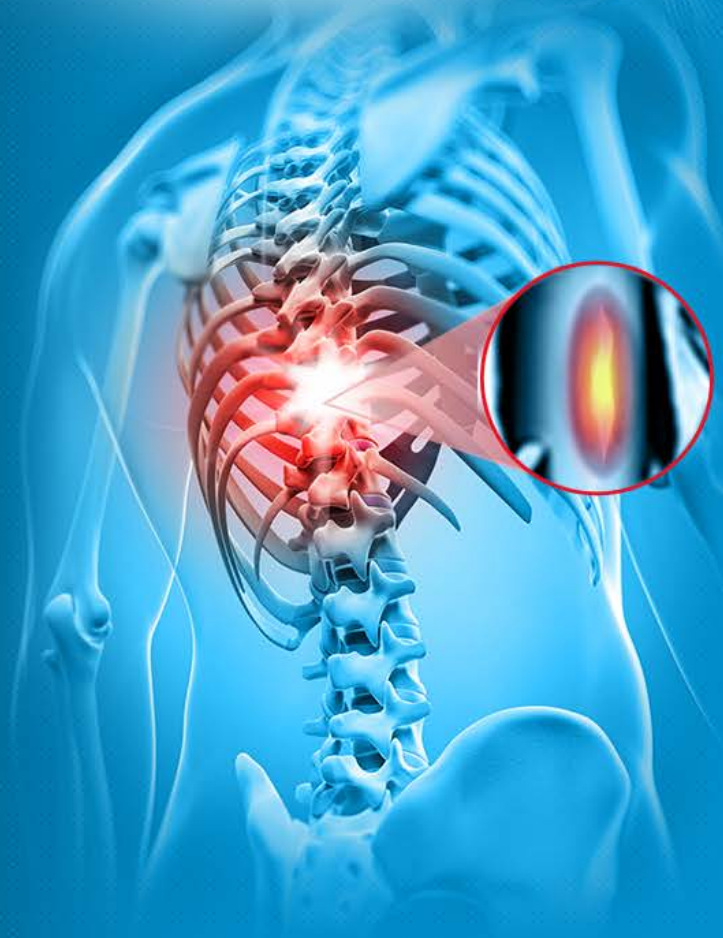
INVIVO THERAPEUTICS™



# The Neuro-Spinal Scaffold Promotes Tissue Remodeling, Axonal Sprouting, and Schwann Cell Myelination Following Acute Spinal Cord Contusion Injury in Rats

***Simon Moore, PhD***
*Director of Research*
*InVivo Therapeutics Corp.*

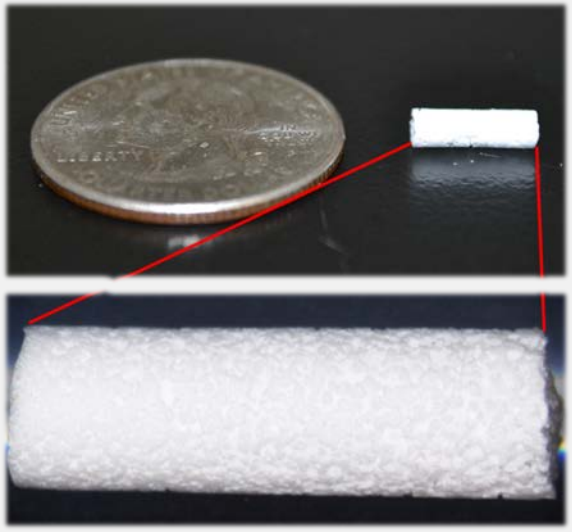
# Forward-Looking Statements

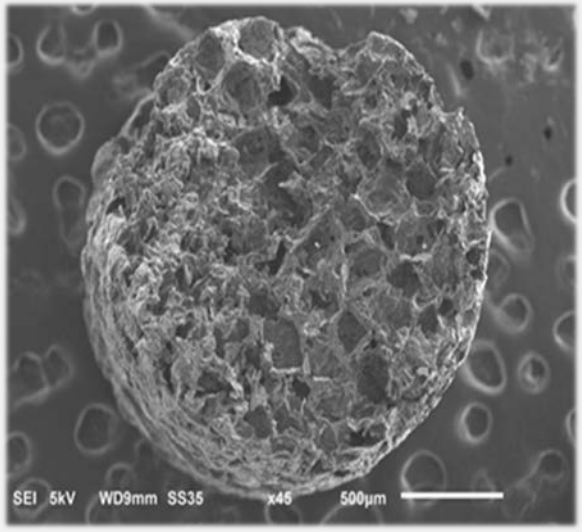
Before we begin, we would like to remind everyone that during our presentation, we will be making forward-looking statements about our business, plans, and objectives. These statements are based on how we see things today. These statements can be identified by words such as believes, estimates, expects, 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.

