Biomateriales instructivos para mejorar la salud

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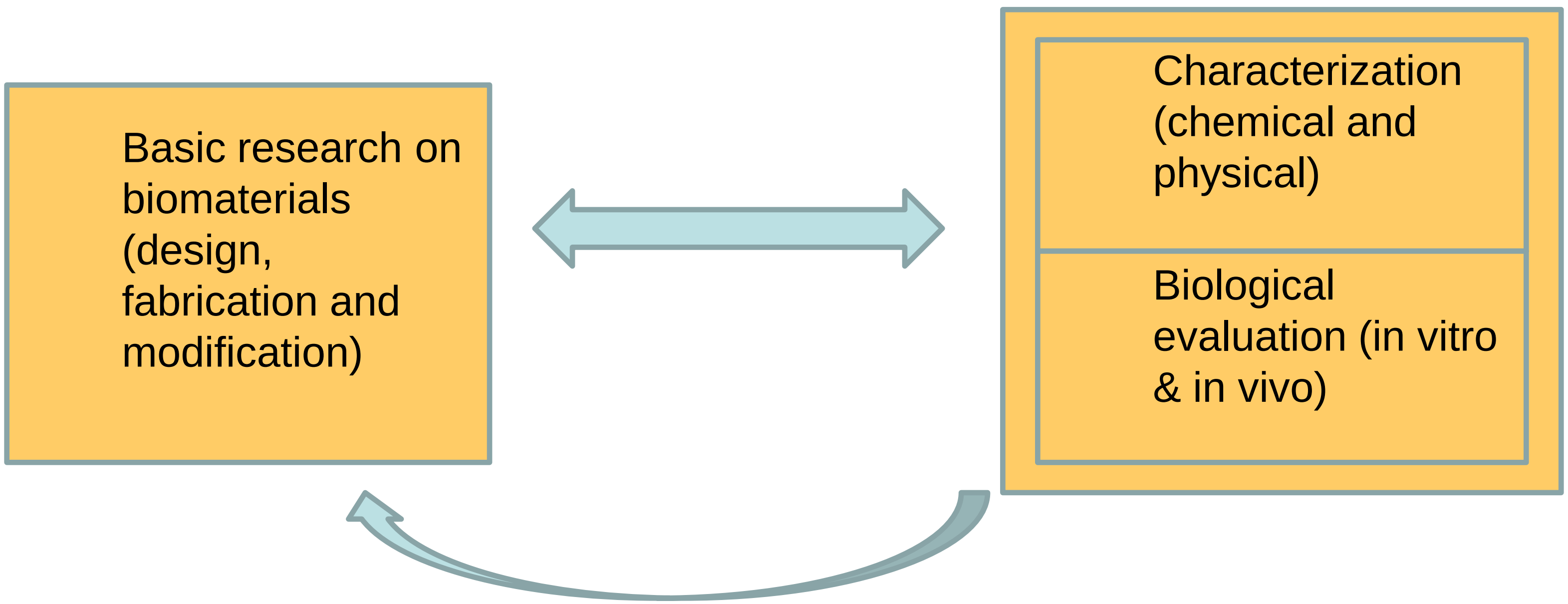
Objetivo

- Desarrollar nuevos materiales para regeneración tisular. Estudiamos materiales bioactivos y biodegradables y aplicamos el conocimiento fundamental y las interacciones con el ambiente biológico para comprender y aplicarlo a la medicna regenerativa.



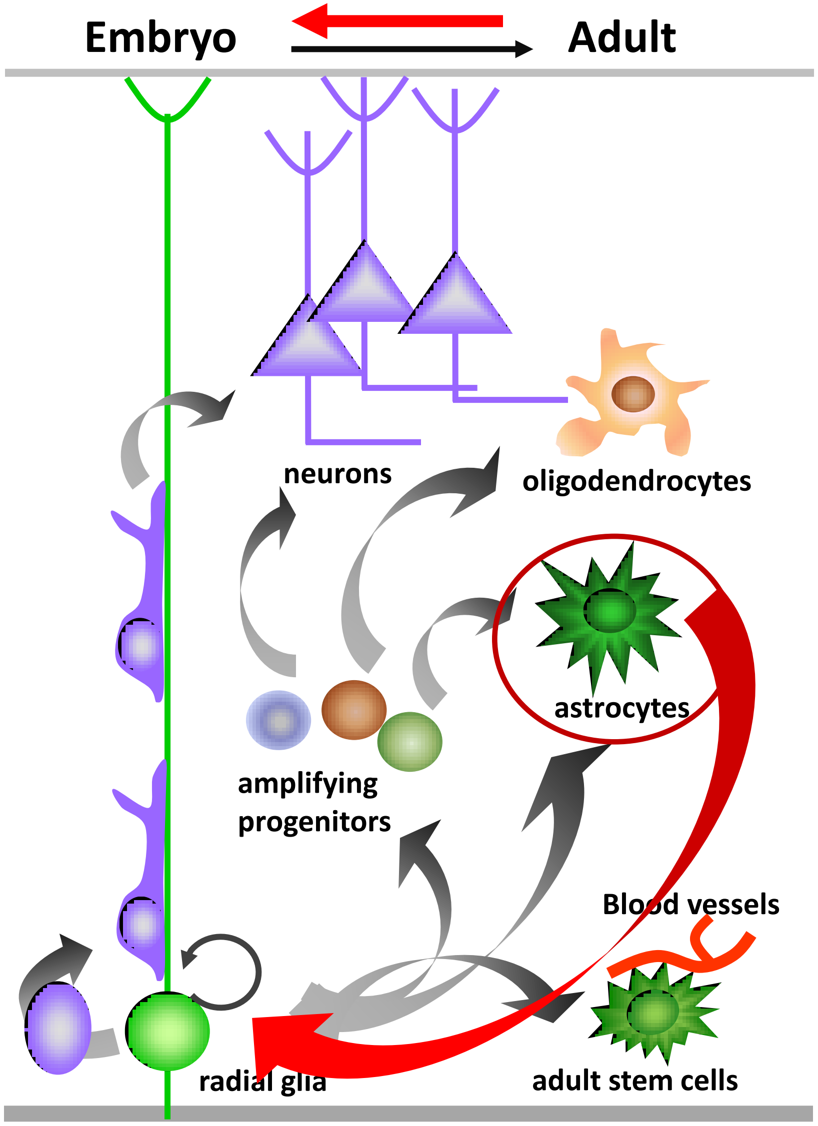
Ictus, traumatismos y procedimientos quirúrjicos destruyen la unidad neurovascular y producen una perdida extensiva de tejido neural.

Espacio vacio años después de un traumatismo cerebral.

El SNC adulto no se autorepara

Daño Cerebral

Potenciar la regeneración endógena del SNC

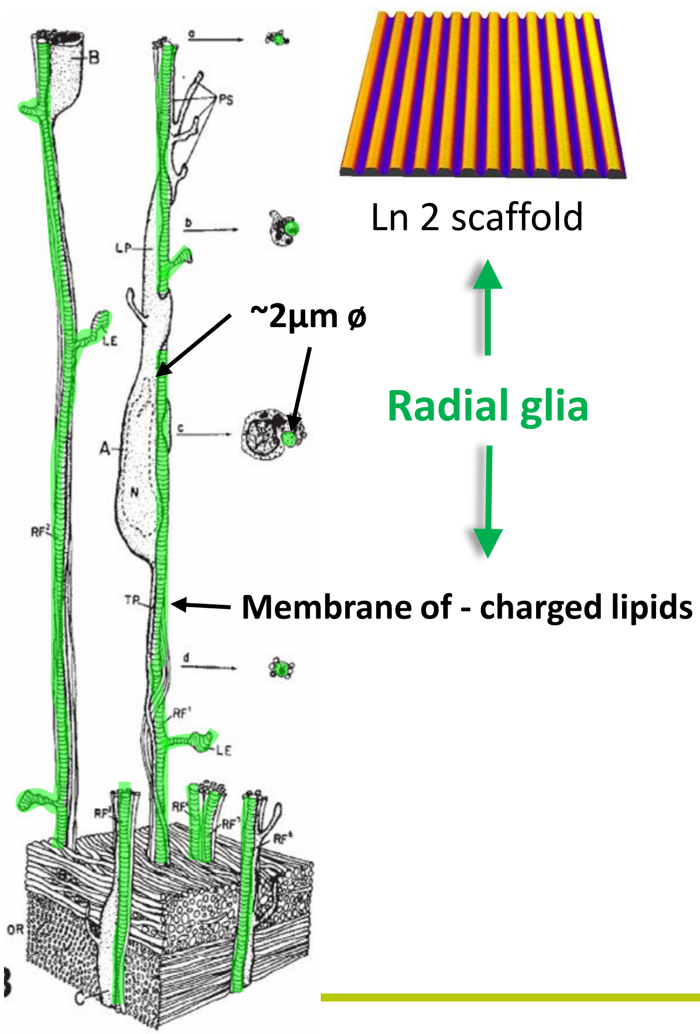


- NSC
- scaffold for neuron migration

Inducir la de-diferenciación de los Astrocitos en Glia Radial

Inducir la Glia Radial funcional

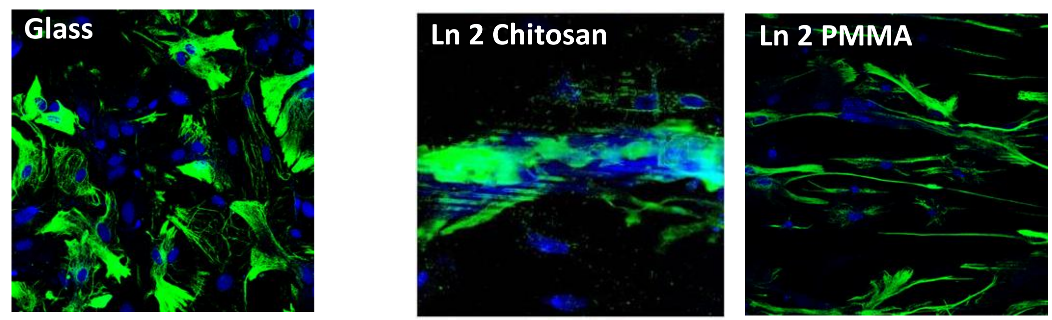
- Tamaño y forma importan



Rakic 1972

Microestructuras que mimetizan el tamaño y la forma de los procesos de la glia radial …

