: The *Neuro-Spinal Scaffold*™ and Bioengineered Neural Trails

Alex A. Aimetti, PhD

Sr. Director, Medical Education

October 29, 2016

Forward-Looking Statements

Before we begin, we would like to remind everyone that during our presentation, we will be making forward-looking statements about our business, plans, and objectives. These statements are based on how we see things today. These statements can be identified by words such as believes, estimates, expects, or similar references to the future, and include statements we may make regarding our product development strategy, business prospects, and clinical and operational milestones. We wish to caution you that actual events or results may differ materially from those expressed in forward-looking statements made by us or on our behalf. For more information on the many factors that can result in actual performance differing from our forward-looking statements, please see our filings made with the SEC, including our 2015 Annual Report on Form 10-K filed on March 4, 2016 and our Quarterly Reports on Form 10-Q filed on May 6, 2016 and August 4, 2016.

Progress Made to Advance Therapies that Aim to Improve the Lives of Individuals with SCI

New executive leadership

Company focused solely on SCI

Initiated pilot clinical study for acute SCI

First individual implanted with *Neuro-Spinal Scaffold*

Neuro-Spinal Scaffold™ receives 2015 Becker's Healthcare Spine Device Award

Announced Bioengineered Neural Trails program (pre-clinical) for chronic SCI

Converted pilot clinical study to INSPIRE Pivotal Probable Benefit Study

Expanded clinical study into Canada

Implanted 10th individual with *Neuro-Spinal Scaffold*

Designed & developed new stem cell injection device

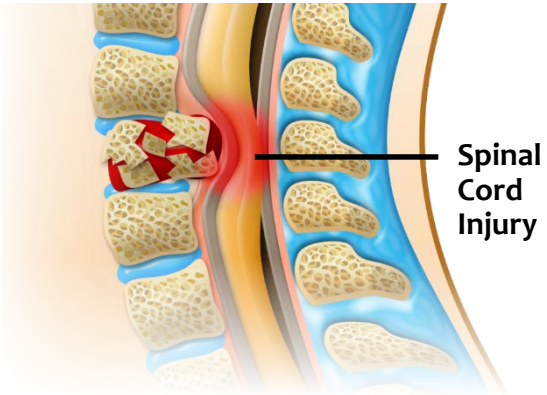
2014 **2015** **2016**

Agenda

- *Neuro-Spinal Scaffold*™: Our approach to acute SCI
  - Technology & mechanism of action
  - Translation to the clinic
  - Clinical results to date and future clinical development plans

- Bioengineered Neural Trails™: Our approach to chronic SCI
  - Rationale
  - Pre-clinical development and results to date
  - Future plans

Progression of Acute SCI to Post-Traumatic Cavity in Contusion Injuries



Hemorrhage & Spinal Cord Swelling

Reduced Blood Flow & Ischemic Necrosis

Cavity Development & White Matter Reduction

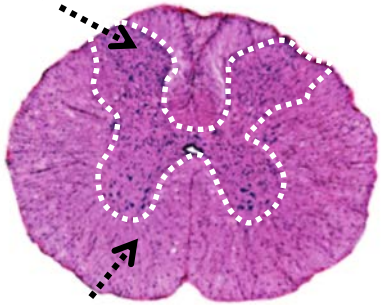
Chronic injury and mature cavity formation

Acute SCI:
Neuro-Spinal Scaffold™

Chronic SCI:
Bioengineered Neural Trails™

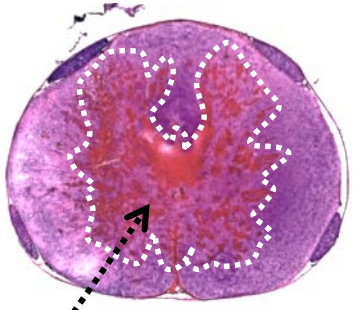
Normal

Highly vascularized gray matter



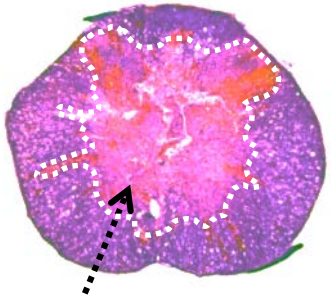
White matter

2 hours after SCI



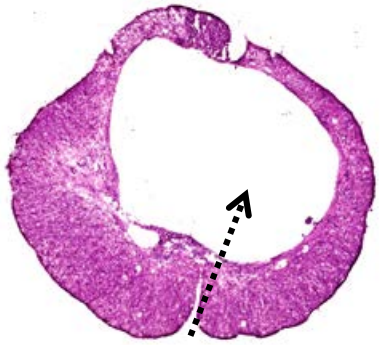
Acute hemorrhage & necrosis

24 hours after SCI



Liquefactive necrosis

12 weeks after SCI



Mature cavity

Histology from rat contusion model of SCI

Poster D8-06; National Neurotrauma Society 2015 Symposium; Santa Fe, NM.

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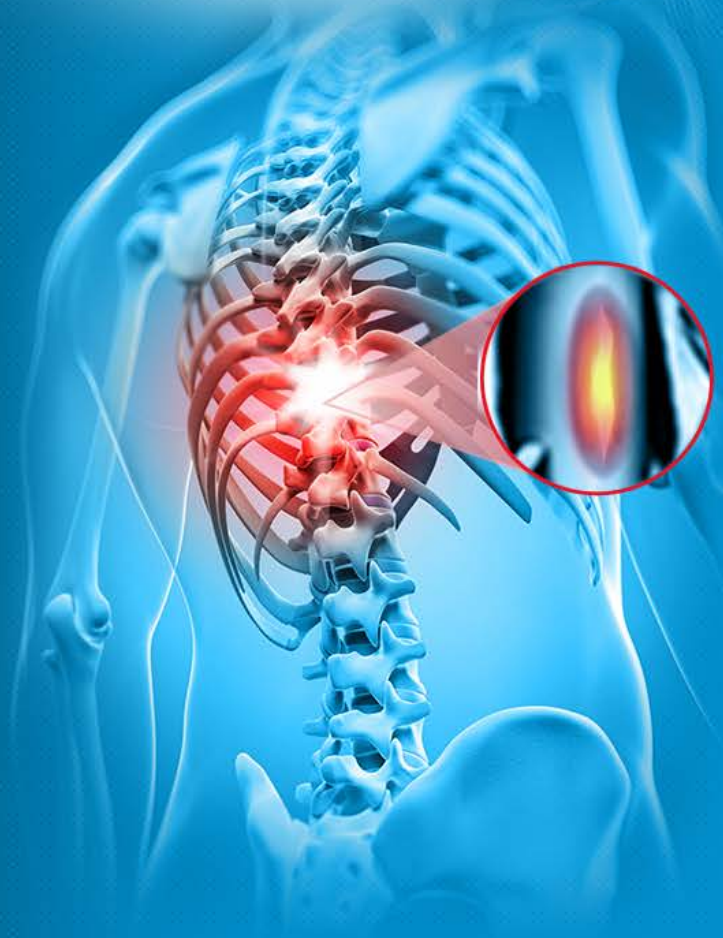
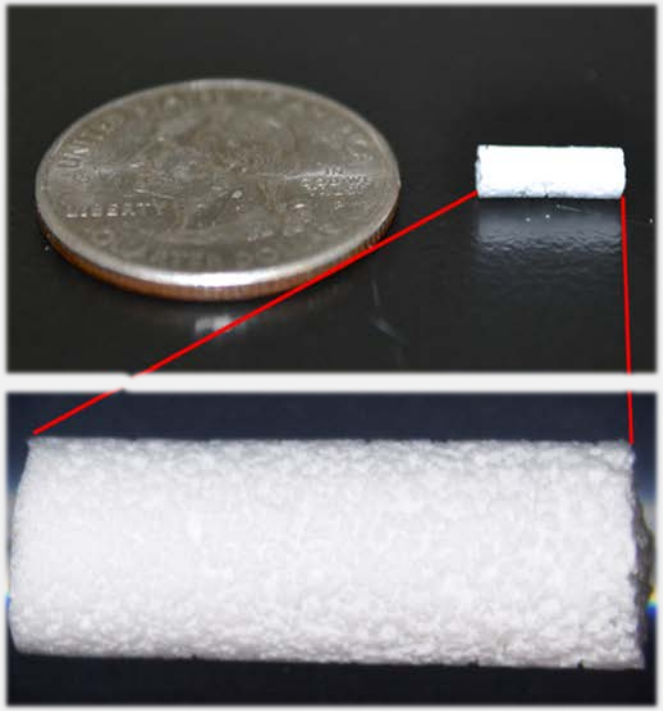
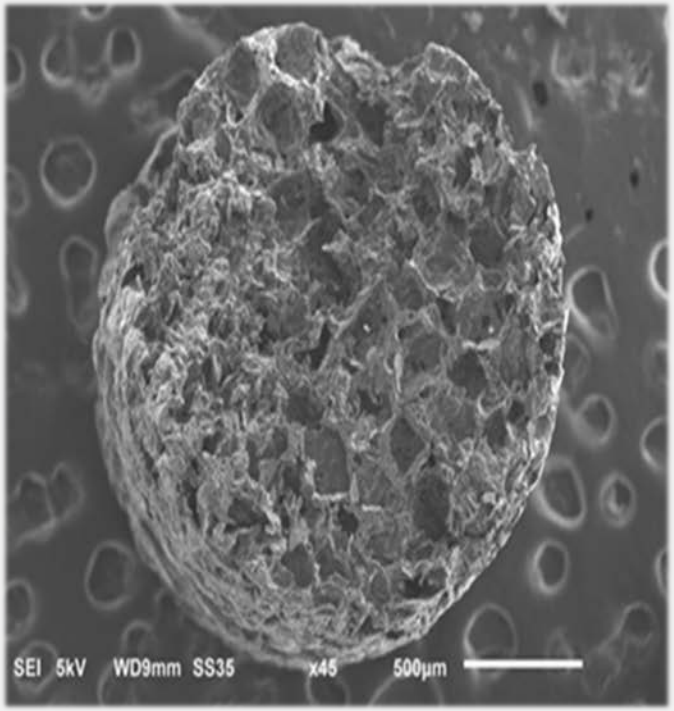