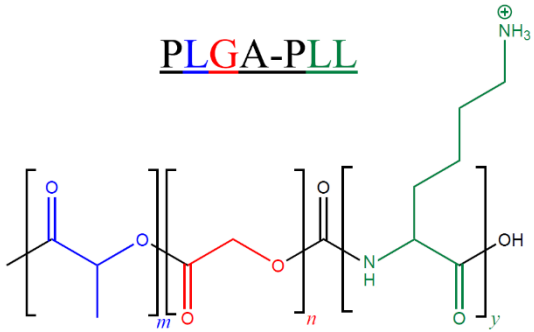
# InVivo Therapeutics

- Located in Cambridge, Massachusetts
- Focused on spinal cord injury
- Two Programs:
  - **Bioengineered Neural Trails™:**
    - For sub-acute and chronic spinal cord injuries
    - Create a trail of neural stem cells that bridges either side of the injury
    - Research stage
  - **Neuro-Spinal Scaffold™:**
    - For acute spinal cord injuries (within 4 days)
    - Insert a degradable scaffold into injury epicenter
    - Clinical stage

# *Neuro-Spinal Scaffold*™ – A Cylindrical, Porous Biodegradable PLGA-PLL Polymer Scaffold

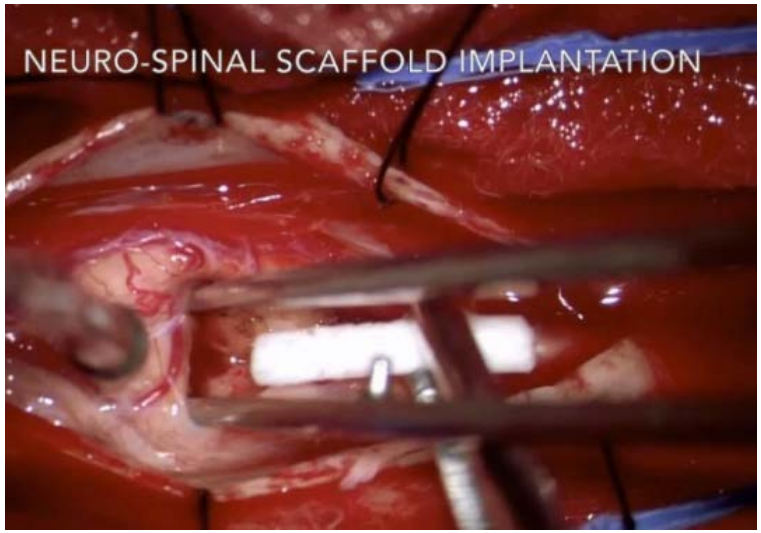




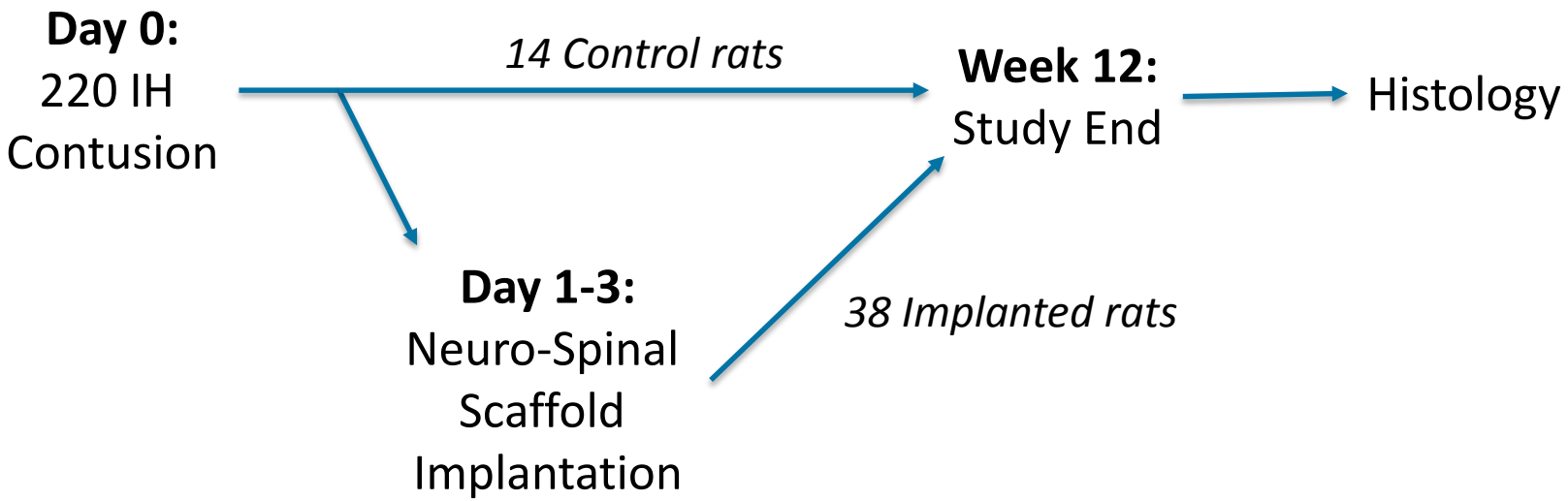

- **PLGA:** Poly(lactic-co-glycolic acid), a biodegradable skeleton
- **PLL:** Poly(L-lysine), promotes cellular adhesion
- 10mm long, 2 or 3mm diameter
- 84-92% porous
- Degrade within 4-8 weeks *in vivo*