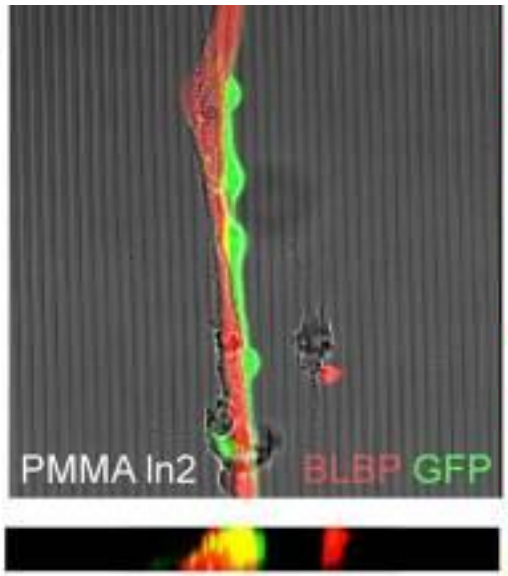
- Propiedades de las superficies

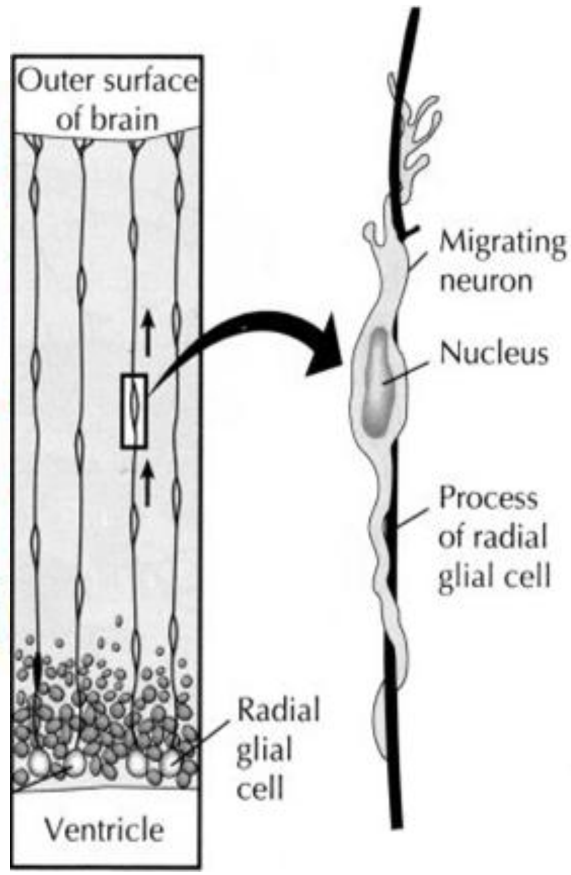


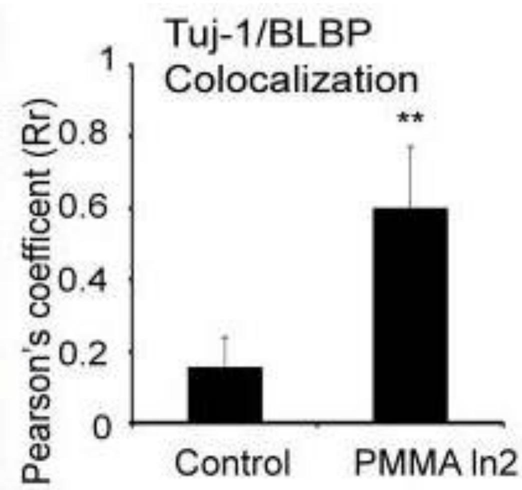
Parameter	Chitosan	PMMA
Chemistry	$-CH_2OH$ $-NH_2$ $-OH$	$-CH_3$ $-CHO$ $-OCH_3$
Contact angle (°)	34 ± 3 Hydophilic	76 ± 4 Hydophobic
Z Potencial (mV)	15 ± 3	-45 ± 5

Hidrofóbicas y cargadas negativamente, como las membranas de la glia…

5days







z

z

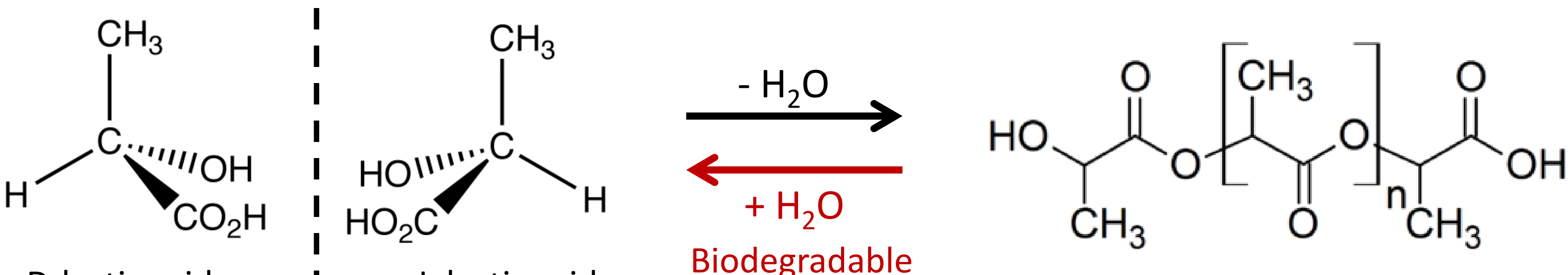
Promote glial-neural adhesion

Mattotti et al. Biomaterials 2012

PLA como material implantable en el SNC

Polylactic acid (PLA)

- Poliéster alifático del ácido láctico
- Biodegradable y termoplástico



D-lactic acid

L-lactic acid

Poly L/DL lactic acid (PLA)

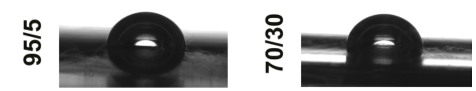
Propiedades físicas y químicas del PLA dependen del % de isómeros L- y D-

L-Lactato es un metabolito intermediario en el metabolismo de los hidratos de carbono

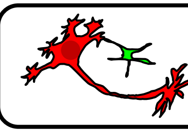
PLA como material implantable en el SNC

Efecto del ratio de L/LD of L /LD en las propiedades físicas de los films de PLA

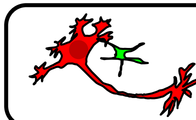
	PLA 95/5	PLA 70/30
Contact angle (º)	75.6 ± 5,2	78.1 ± 8,7
Z potential (mV) (pH=7,4)	- 73.3 ± 1,8	- 36.7 ± 1,9
Young's Modulus	9,5 ± 0,3 GPa	63.7± 1,3 MPa