Neuro-Spinal Scaffold™ for Acute SCI

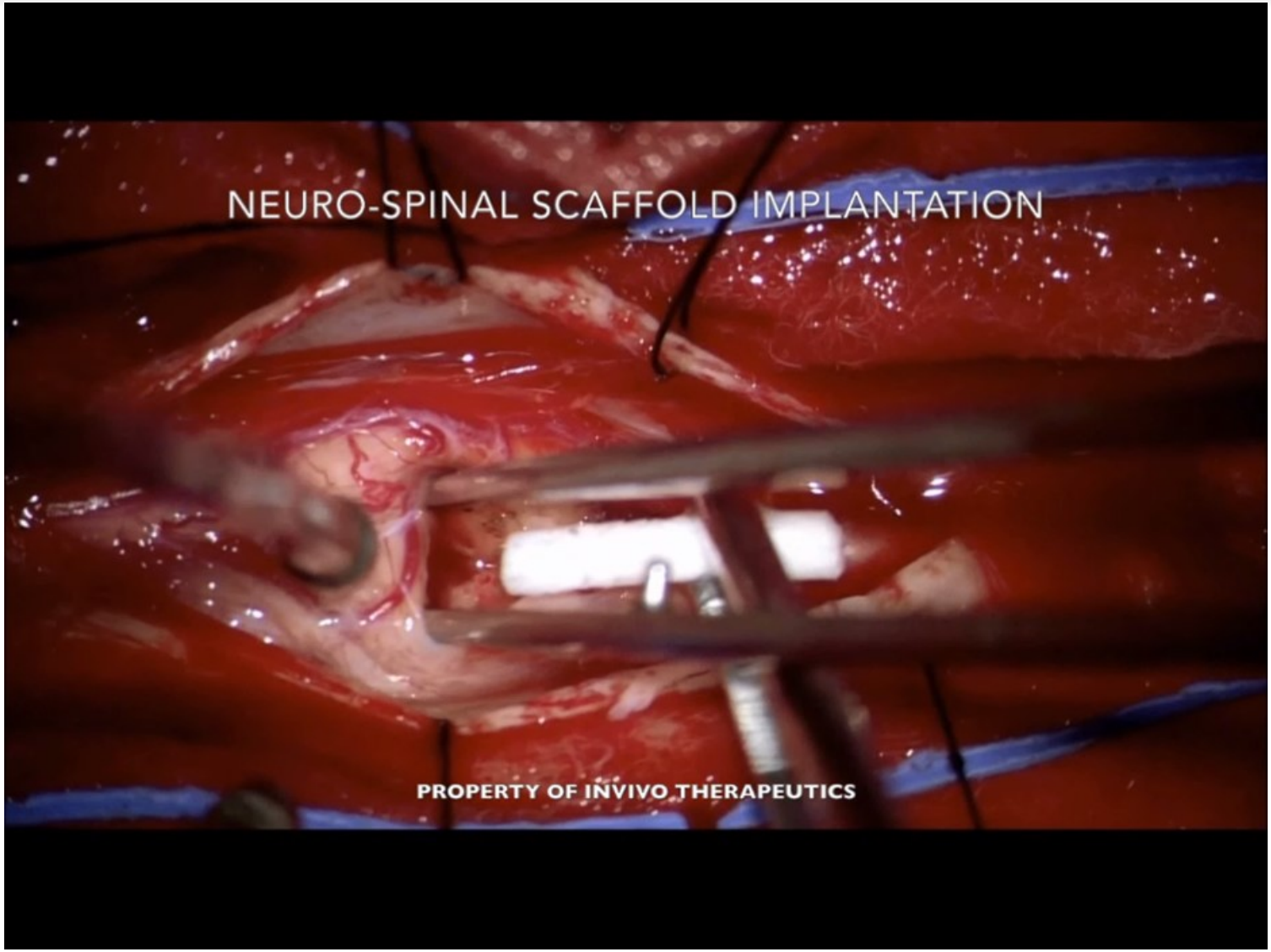
Designed to Promote Healing in Spinal Cord Injury

Novel Clinical Approach for Acute SCI: The *Neuro-Spinal Scaffold*™



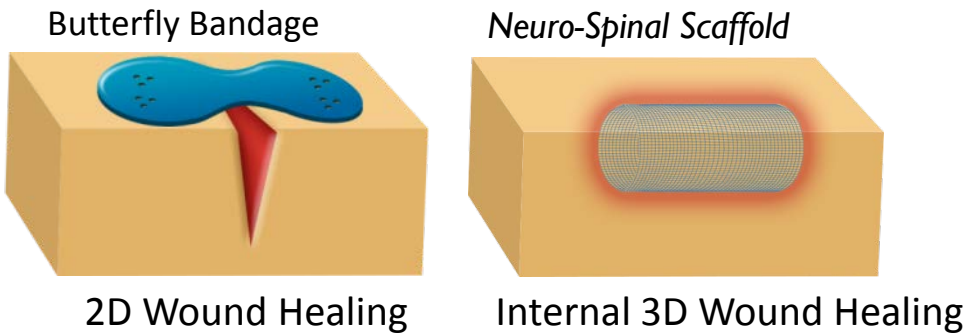


First *Neuro-Spinal Scaffold*™ Implantation in Human Contusion Injury

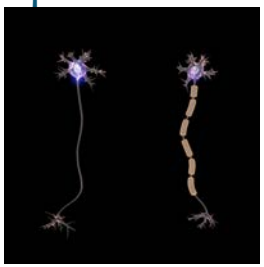


Neuro-Spinal Scaffold™ Mechanism of Action

- Provides structural support to surrounding viable tissue
- Promotes the formation of neuro-permissive remodeled tissue that supports neural regeneration
- Serves as a locus for 3-dimensional appositional healing



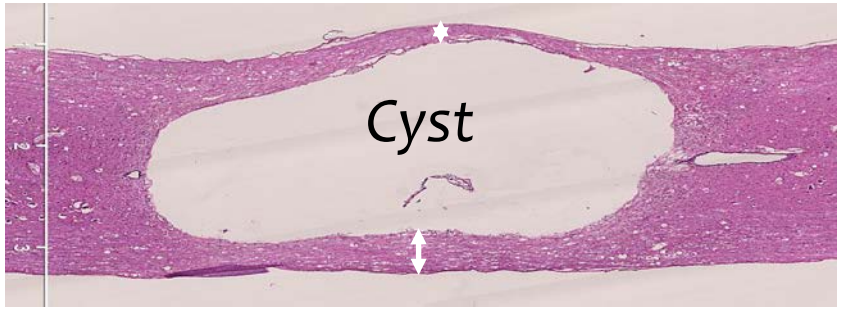
- Preserves macroscopic spinal cord architecture and decreases cyst volume
- Increases spared white matter and promotes remyelination of denuded axons



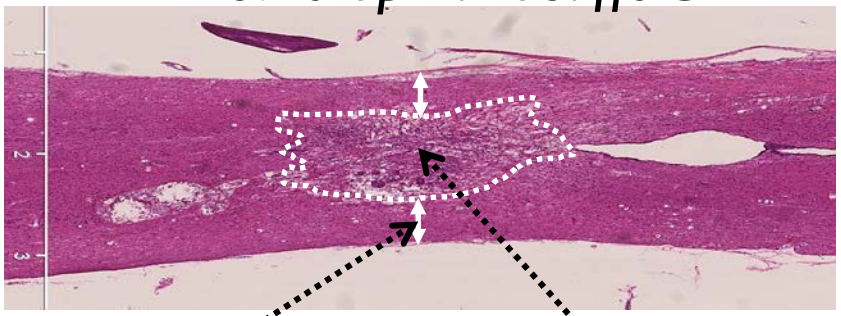
The *Neuro-Spinal Scaffold*™ Preserves Macroscopic Spinal Cord Architecture

Rat Acute Spinal Cord Contusion Injury (at 12 weeks)