# *Neuro-Spinal Scaffold*™ in the Clinic: INSPIRE Study



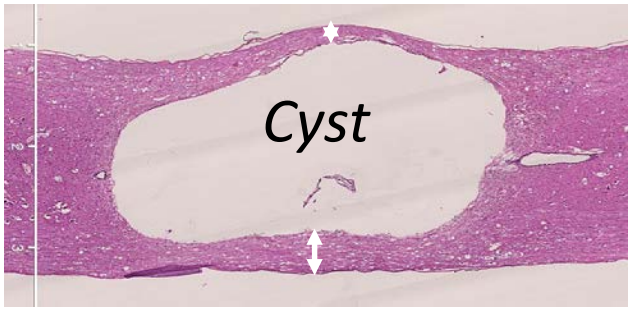

- NCT02138110
- Implanted into the injury epicenter within 96 hours of injury
- Complete (AIS A) thoracic injuries
- Humanitarian Device Exemption (HDE)
- 27 clinical sites across the US and Canada
- Of the 8 patients in follow up, 5 have improved to AIS B or better.

# 12-Week Rat Contusion Study

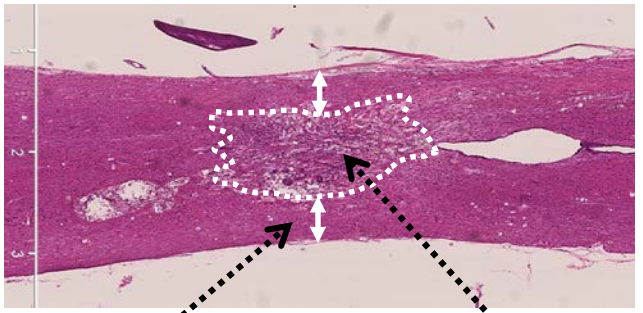


# *Neuro-Spinal Scaffold*™ Implantation Reduces Cyst Size, White Matter Loss and Creates Novel Tissue

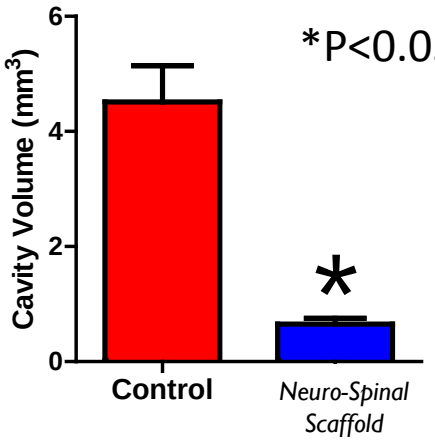
**Control** *(n = 14)*



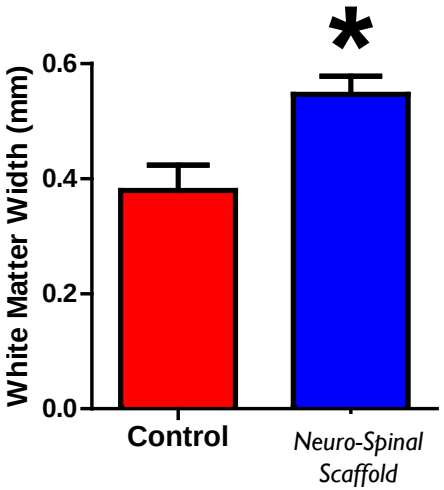

**Neuro-Spinal Scaffold** *(n = 38)*



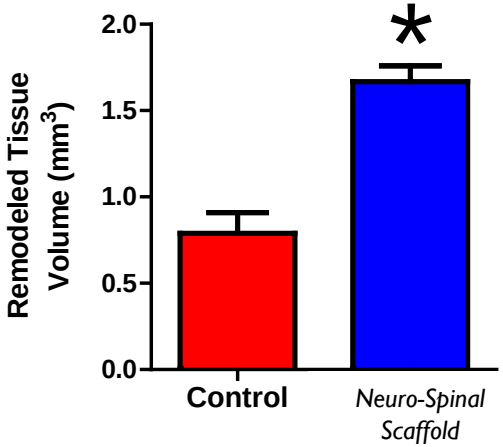
Cyst Reduction




White Matter Sparing

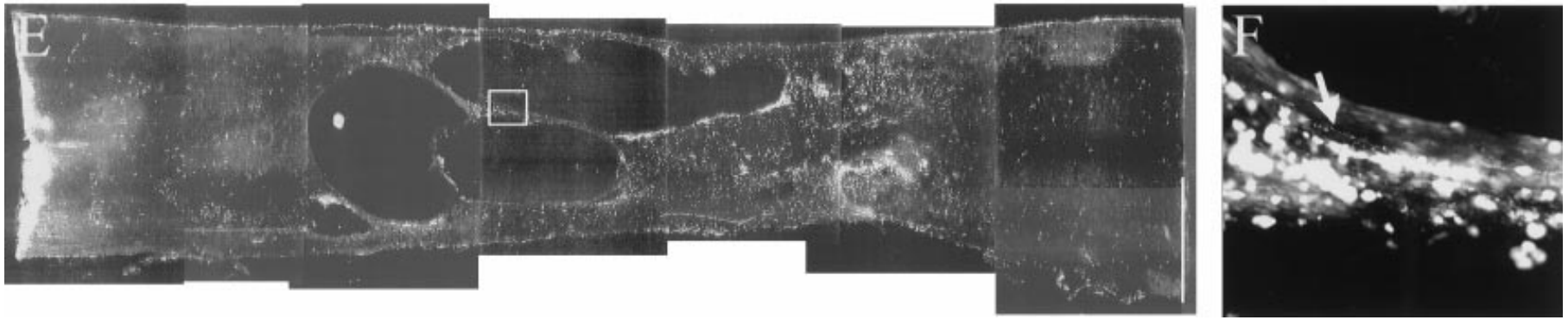



Novel Tissue



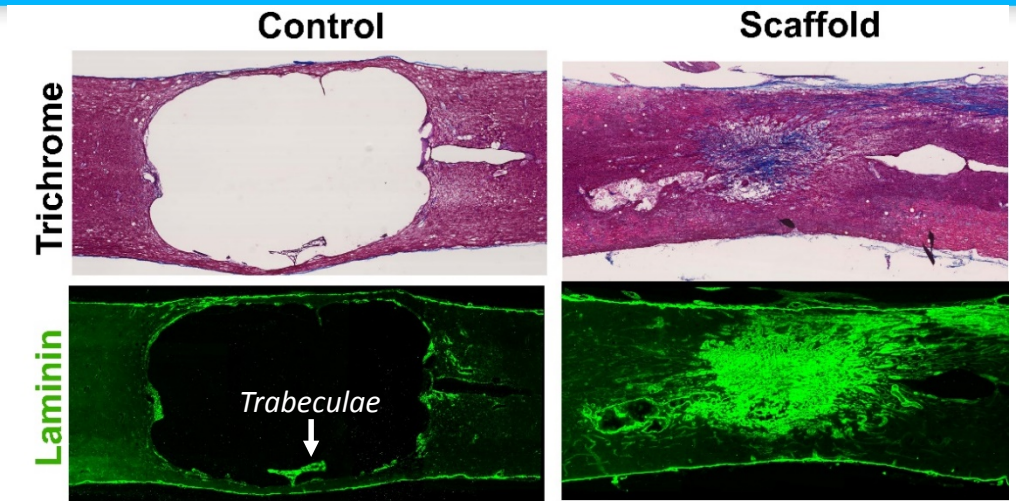
# Novel Tissue from *Neuro-Spinal Scaffold*™ as Expanded Trabeculae

- Cellular bridges known as trabeculae have been observed to divide cavities
- These trabeculae contain ECM, axons, macrophages, and myelinating Schwann cells (Guizar-Sahagun et al., 1994; Beattie et al., 1997; Hill et al, 2001)