Hydrophobic

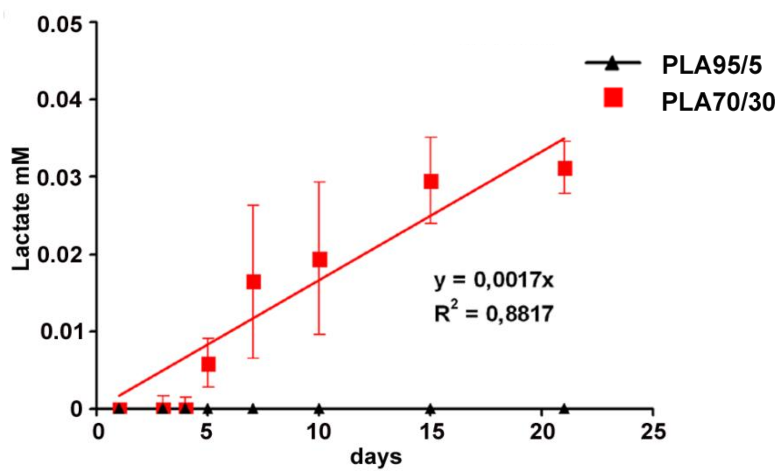


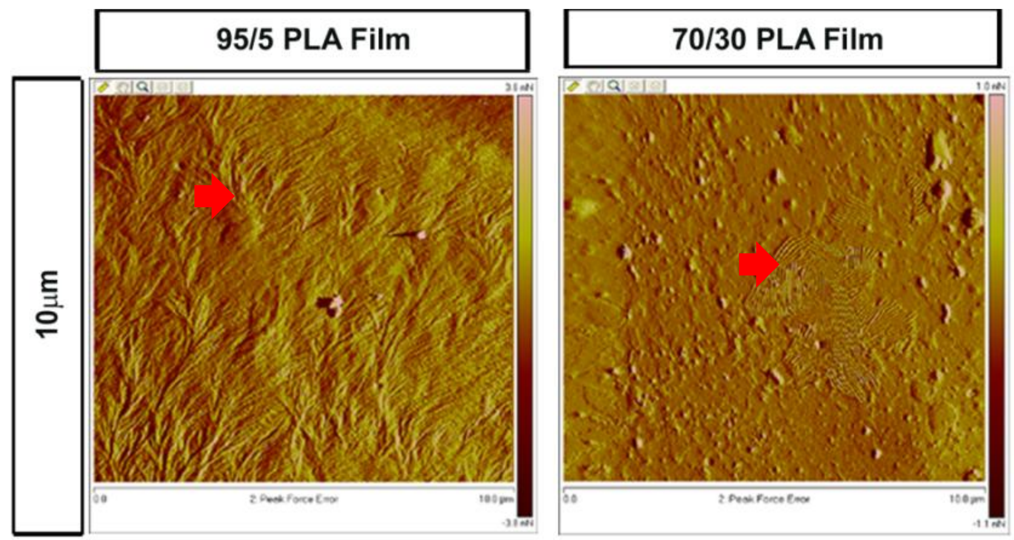
Membrane potential -40 to -90 mV



Elasticity < 1 KPa

Degradación del Lactato





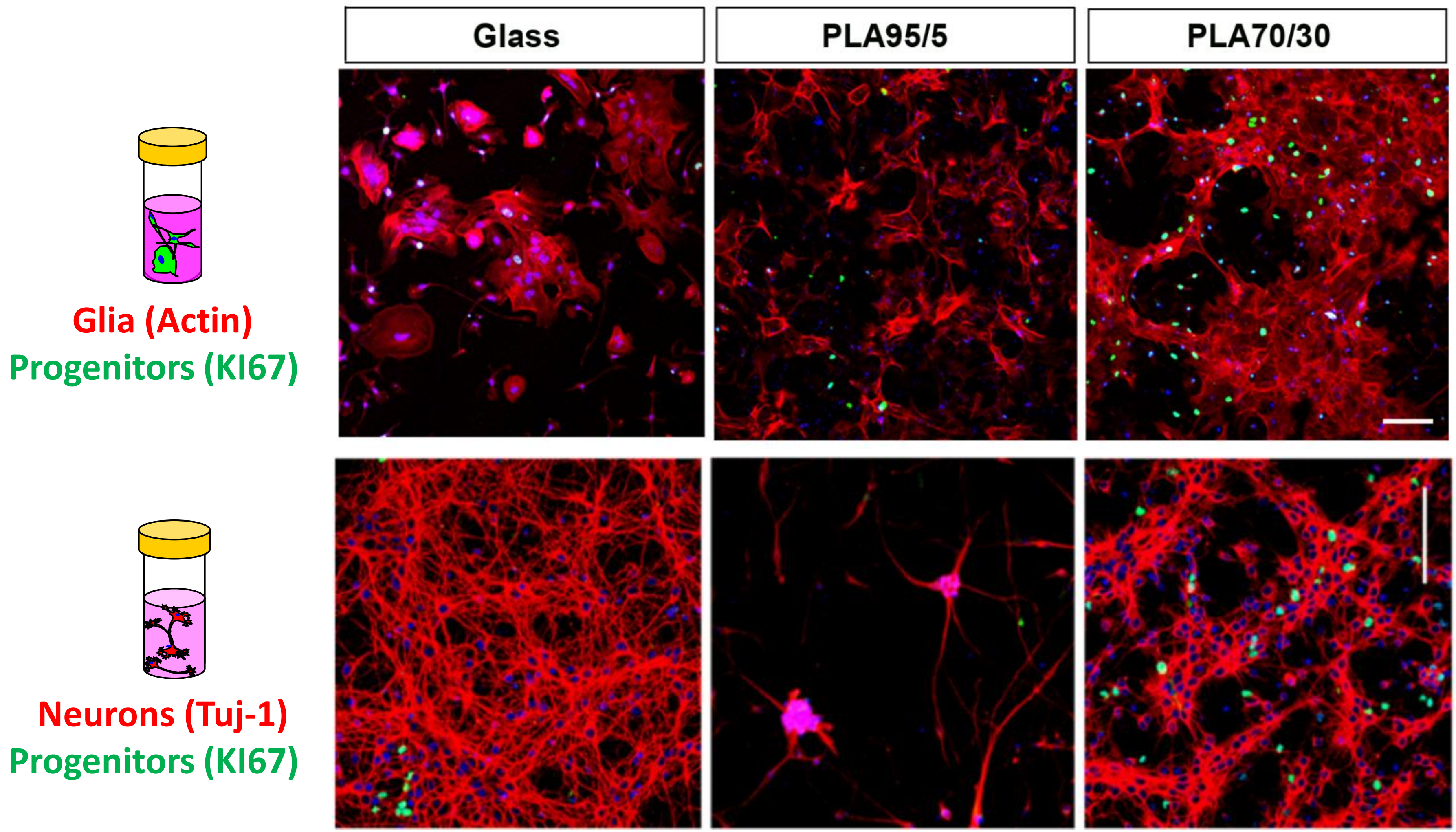
Cristalino

Amorfo

AFM images

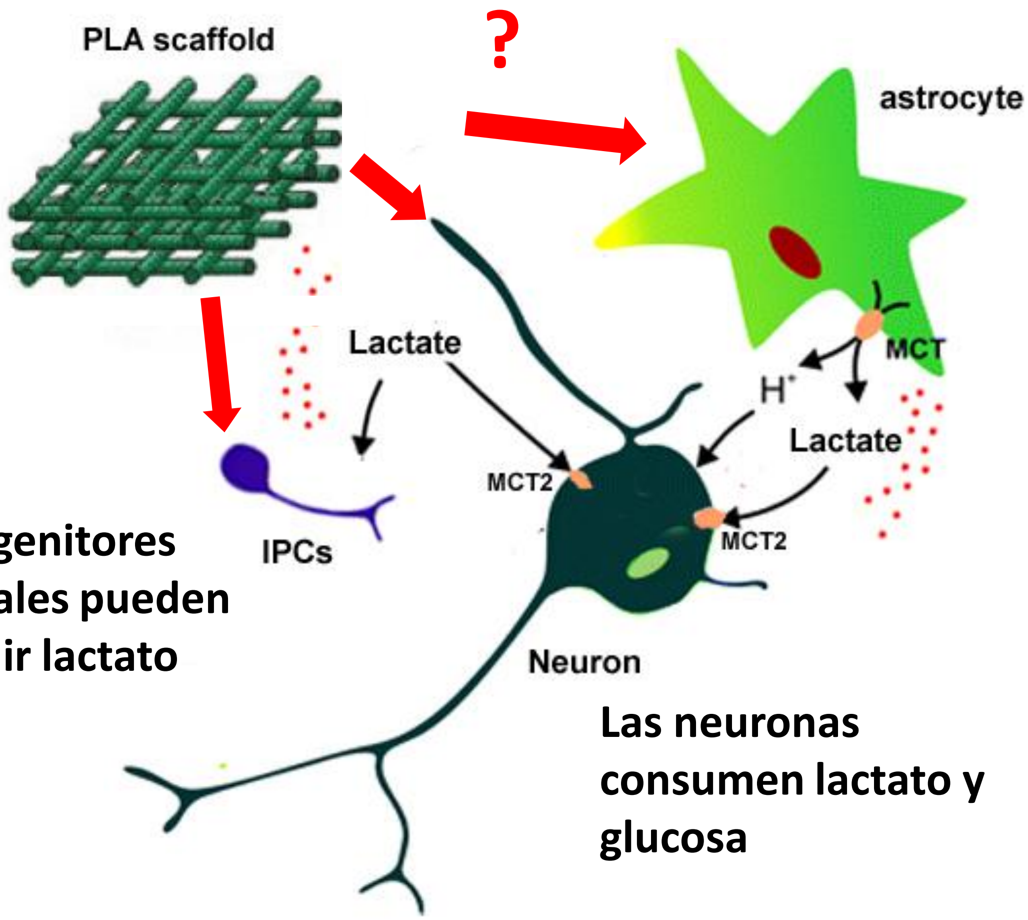
Z. Álvarez et al. / Biomaterials 34 (2013) 2221-2233

PLA 70/30 mantiene la Glia, las Neuronas y los Progenitores



El Lactato es fuente de energía para Neuronas y Progenitores

Puede el PLA 70/30 "alimentar" a las células neurales?