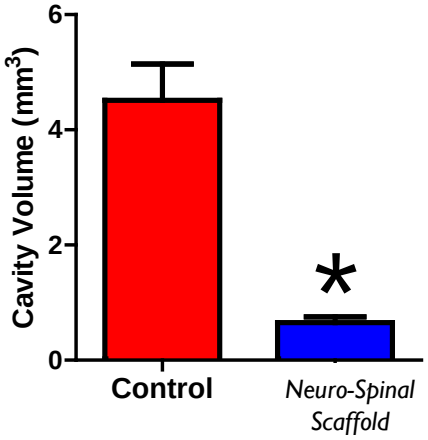
Control



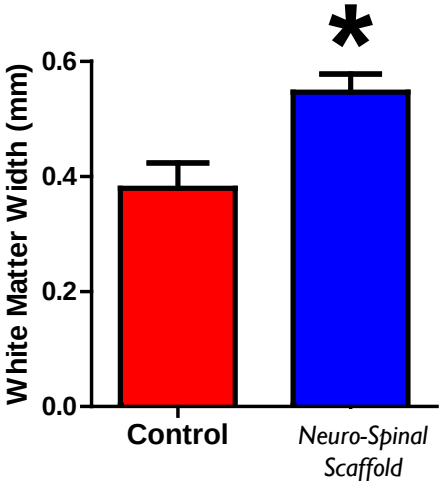
Neuro-Spinal Scaffold



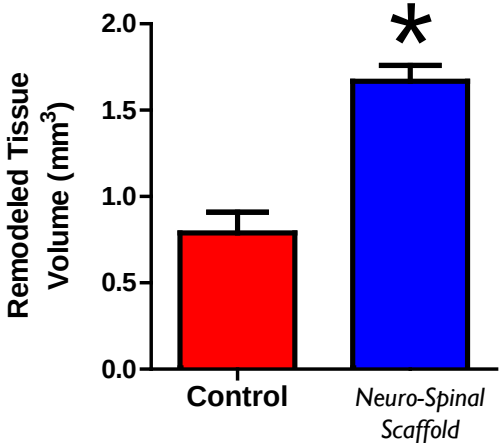
Cyst Reduction



White Matter Sparing



Remodeled Tissue



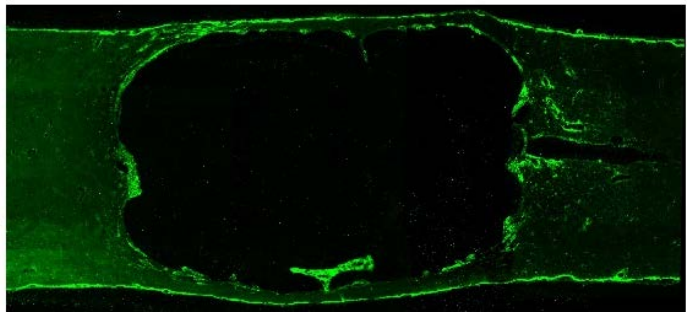
*P<0.05

Poster D8-06; National Neurotrauma Society 2015 Symposium; Santa Fe, NM.

The *Neuro Spinal Scaffold*™ Increases Remodeled Tissue Supporting Neural Regeneration

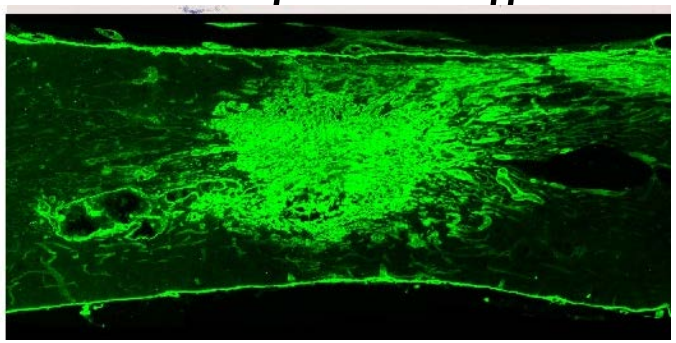
Rat Acute Spinal Cord Contusion Injury (at 12 weeks)

Control

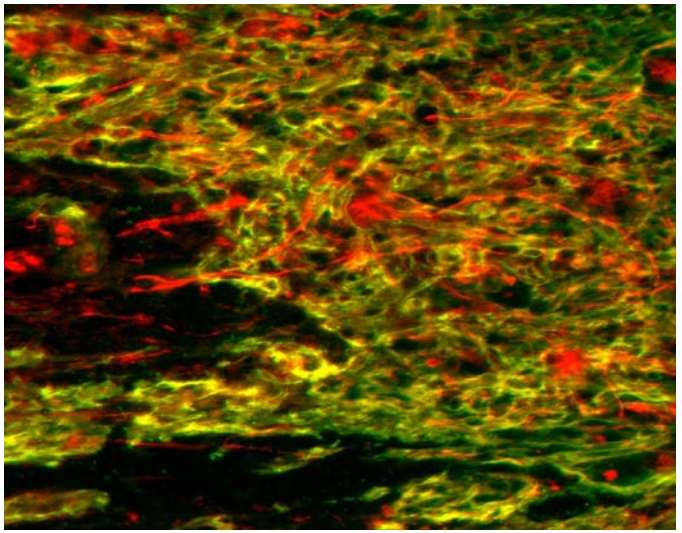


Minimal neuro-permissive matrix

Neuro-Spinal Scaffold



Remodeled tissue with extensive neuro-permissive matrix



Neuro-permissive matrix supports neural regeneration

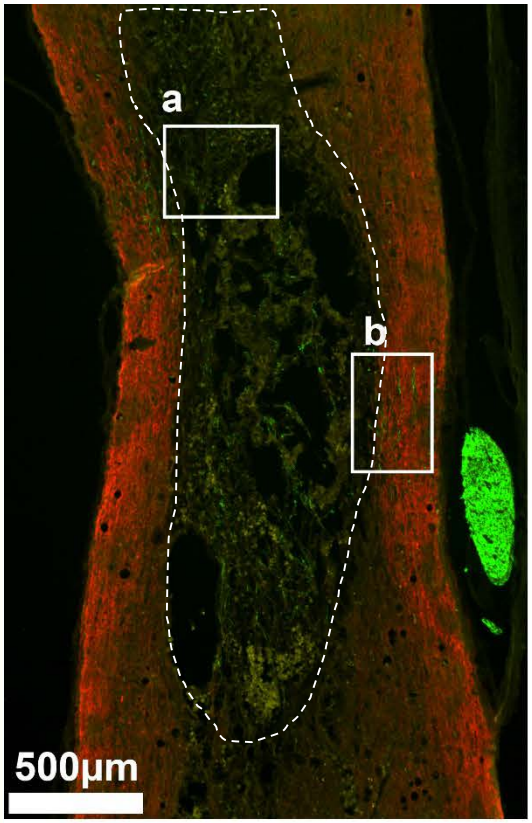
Company images

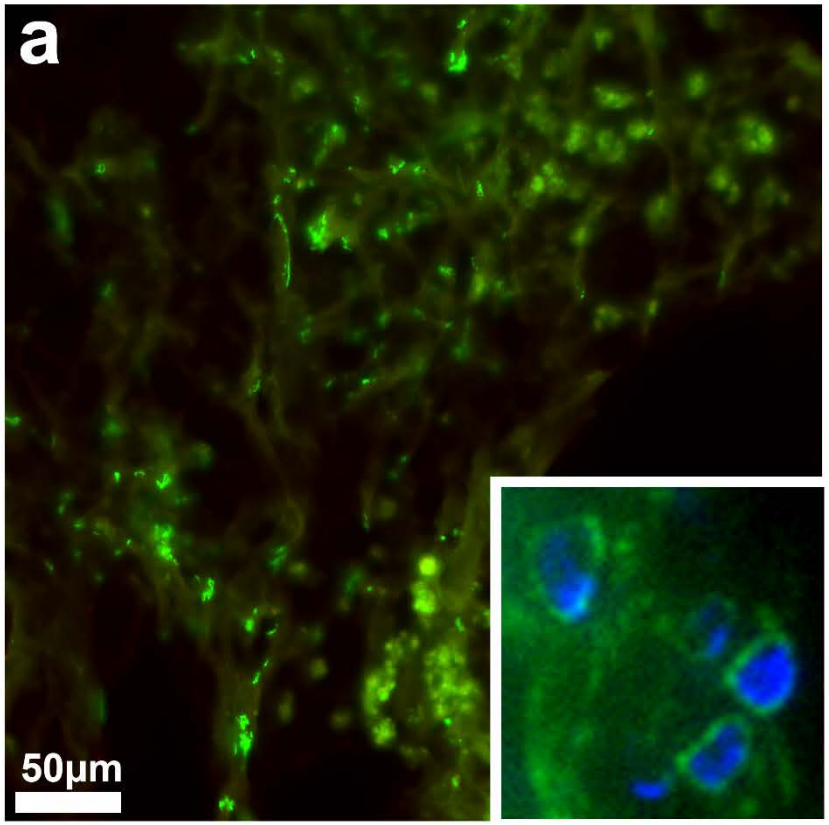
Neural Regeneration and Remyelination with Schwann Cells after *Neuro-Spinal Scaffold*™ Implantation