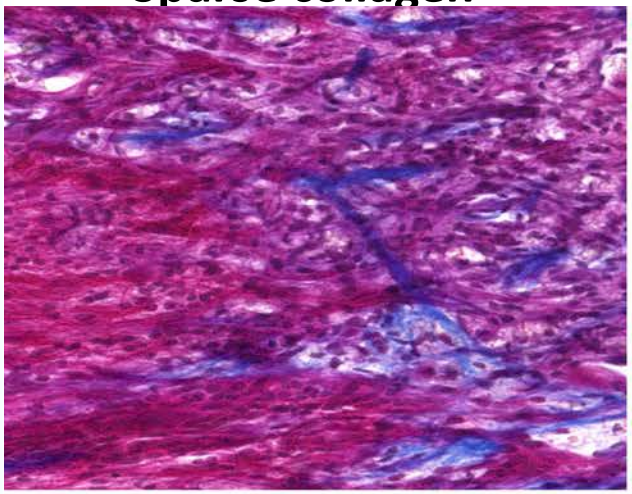



Hill *et al.,* 2001

# Novel Tissue Contains ECM that is Permissive to Axon Regrowth

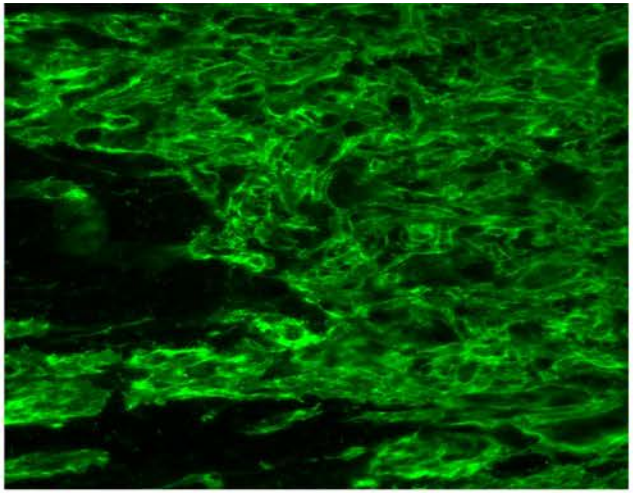