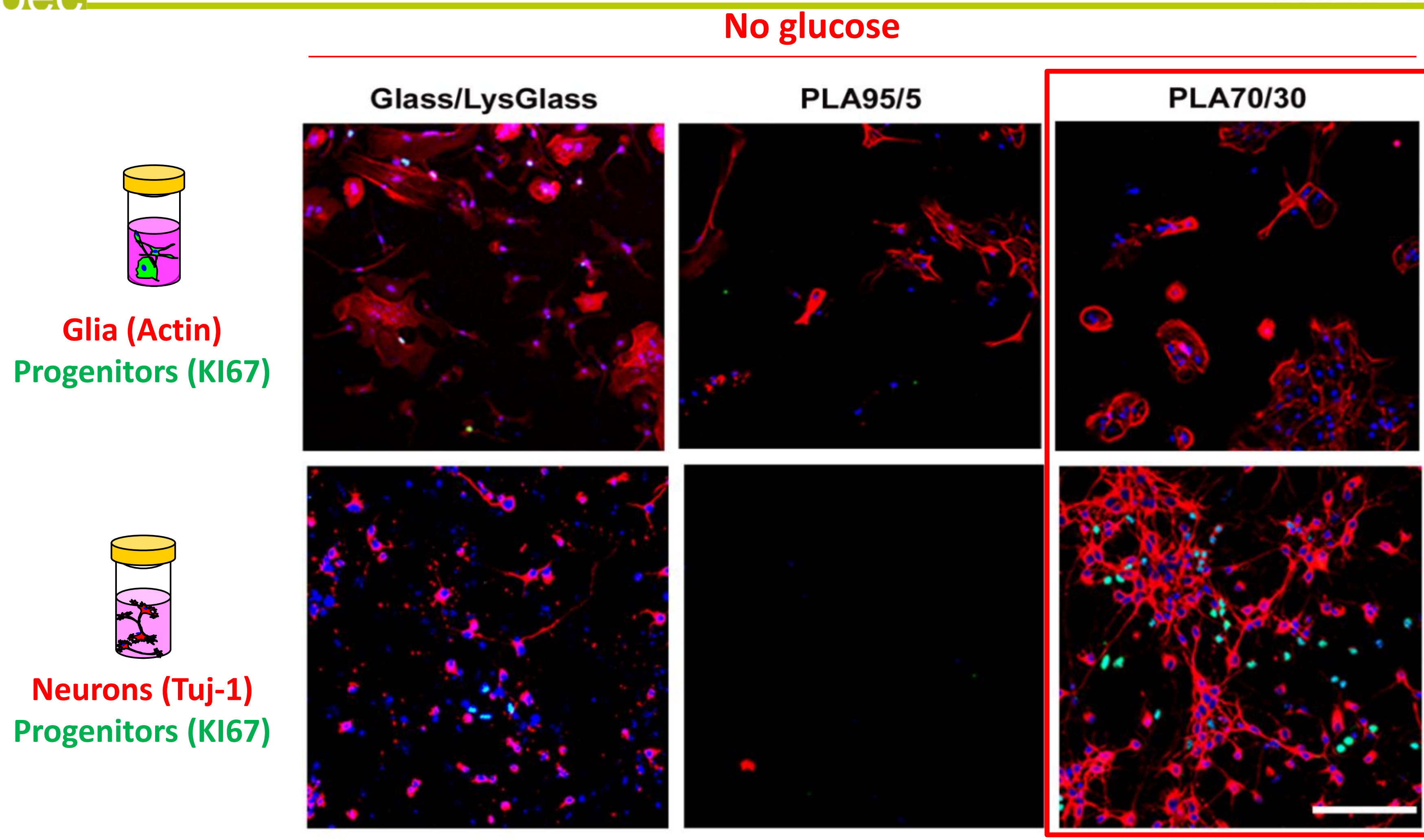


Los astrocitos consumen glucosa y liberan lactato

Los progenitores neuronales pueden consumir lactato

Las neuronas consumen lactato y glucosa

El PLA 70/30 alimenta a las células neurales?

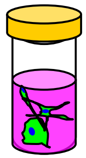


- PLA 70/30 “feed” glia neurons and progenitors in the absence of glucose

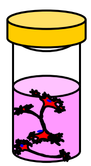
Z. Álvarez et al. / Biomaterials 34 (2013) 2221-2233

El Lactato alimenta a las células neurales?

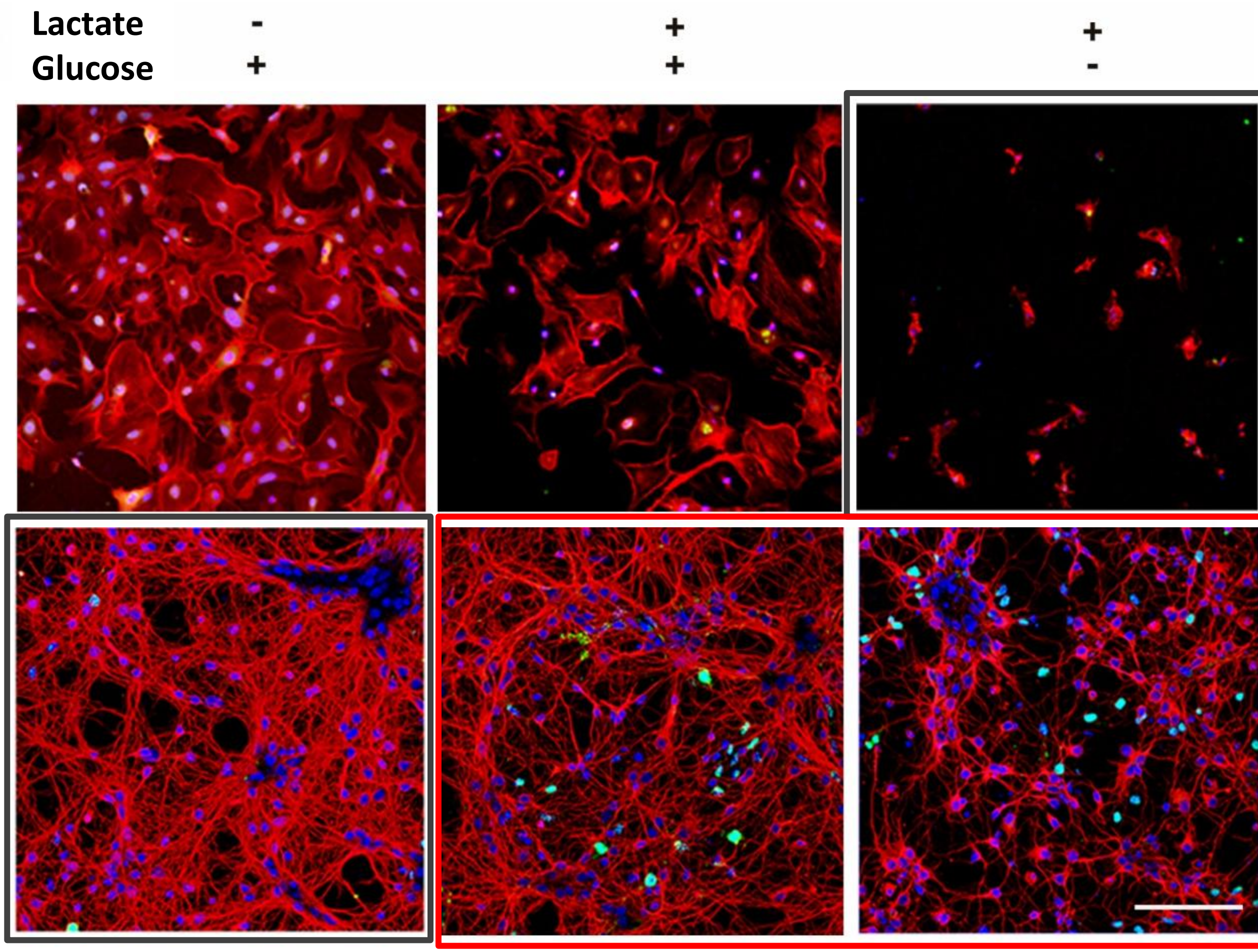
Lysglass substrate



Glia (Actin)
Progenitors (KI67)



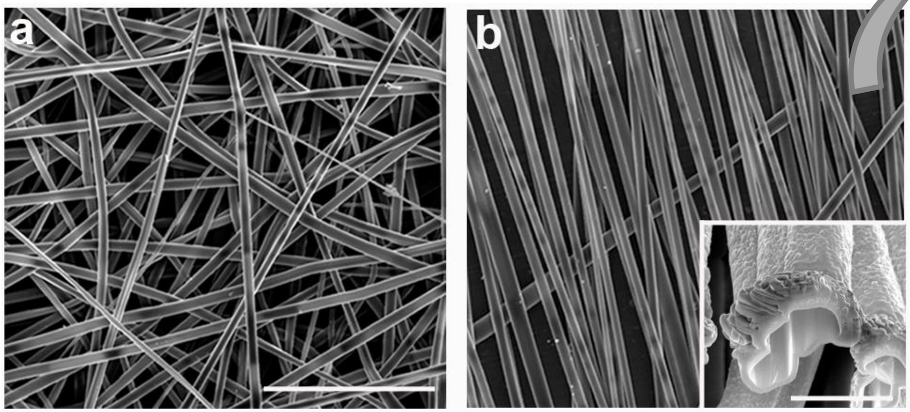
Neurons (Tuj-1)
Progenitors (KI67)



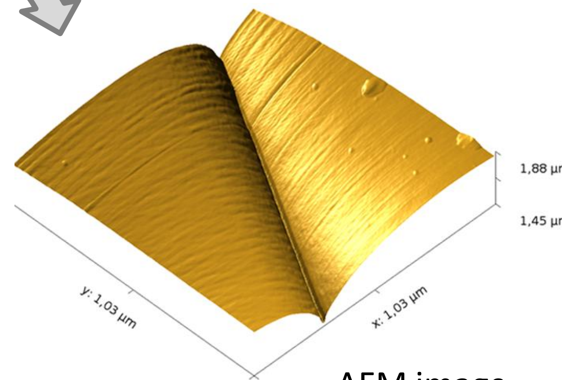
- Glial cells need glucose to survive
- Neurons use glucose and L-lactate
- Neural progenitors need L-lactate to survive