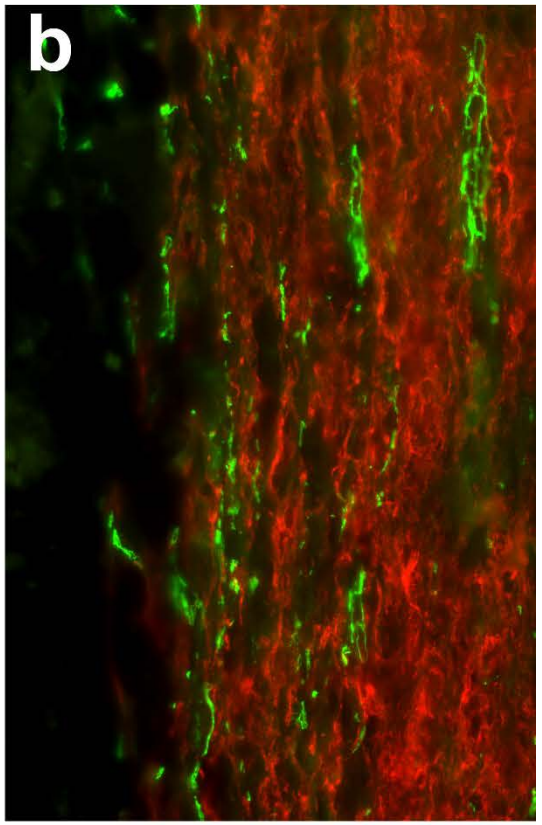
Contusion Injury
Central epicenter (a) and white matter (b)

Epicenter
Schwann Cells aid neural regeneration

White Matter
Schwann Cells restore signal transduction







Rat Acute Spinal Cord Contusion Injury (at 12 weeks)

Inset: Schwann cells ensheathing axons

Oligodendrocytes Schwann Cells

The INSPIRE Study
A Pivotal Trial for Regulatory Approval

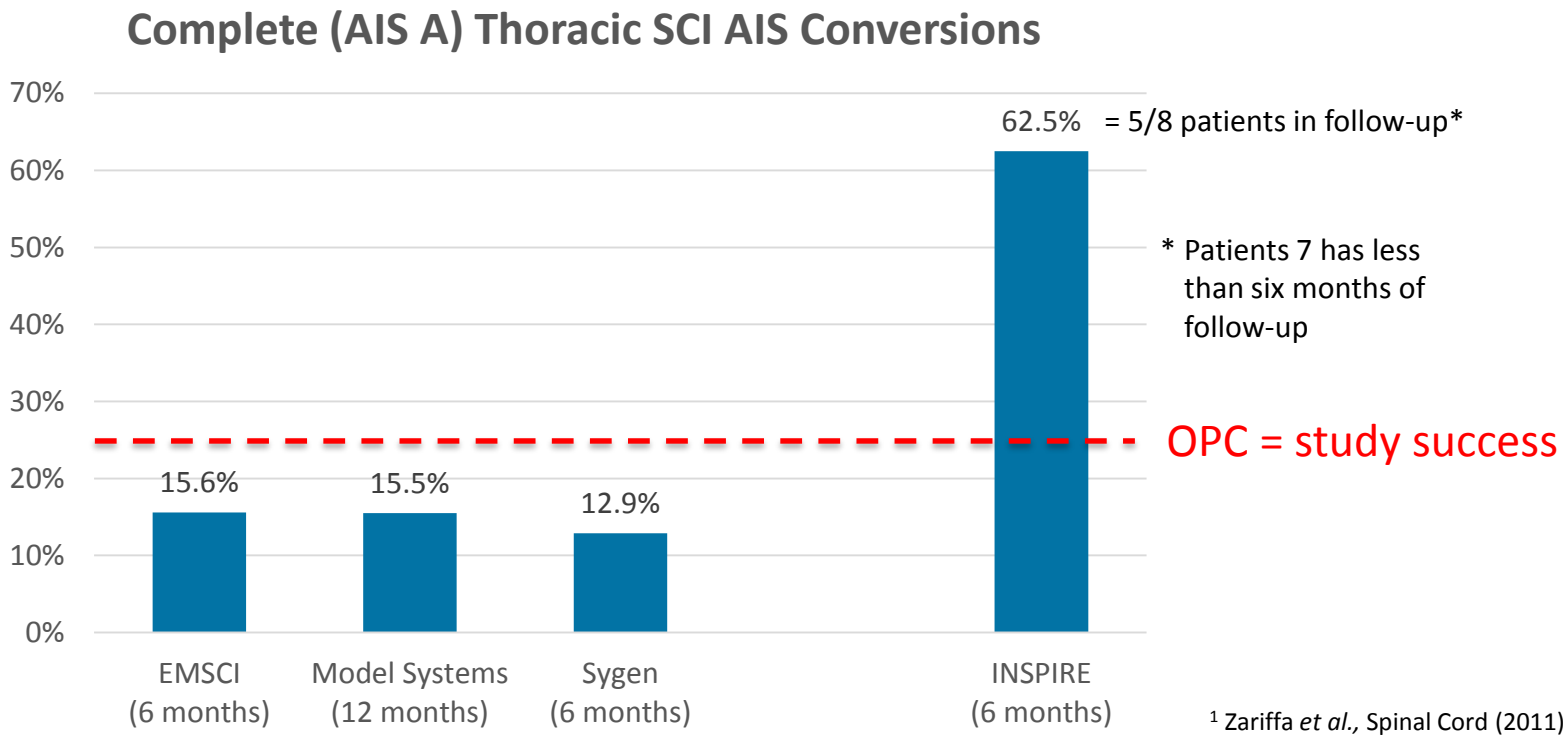
InVivo Study of Probable Benefit of the *Neuro-**Spi**nal Scaffold*™ for Safety and Neurologic **Re**covery in Subjects with Complete Thoracic AIS A Spinal Cord Injury

- Designed as 20-patient pivotal study to be used for HDE application
  - Endpoint: improvement in ASIA Impairment Scale (AIS) grade by 6 months
- Objective Performance Criterion (study success definition) – at least 25% of patients improve AIS grade by 6 months
- Additional Endpoints: sensory and motor scores, bladder and bowel function, Spinal Cord Independence Measure, pain, quality of life
- 23 clinical sites (US and Canada)
  - Plan also to include United Kingdom clinical sites

NOTE: FDA has recommended inclusion of a control arm in the study as part of a Study Design Consideration (SDC). As is typical of the regulatory process, InVivo has previously addressed a number of SDCs regarding the study. InVivo is engaged in a discussion with the FDA regarding this SDC and will provide an update if substantial changes are made to the study protocol. InVivo continues to believe that the current study design is sufficient to demonstrate safety and probable benefit in support of an HDE application for marketing approval.

Objective Performance Criterion: 25% AIS Grade Conversion by 6 months

- Historical benchmarks for AIS conversion rates
  - European Multicenter Study about Spinal Cord Injury (EMSCI)[1]; *n* = 256
  - Spinal Cord Injury Model System (US)[2]; *n* = 265
  - Sygen clinical trial in spinal cord injury[3]; *n* = 139



[1] Zariffa *et al.,* Spinal Cord (2011)
[2] Lee *et al.,* J. Spinal Cord Med. (2014)
[3] Fawcett *et al.,* Spinal Cord (2007)

NOTE: Approval is not guaranteed if the OPC is met and HDE approval may still be obtained if OPC is not met.

Promising Neurologic Outcomes and Favorable Safety Profile in The INSPIRE Study

Sex	Age	Neurologic Level of Injury	Time to Implant	Neurologic Outcome to Date
M	**Adult**	**T11**	**9 hrs.**	**Converted to AIS C at 1 month**
M	**Adult**	**T4**	**83 hrs.**	**Converted to AIS B at 1 month**
F	**Pediatric**	**T8**	**69 hrs.**	**Converted to AIS B at 6 months**
M	**Pediatric**	**T10**	**9 hrs.**	**Converted to AIS B at 2 months**
M	**Adult**	**T4**	**40 hrs.**	**Converted to AIS B at 3 months**
F	Adult	T7	46 hrs.	Remains AIS A at 12 months
M	Adult	T3	53 hrs.	Remains AIS A at 6 months
M	Adult	T3	21 hrs.	Remains AIS A at 3 months

Note: Two subjects passed away with the cause of death deemed unrelated to *Neuro-Spinal Scaffold*™ or implantation

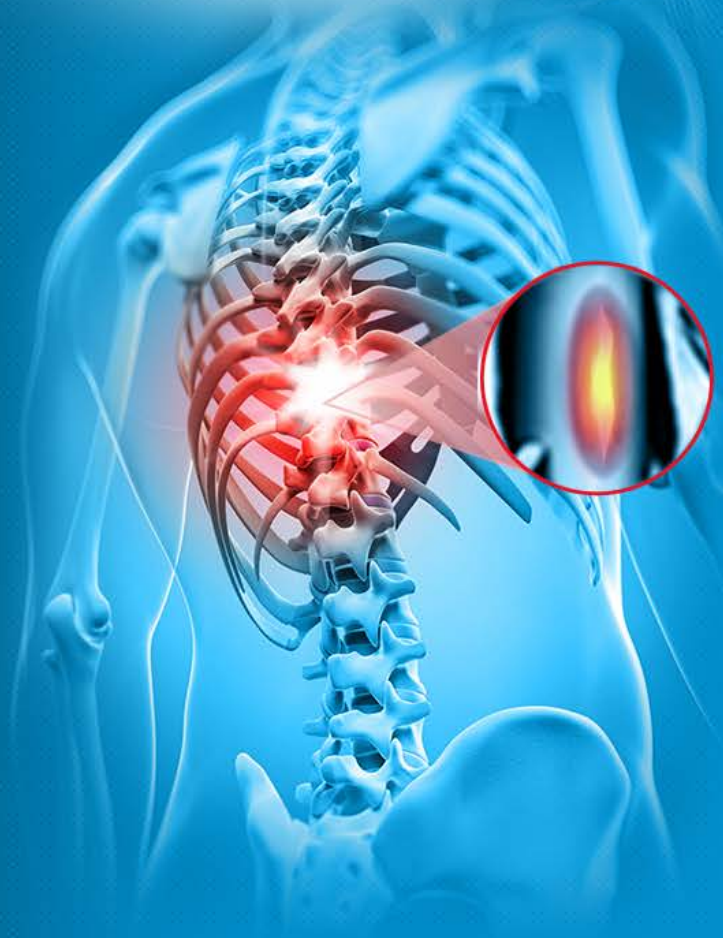
- No obvious correlations between AIS conversions and injury level or time to implant
- No Serious Adverse Events related to *Neuro-Spinal Scaffold*™ or implantation procedure