**Sparse collagen**



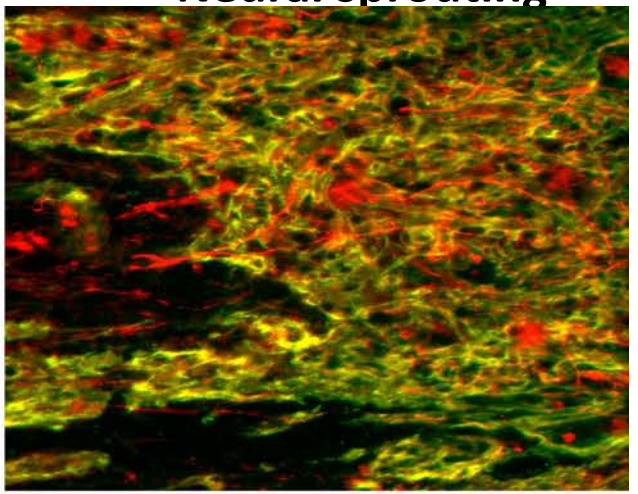
Masson's Trichrome

**Abundant laminin**



Laminin

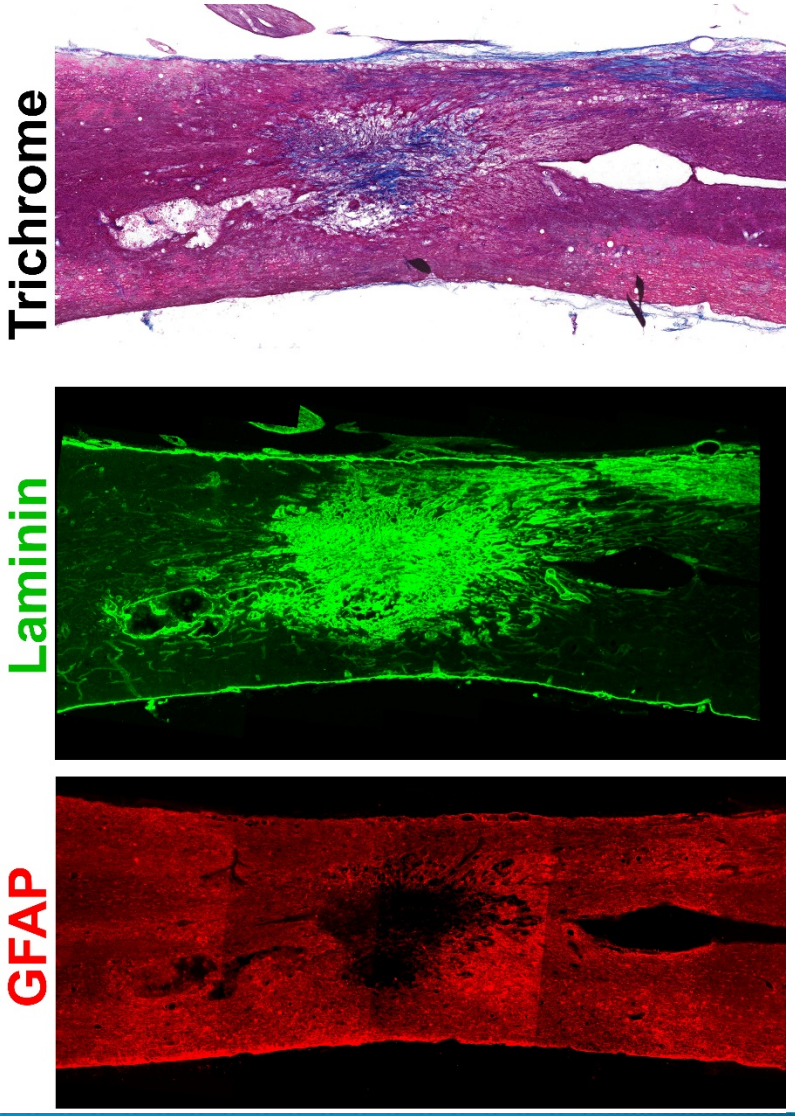
**Neural sprouting**



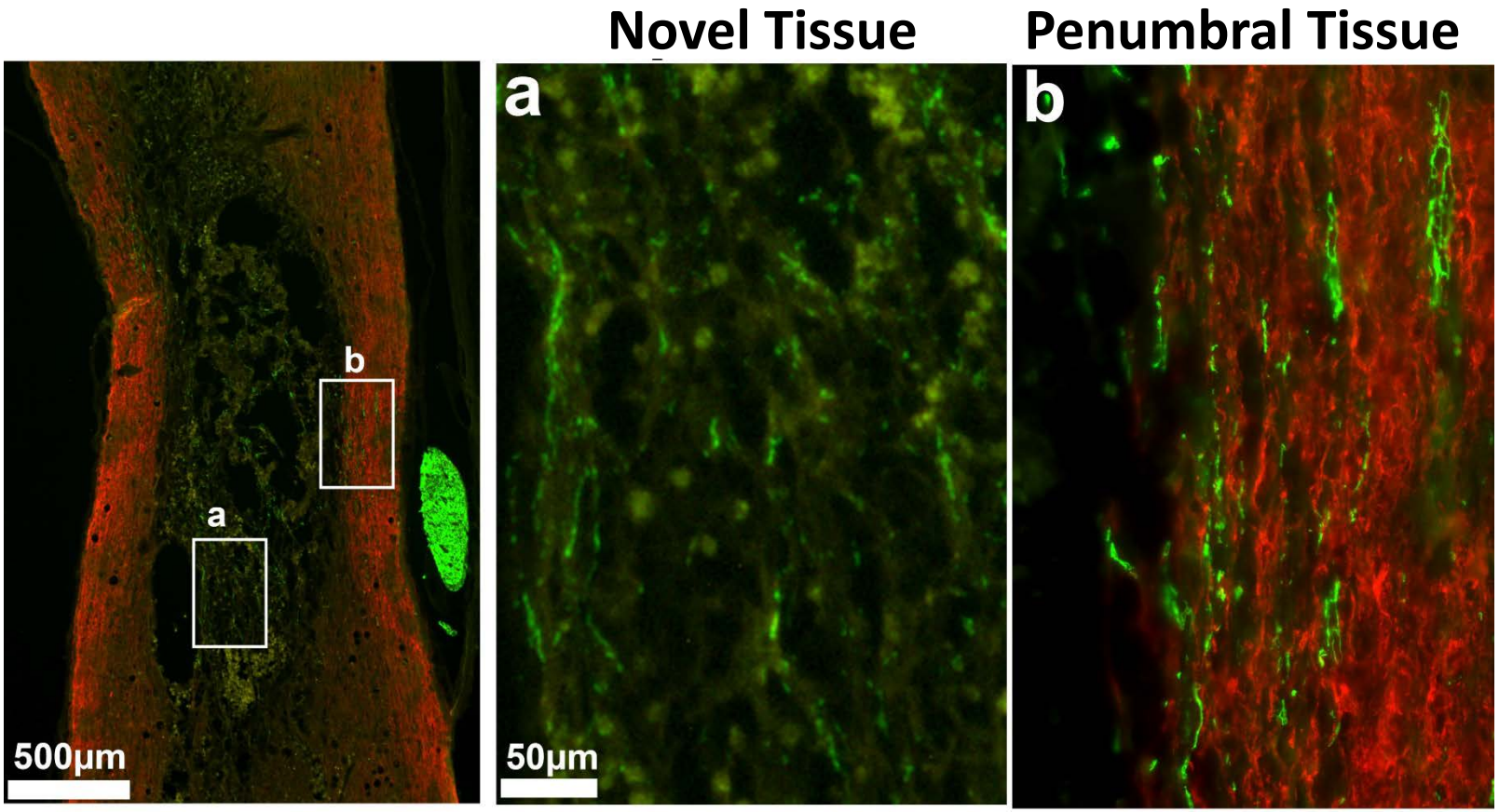