Fibras PLA 70/30 como andamio mimético de glia radial

Random **Aligned**

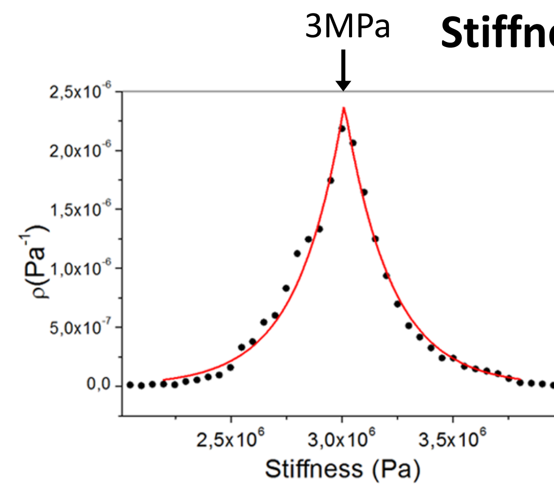


FE-SEM images

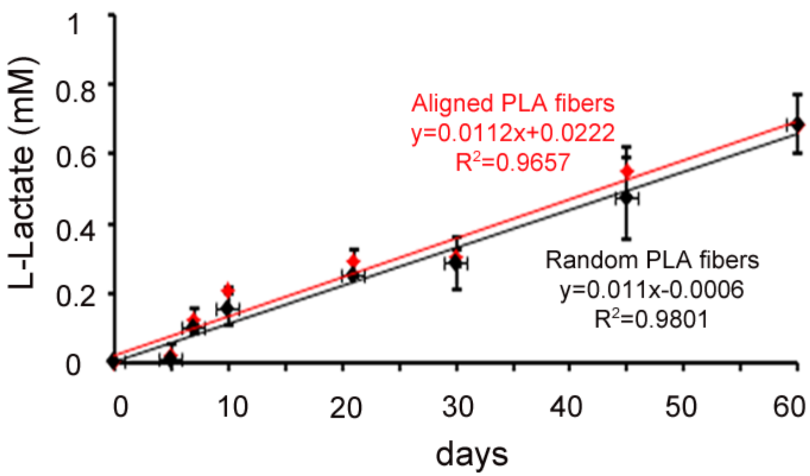


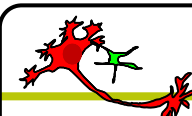
AFM image

Stiffness



L-lactate Release





Elasticity < 1 KPa

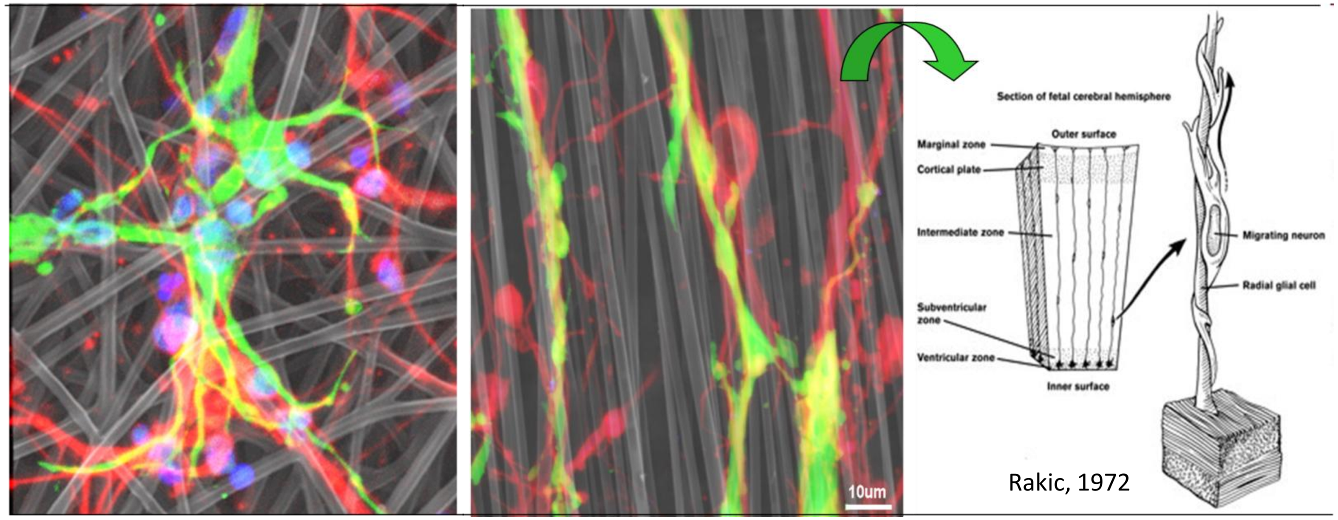
Z. Álvarez et al (2013) submitted

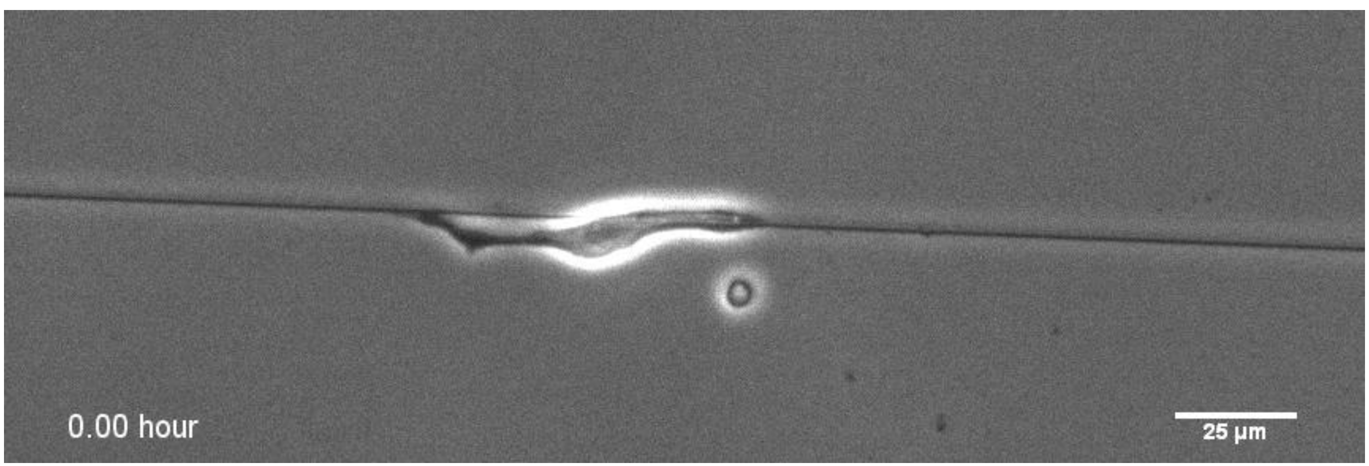
Fibras de PLA 70/30 promueven la migración neuronal

Glia/Neurons

Random

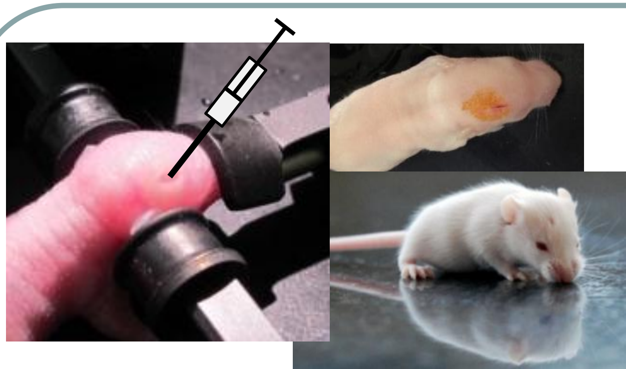
Aligned



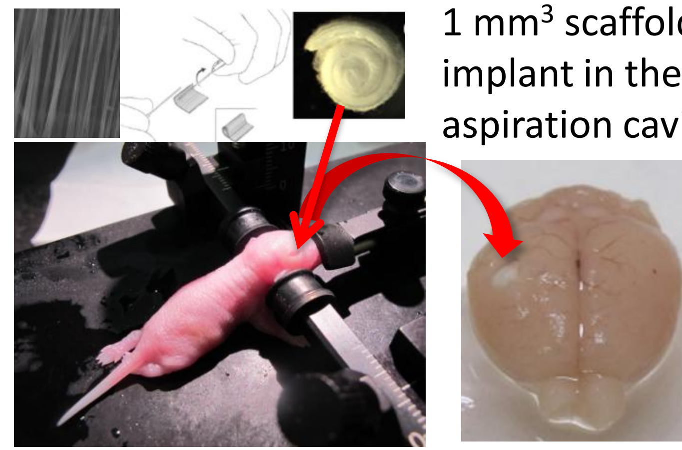


Z. Álvarez et al (2013) submitted

Modelo de daño cerebral



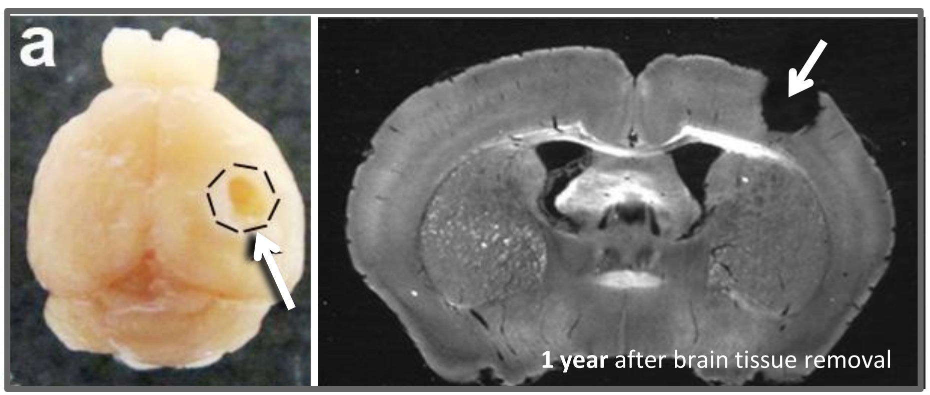
Aspiration of 1 mm^3 brain piece in 4 days old mice