Neuro-Spinal Scaffold™
A Robust Clinical Development Portfolio

- Acute Complete (AIS A) Thoracic SCI via HDE
  - **Target full enrollment in H1-2017 and completion of INSPIRE in H2-2017**
  - **Target Regulatory submission in late 2017 or early 2018**
- Acute Complete (AIS A) Cervical SCI via HDE
  - Projected pilot study approval and initiation in Canada in H1-2017
  - Planned expansion into European countries
  - FDA has requested data from INSPIRE before U.S. study approval [1]
  - Pursuing U.S. and Ex-U.S. pathways in parallel
- Acute Incomplete (AIS B, AIS C) SCI
  - Expand to larger acute SCI population (thoracic and cervical injuries)

[1] On September 30, 2016, FDA notified InVivo that its proposed cervical study was disapproved pending submission of results from the INSPIRE study. Previously, the FDA had communicated that data from the first five patients in INSPIRE would be required before considering approval. InVivo will initiate discussions with FDA regarding the disapproval and believes that data generated to date in INSPIRE support moving into cervical SCI.

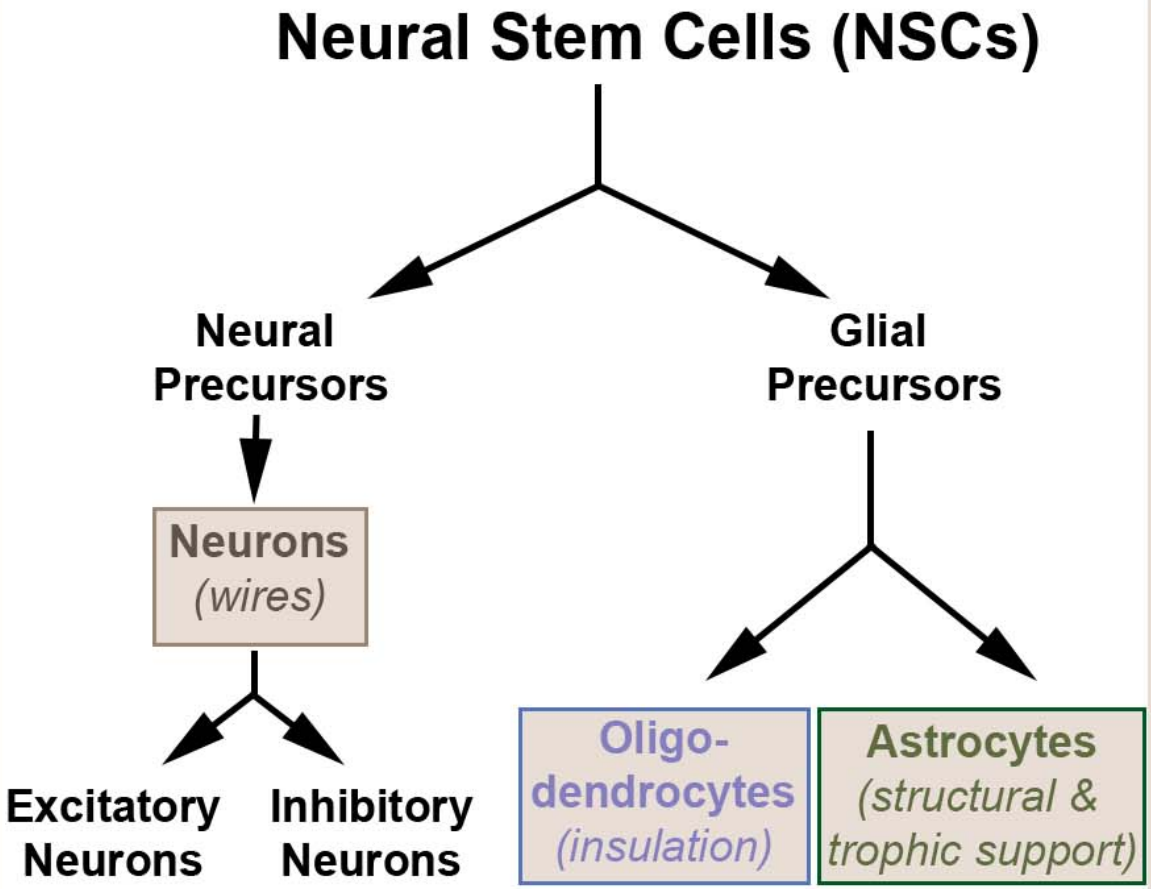
INVIVO THERAPEUTICS™

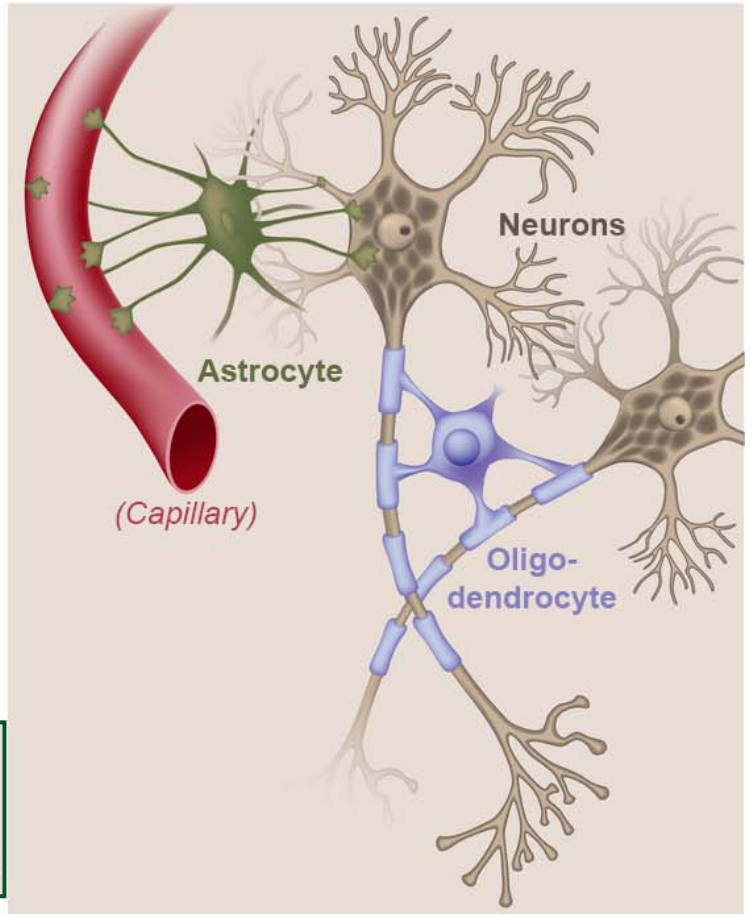


InVivo's Chronic SCI Product: Bioengineered Neural Trails™

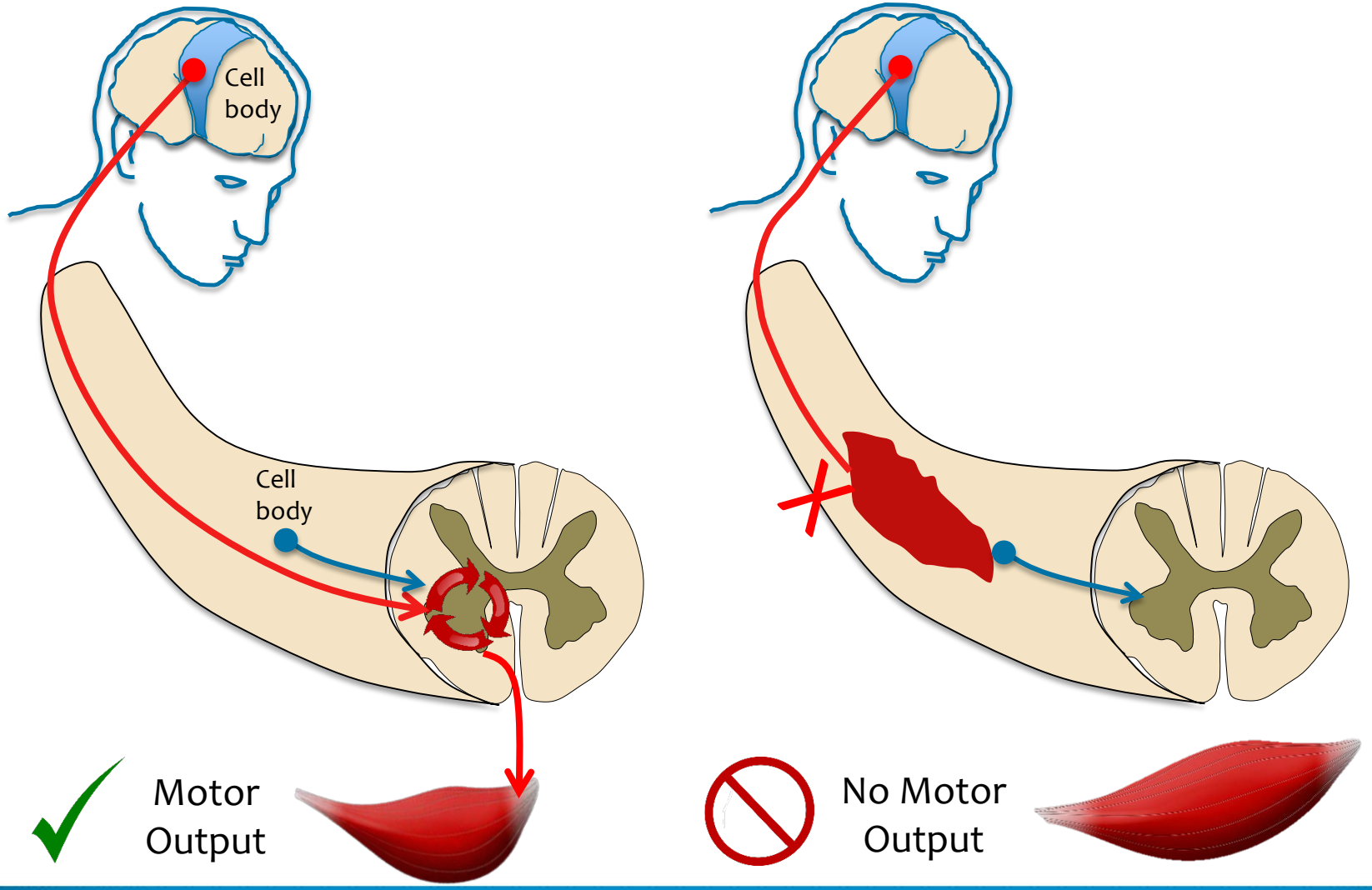
Neural Stem Cells Incorporated into an Injectable Scaffold for Minimally-Invasive Delivery

Neural Stem Cells Can Differentiate into the Major Three Cell Types of the Central Nervous System

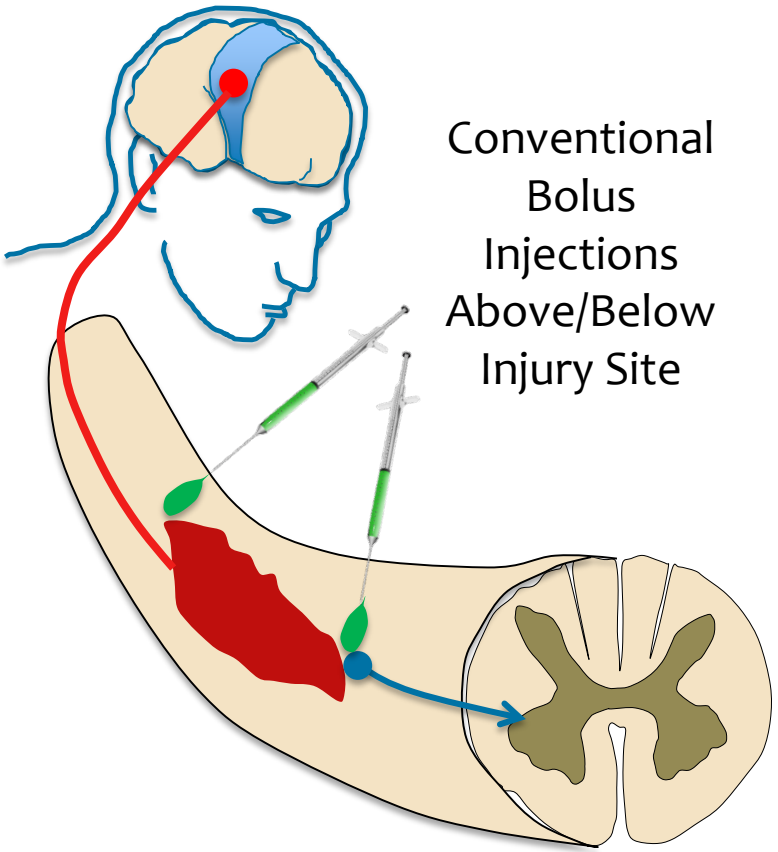




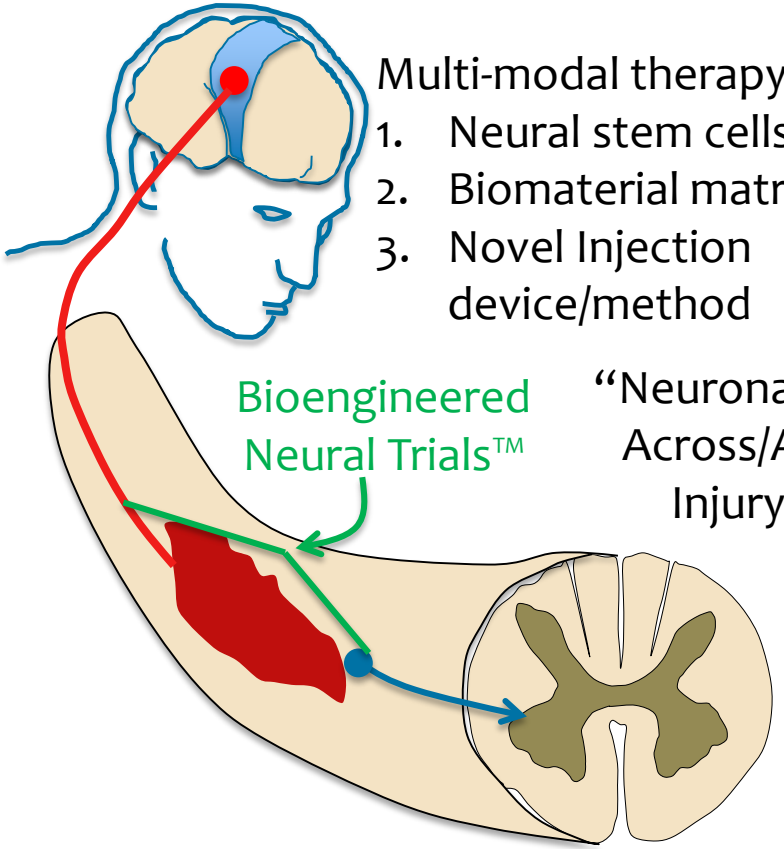
Disruption of Motor Control within the Spinal Cord Following Injury



Trails of Transplanted Cells May Provide a Preferred Delivery Approach to Bridge the Injury



Conventional Bolus Injections Above/Below Injury Site



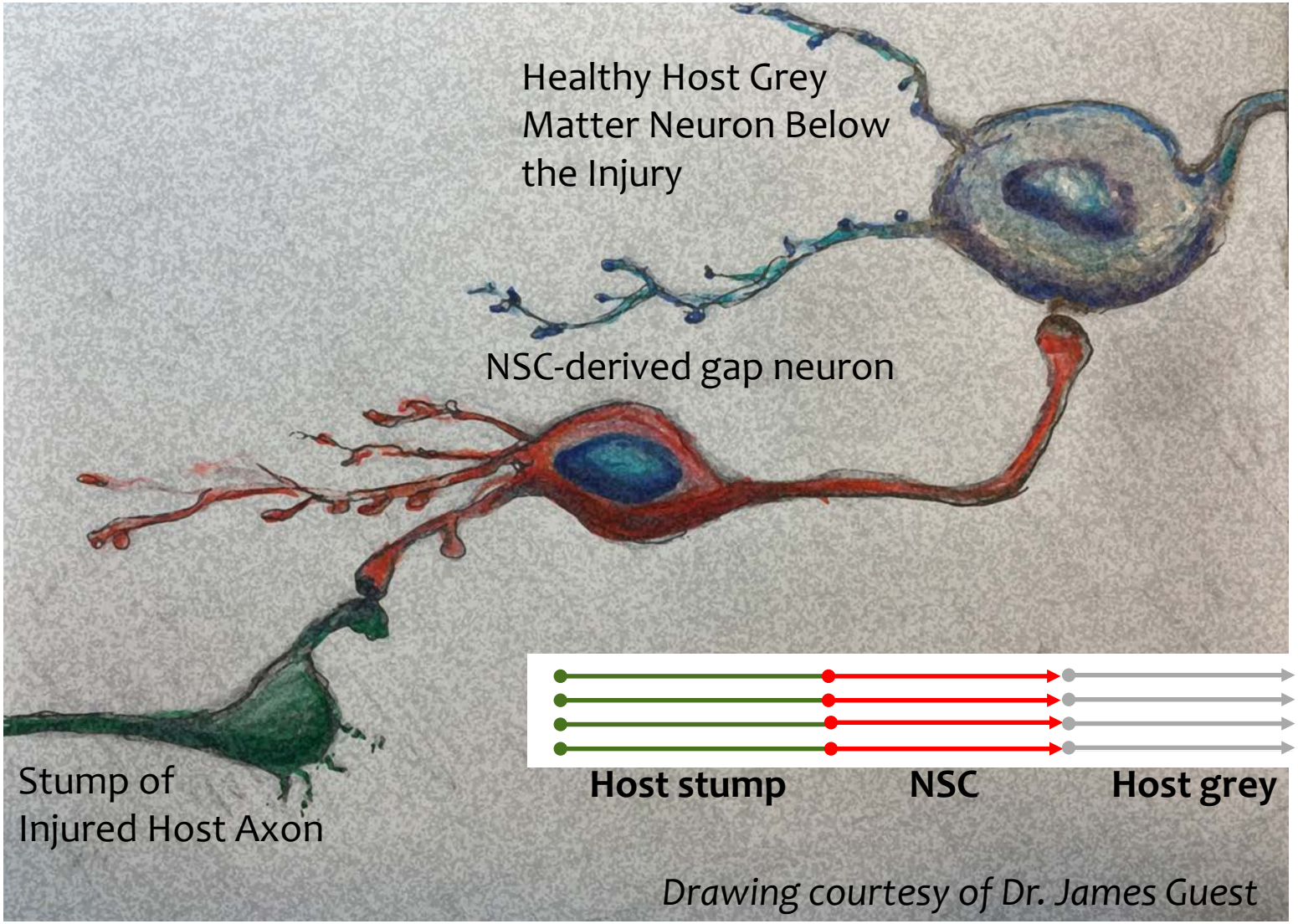
Multi-modal therapy includes:

1. Neural stem cells
2. Biomaterial matrix
3. Novel Injection device/method

Bioengineered Neural Trials™

"Neuronal Relay" Across/Around Injury Site

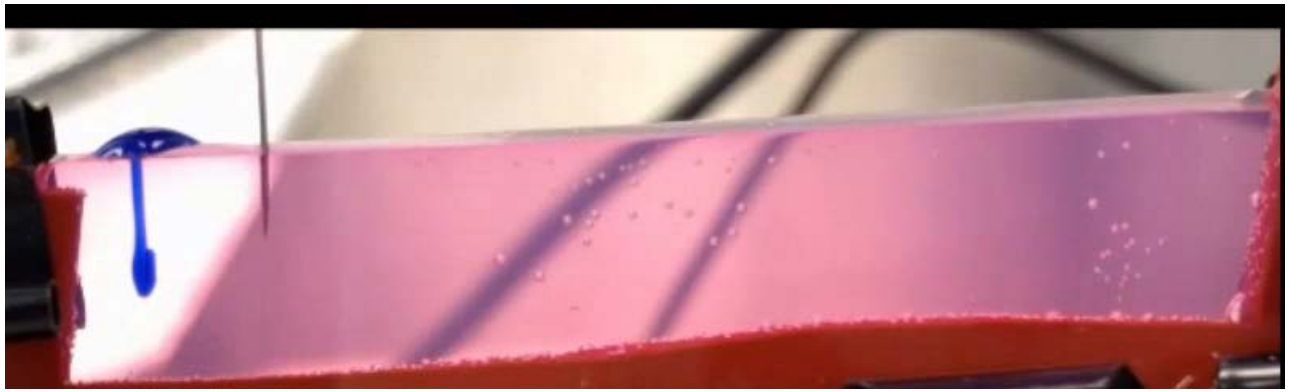
The Gap Neuron Hypothesis



Bioengineered Neural Trails™ Provide Many Advantages Over Conventional Bolus Injections

Bolus approach

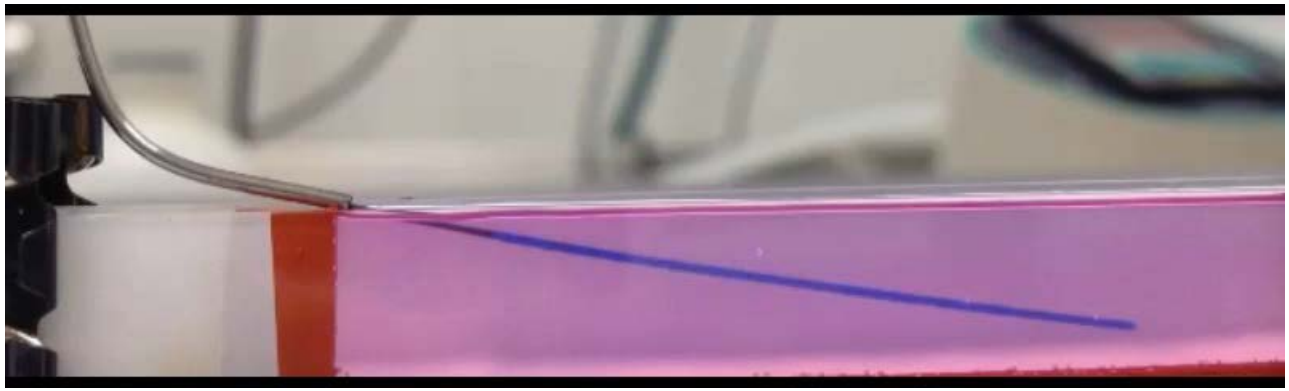
- Reflux at multiple injection sites
- Sub-optimal cell distribution
- No longitudinal connectivity



Collagen matrix to simulate spinal cord

Trail approach

- No reflux at single injection site
- Homogeneous cellular suspension
- Immediate longitudinal connectivity