ß3-Tubulin/Laminin

# Absence of Reactive Astrocytes in Novel Tissue

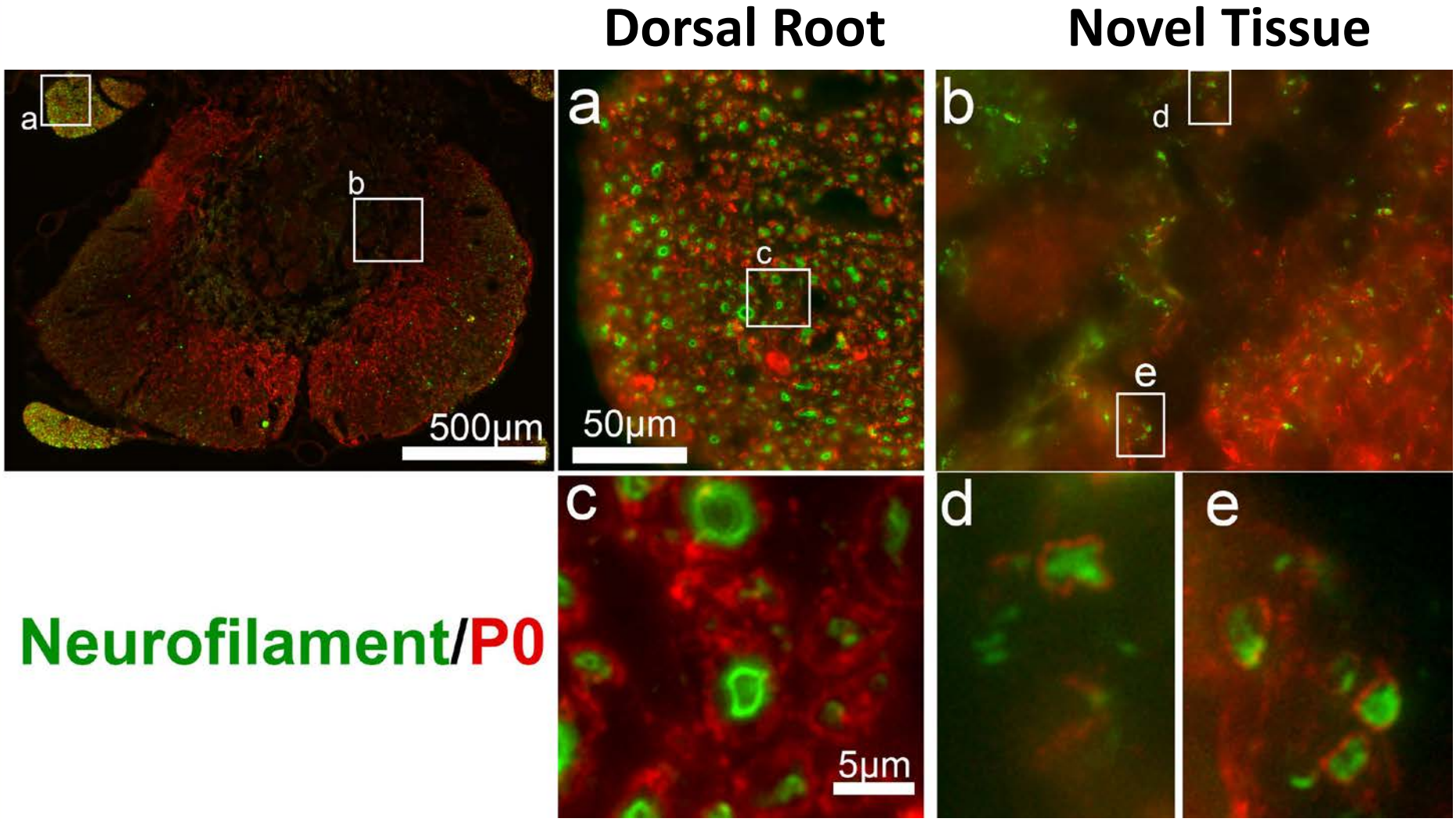
GFAP+ reactive astrocytes have been reported to be sources of ECM (Jones et al., 2003)