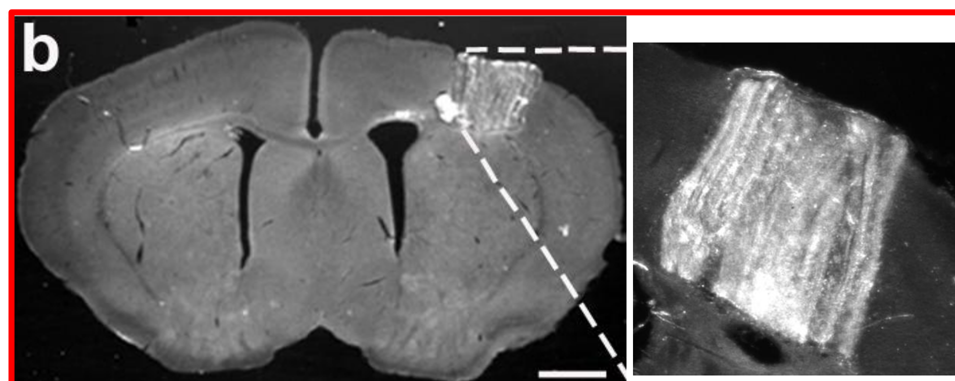


1 mm^3 scaffold implant in the aspiration cavity

No Regeneración !

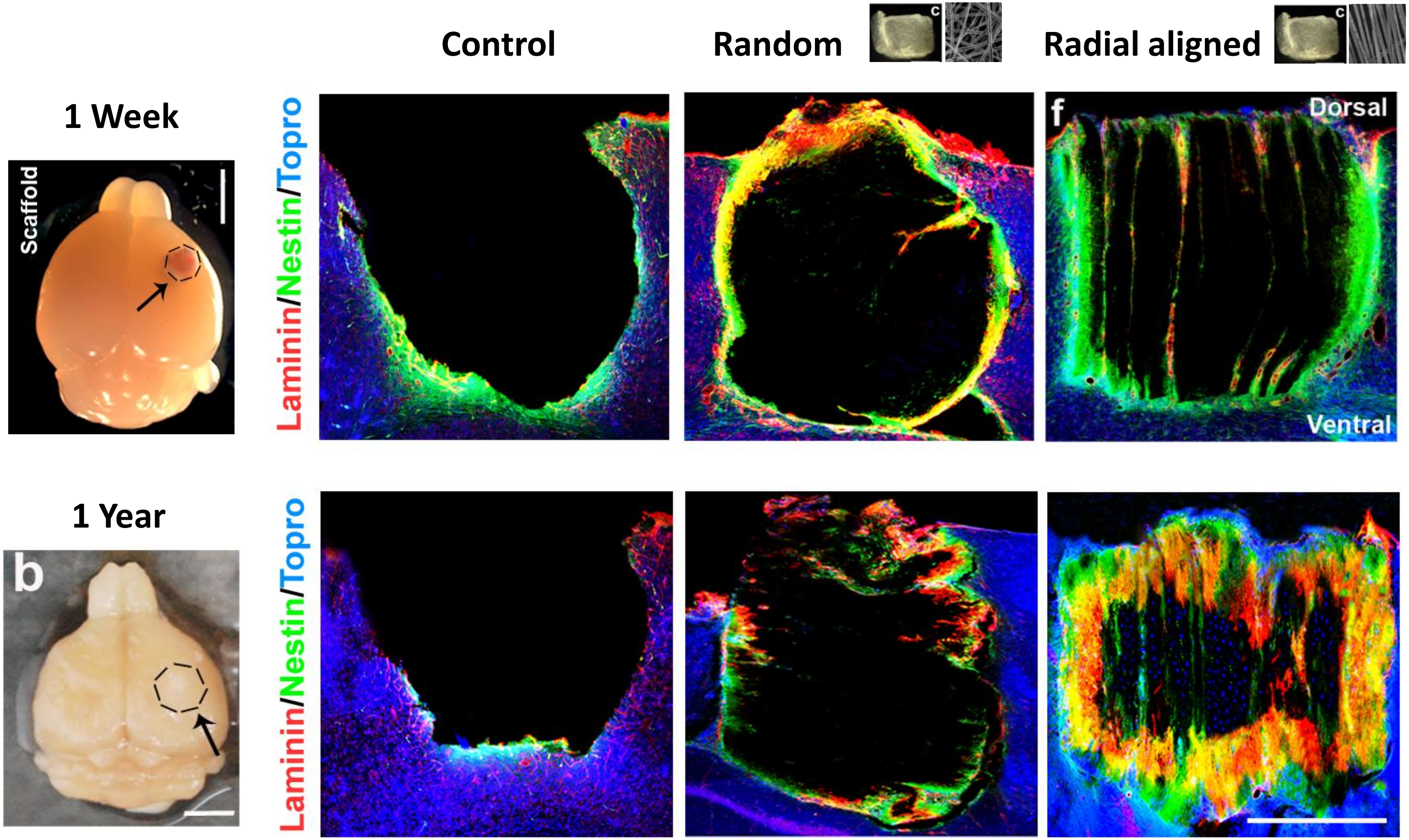
Regeneración ??