Company videos/images

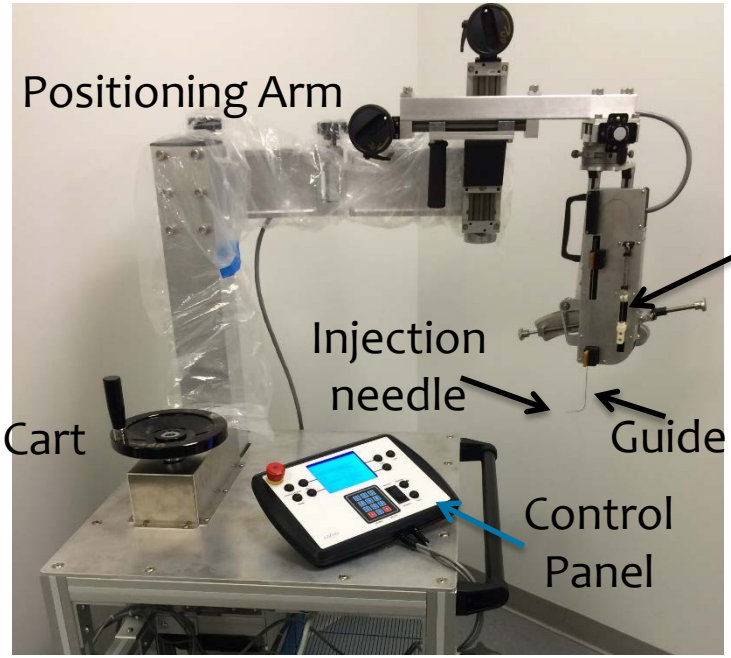
Evolution of the TrailMaker™

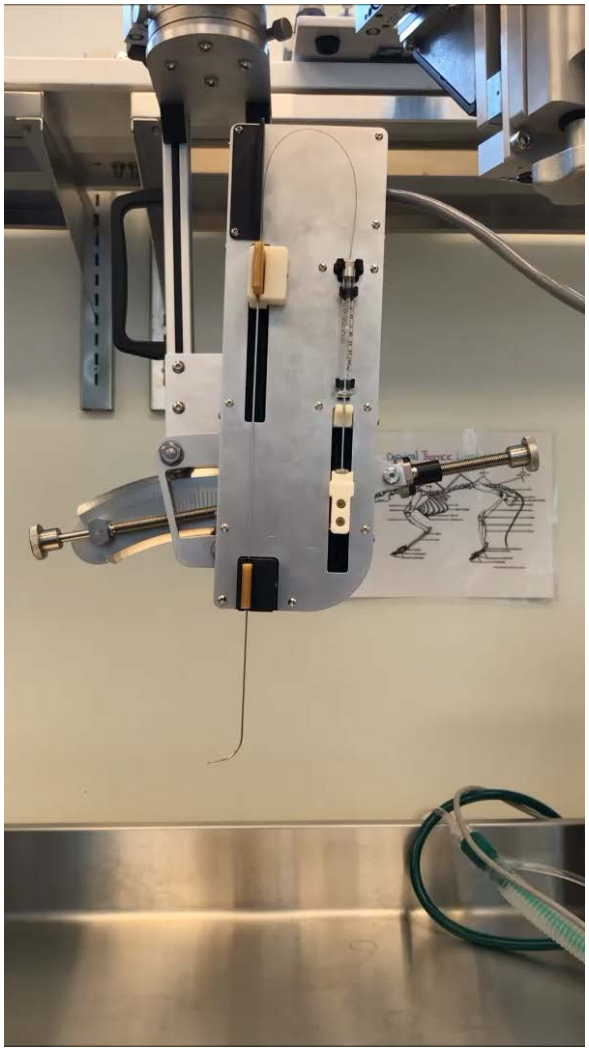
First Generation

Second Generation

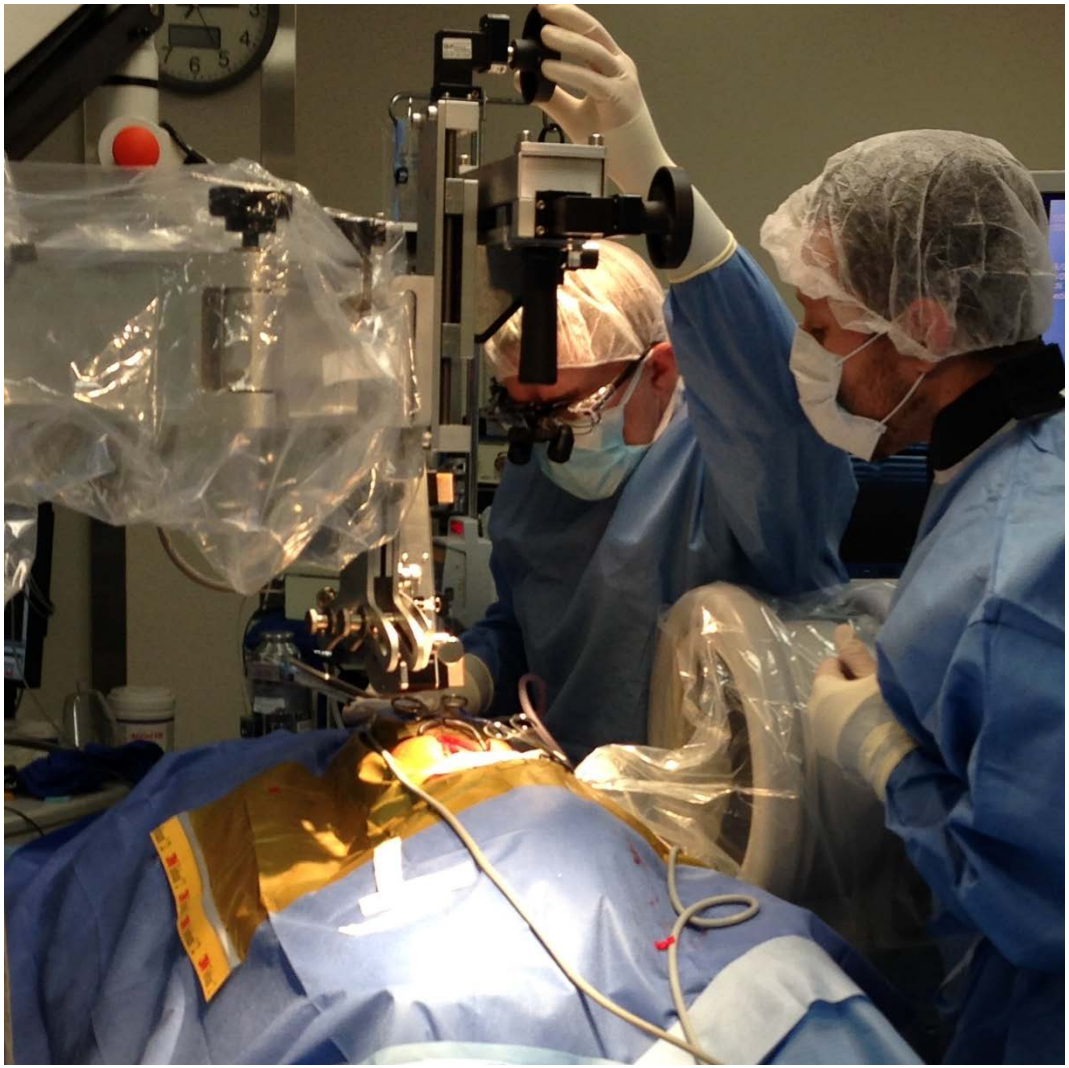
Development of a Novel Device to Inject Therapeutic Trails within the Spinal Cord

The TrailMaker™ Injection Device





Feasibility of Proprietary Device Demonstrated in Pilot Porcine Study

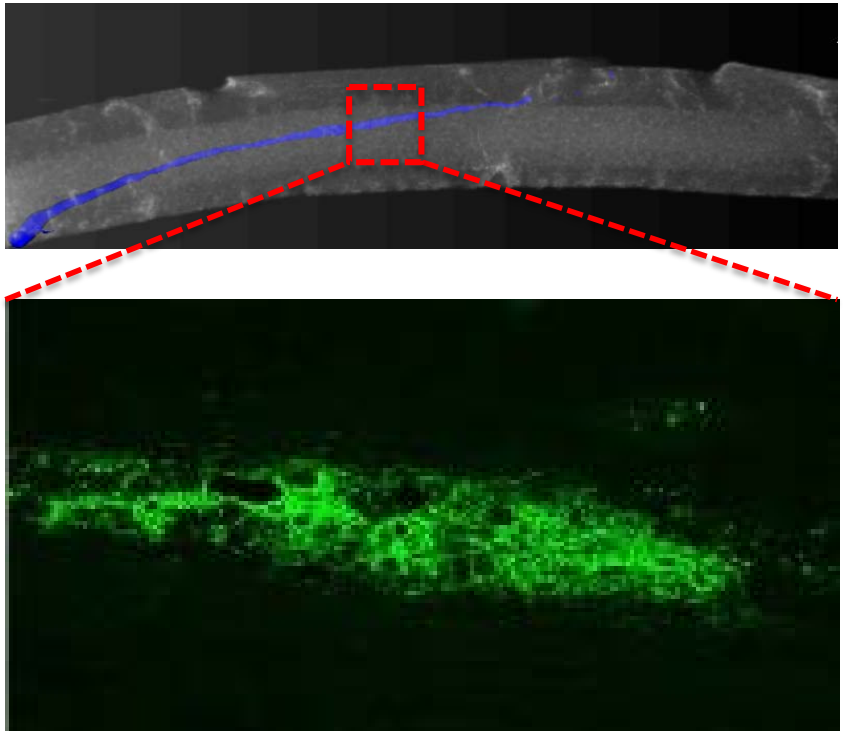


In collaboration with Dr. James Guest

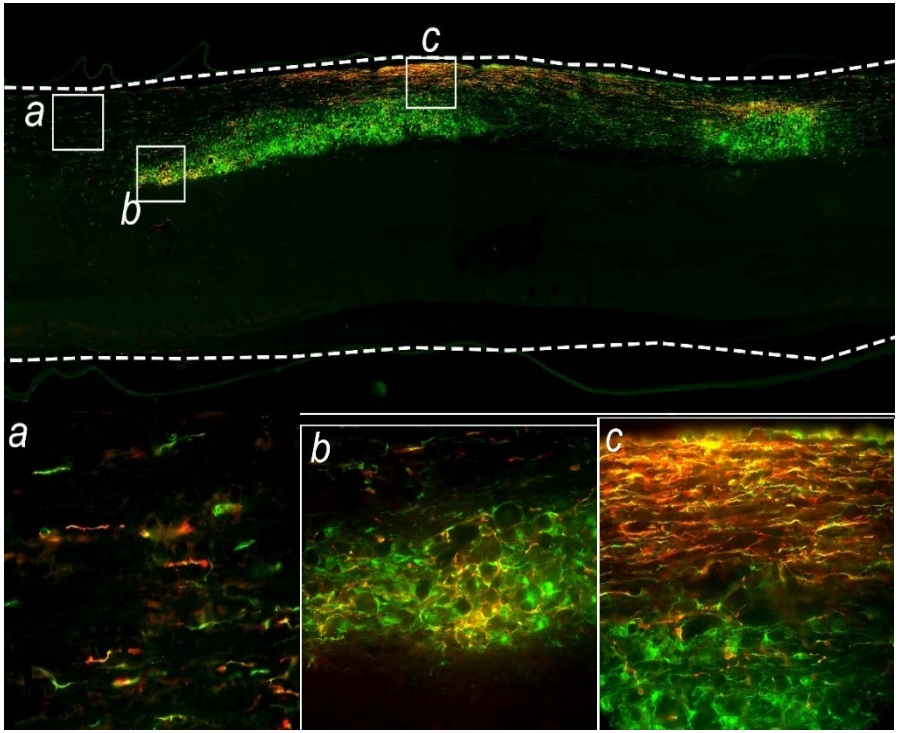
Bioengineered Neural Trails™: InVivo's Novel Neural Stem Cell Product for Chronic SCI

Porcine Model (1 week after injection)

3D MRI of Bioengineered Neural Trail



Rat Model (1 month after injection)



Histology demonstrating interconnected human cells (STEM121) and neural precursors (rat only) (DCX)

Next Steps for Bioengineered Neural Trails Program

- Continue to evaluate surgical feasibility of delivering cell trails within the spinal cord – improve upon device if needed
- Identify neural stem cell source
- Understand biology of stem cells once injected and evaluate for transplant – host integration
- Perform efficacy and GLP safety/toxicology studies that support clinical translation

Conclusions

InVivo is:

- taking a biomaterials/regenerative medicine approach to SCI
- pioneering new surgical approaches to SCI
- building institutional expertise in the translation of SCI therapeutics