# Abundant Schwann Cells in Novel Tissue and in Penumbral White Matter



# Schwann Cells Myelinate Axons in Novel Tissue



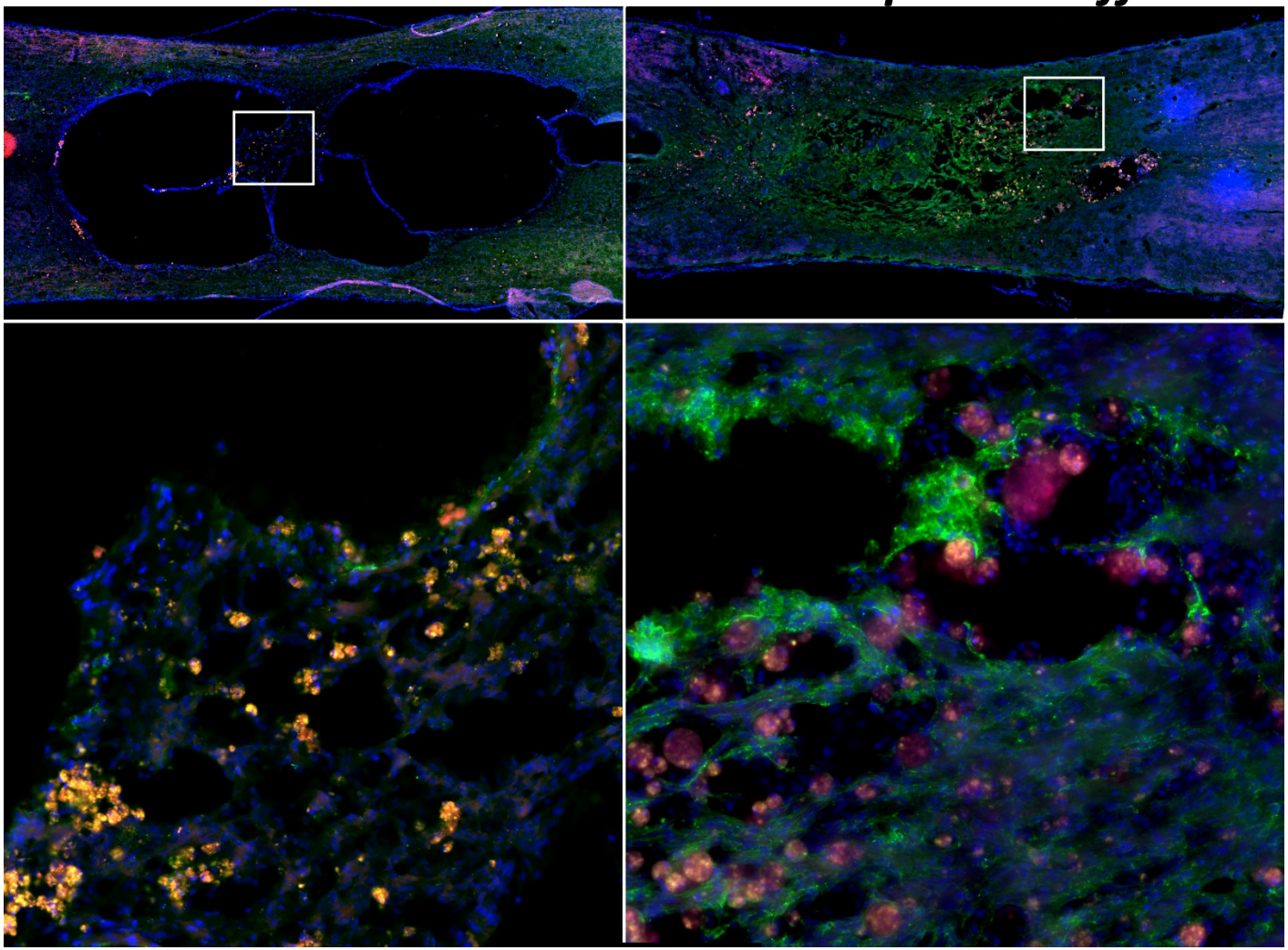
# Emerging Roles of Reparative Macrophages and NG2+ Cells After Spinal Cord Injury:

- After rat contusion injury, there is a persistence of M1-type macrophage >28 days and an early peak of M2-type macrophage at ~5 days (Chen *et al.*, 2015).
- M2-type macrophage promote axon extension on inhibitory substrates (Kigerl et al., 2009).
- M1 and M2-type macrophage attract Schwann cells (Mokarram et al., 2013).
- M1 and M2-type macrophage attract and increase the proliferation of NG2+ precursor cells that can give rise to myelinating oligodendrocytes and Schwann cells (Miron et al., 2013; Zawadzka et al., 2010).
- NG2+ cells are sources of ECM (e.g. laminin) (Jones et al., 2003)

# NG2+ Cells and M2 Macrophage in Novel Tissue

Control

***Neuro-Spinal Scaffold™***

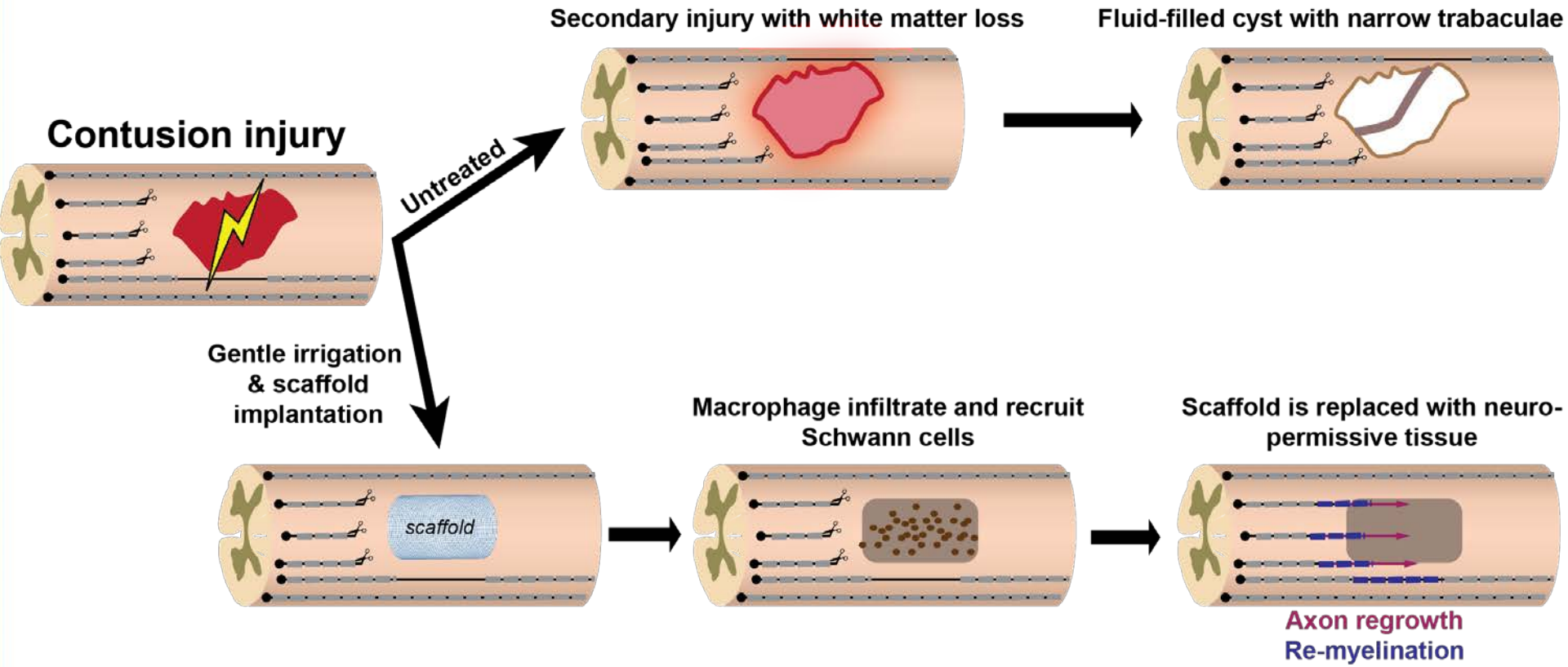


**NG2**

**Reparative M2 macrophage *(Arginase-I)***

**DAPI**

# Neuro-Spinal Scaffold ™ Implantation Reduces Cysts and White Matter Loss, and is Replaced with Neuropermissive Tissue



# Thank You!

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  - Pam Podell
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  - Laura Chamorro

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