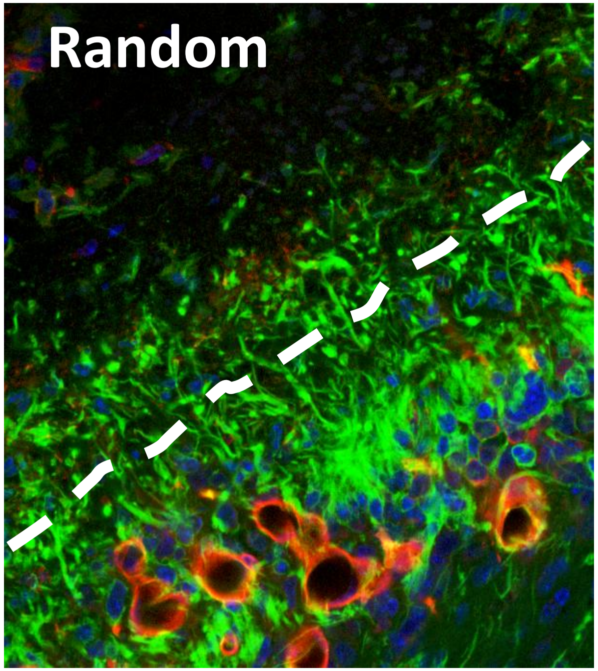
Z. Álvarez et al (2013) submitted

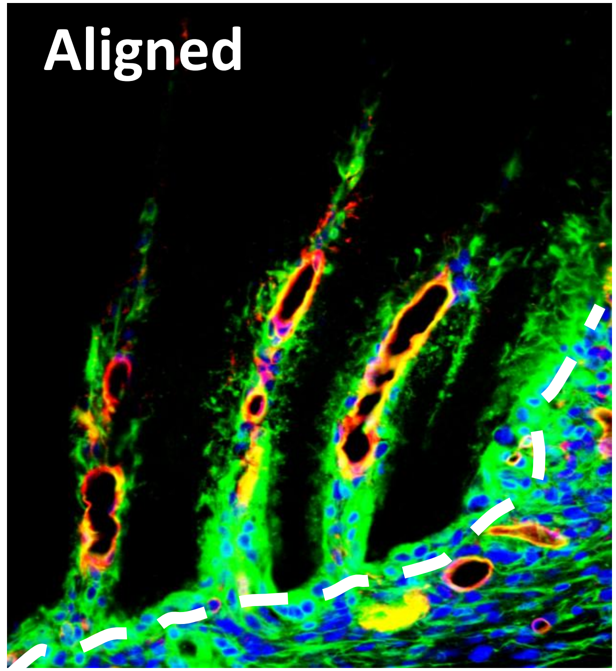
Implantación 1mm^2 fibras

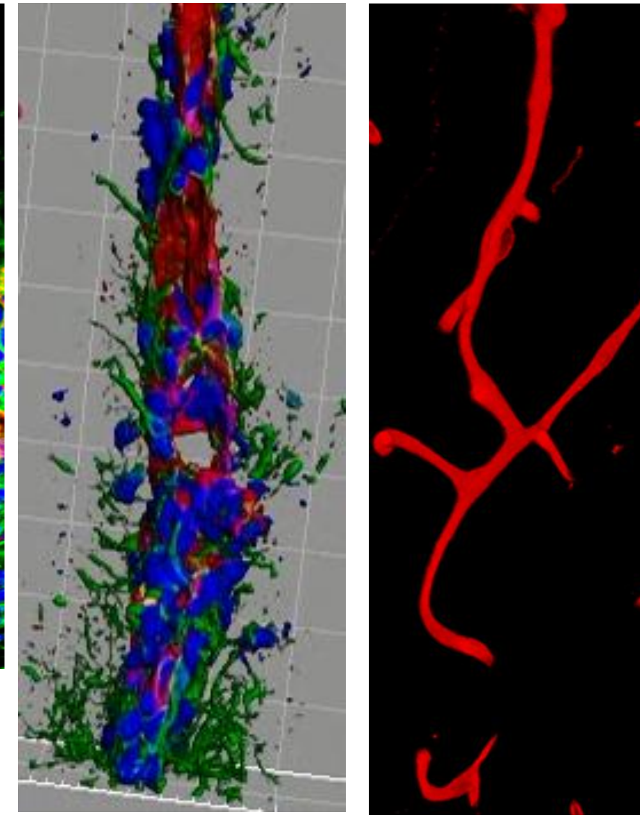


Z. Álvarez et al (2013) submitted

Vasos sanguíneos invades los andamios de fibras alineadas



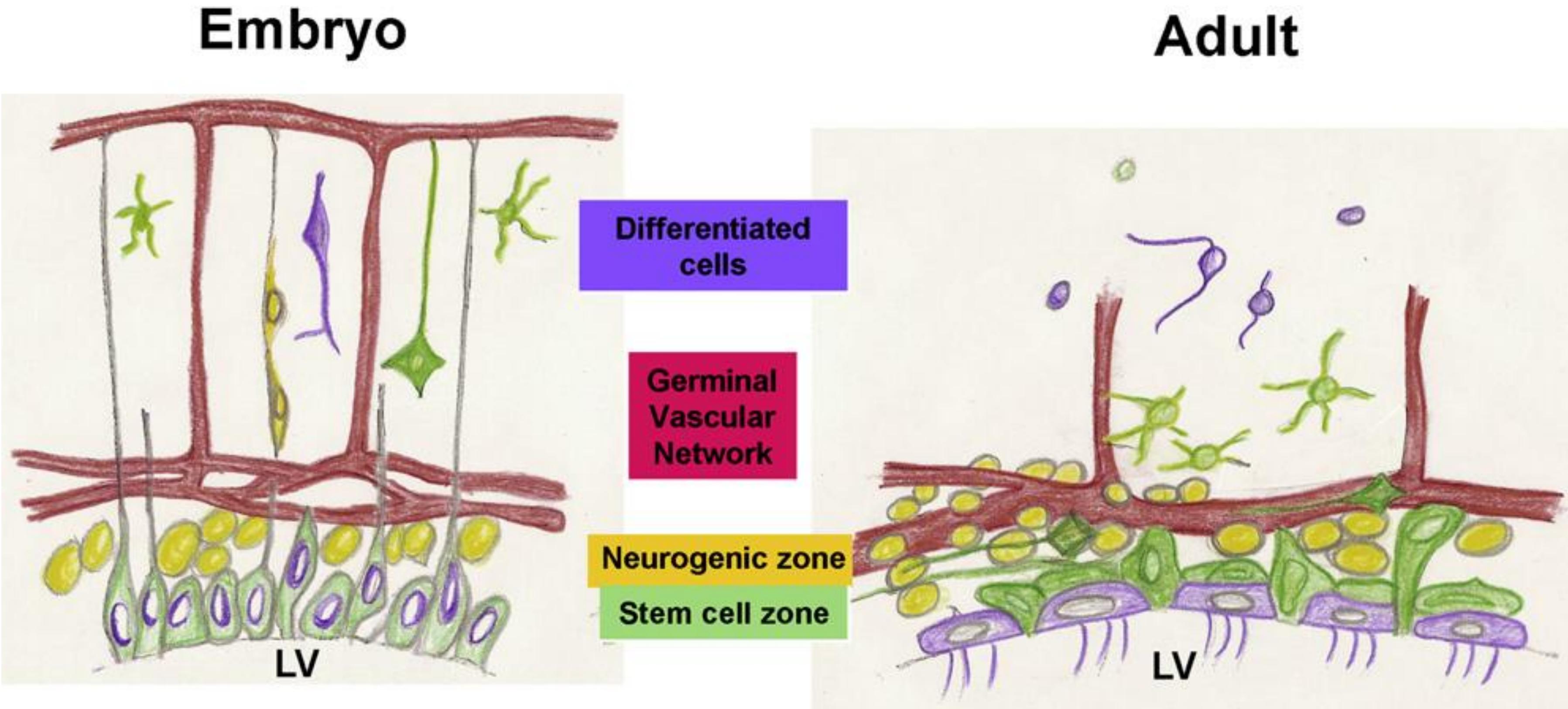




Reconstitución de nichos neurovasculares

Radial glia (Nestin) Blood Vessels (Laminin or DiI perfussion) Nuclei (Topro)

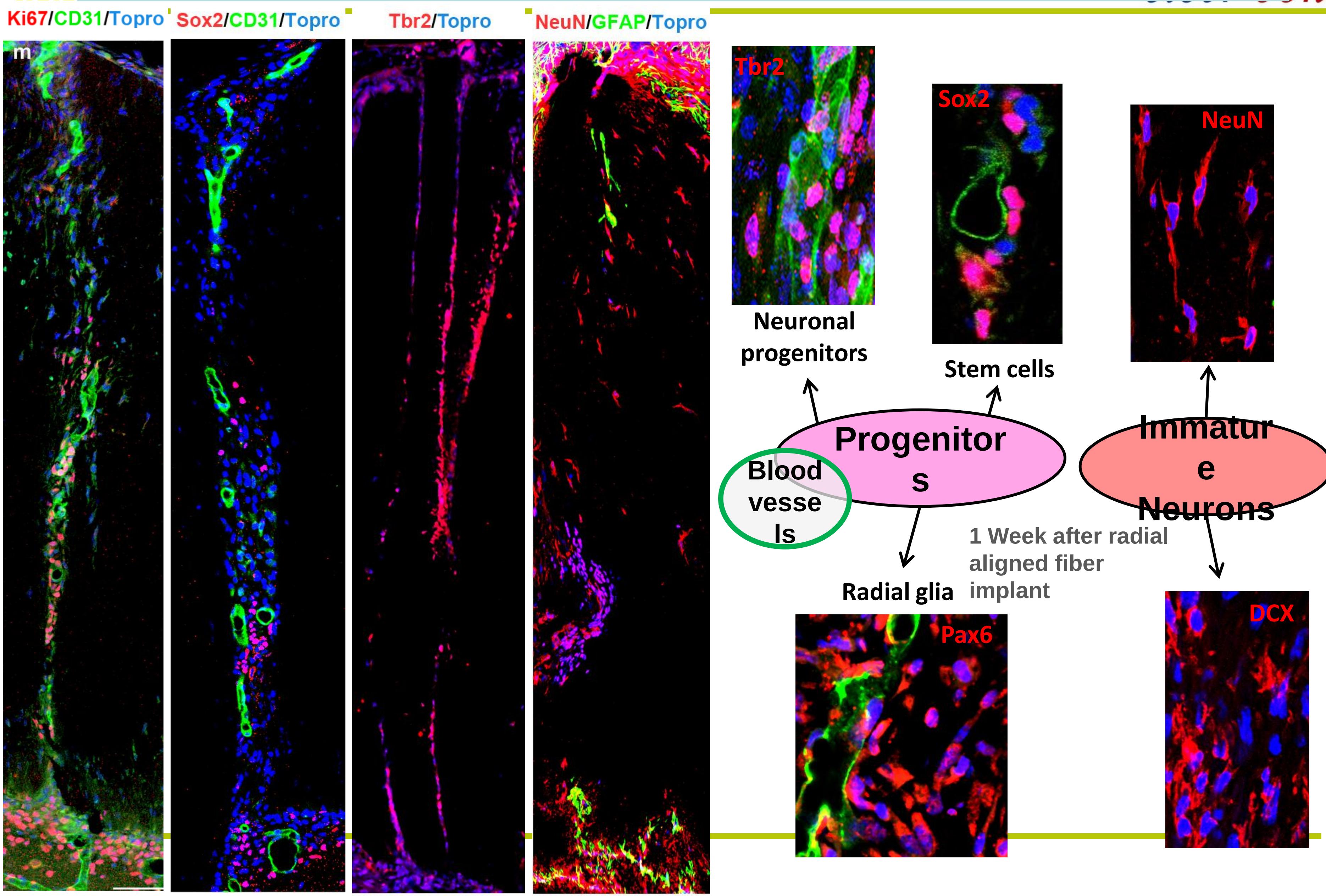
El nicho neurogénico neurovascular



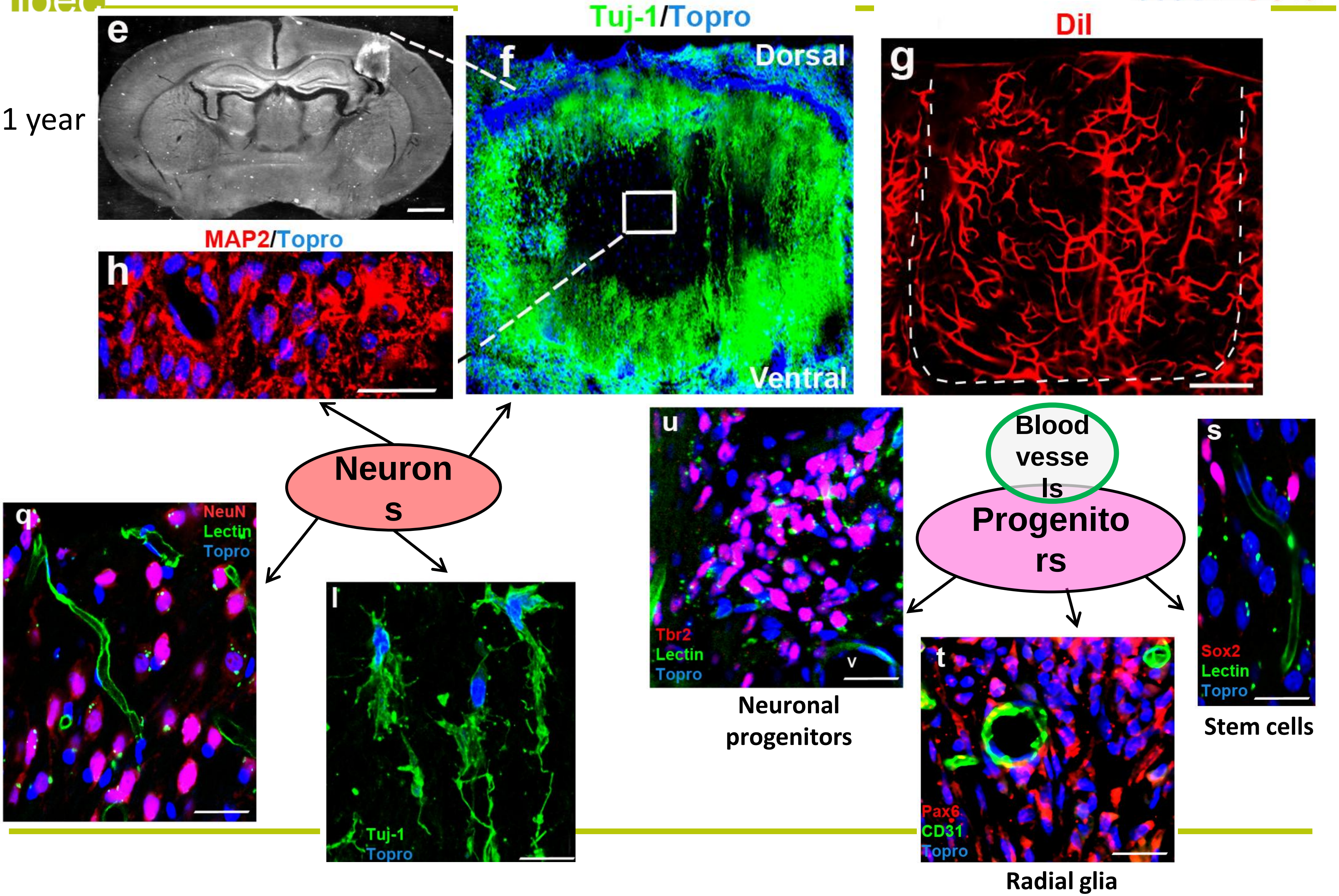
Shen et al., Cell Stem Cell, 2008

Radial aligned PLA fiber scaffolds induce the formation of a regenerative neurogenic neurovascular niches?

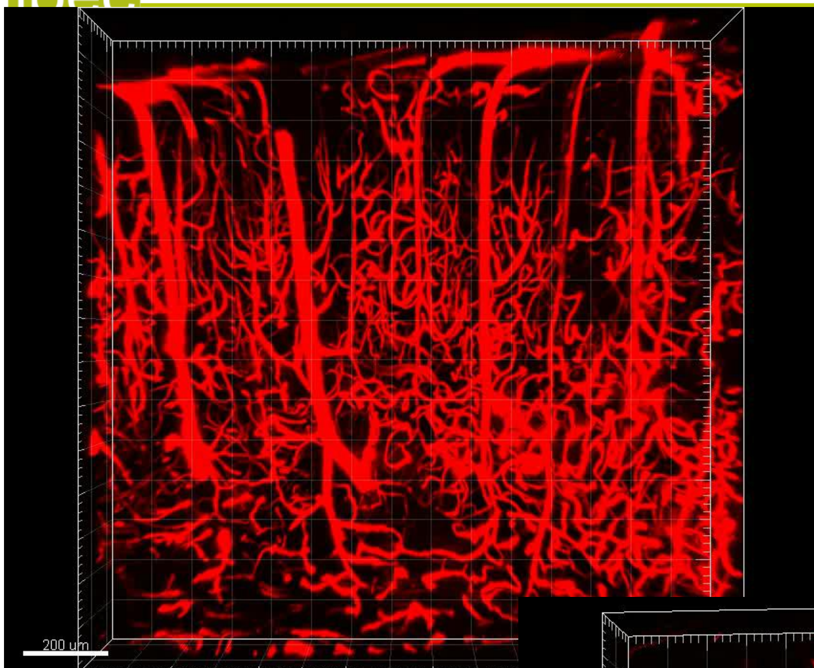
Constitución del nicho neurogénico neurovascular



Regeneración del SNC a 1 año

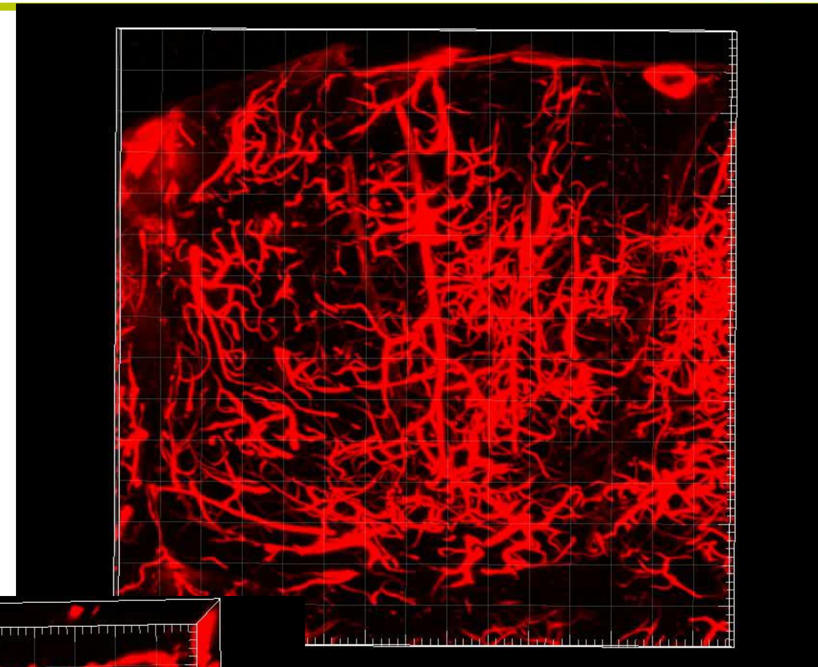


Reconstrución neurovascular después de 1 año

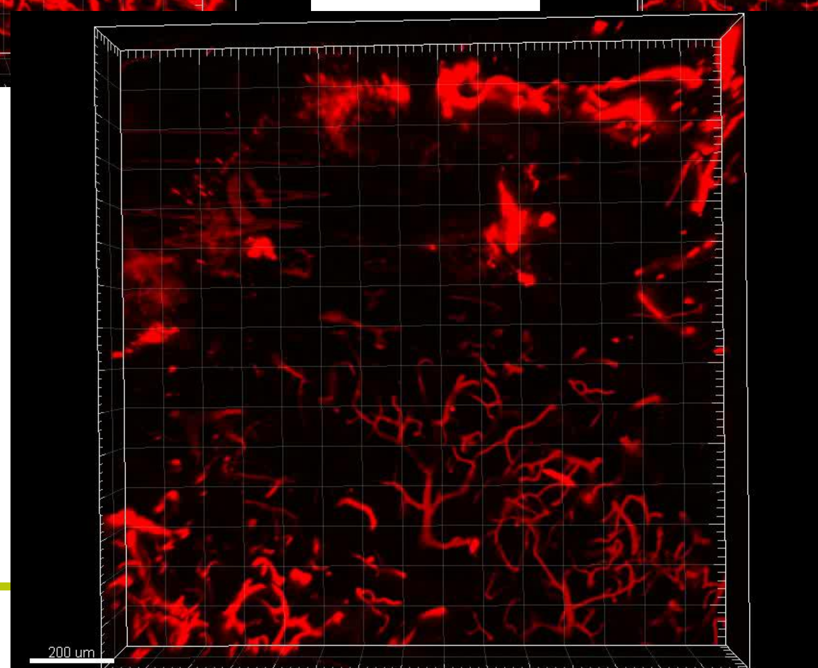


Normal brain

DiI transcardiac prefussion



Radial aligned scaffold



Random scaffold

Biomaterials for Regenerative Therapies

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University of Barcelona
Universtty of Valladolid
University of Liverpool
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Inserm, Bordeaux
Univesity of Wageningen

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Departament d'Innovació, Universitats i Empresa

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