



University  
of Glasgow

# Strategies for CNS repair: focus on in vitro studies

Glial Cell Biology Group:

Sue Barnett

Susan Lindsay

Paul O Neil

Mike McGrath

Mike Whitehead

Sara Hosseinzadeh

George McCanney

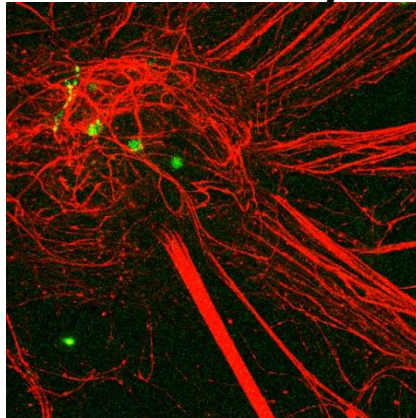
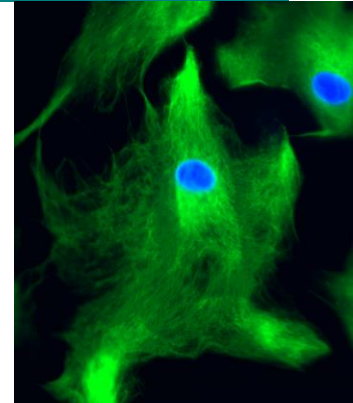


# Methods employed, particularly methods that are unique to the group

- Complex neural cell cultures eg: Myelinating culture and Spinal Cord Injury cultures, proliferation, differentiation, ELISA etc
- Purified PNS, CNS and Olfactory primary neural cell cultures
- Purified Mesenchymal stem cells, and neural progenitor cells
- Immunofluorescence, confocal imaging etc

# Criteria for CNS repair

- Injury cause astrocytes to become reactive;
  - Need to reduce astrogliosis
- Injury cause demyelination and nerve damage;
  - Need to increase myelination and promote axonal regrowth



Will cell transplantation be a useful strategy?  
Identification of novel approaches  
Is the olfactory system a useful supply of cells for transplantation?

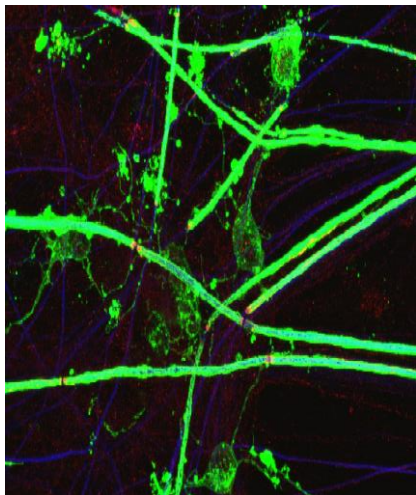


# Strategies to repair the injured / diseased CNS

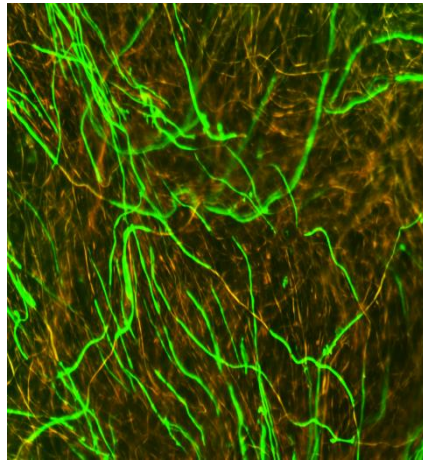
- In vitro models of myelination and SCI, focus on the astrocyte and its reactivity status, chemokines and pro and inhibitory factors, microglia, stem cells, MSCs and cells of the olfactory system.
- Astrocytes affect myelination via chemokines/cytokine secretion
- MSC can promote myelination
- OECs but not Schwann cells promote myelination
- Levels of sulphation around the ECM can influence astrocytosis in vitro

## Myelinating cultures

### CNS myelination

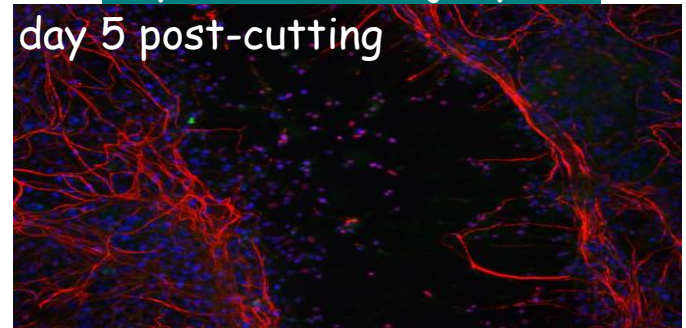


### PNS myelination

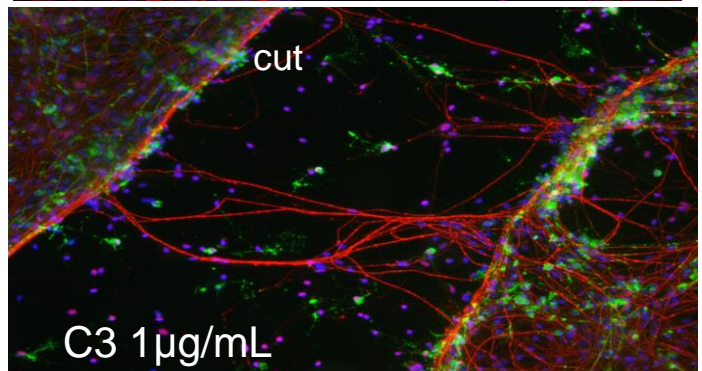


## Spinal cord injury

day 5 post-cutting



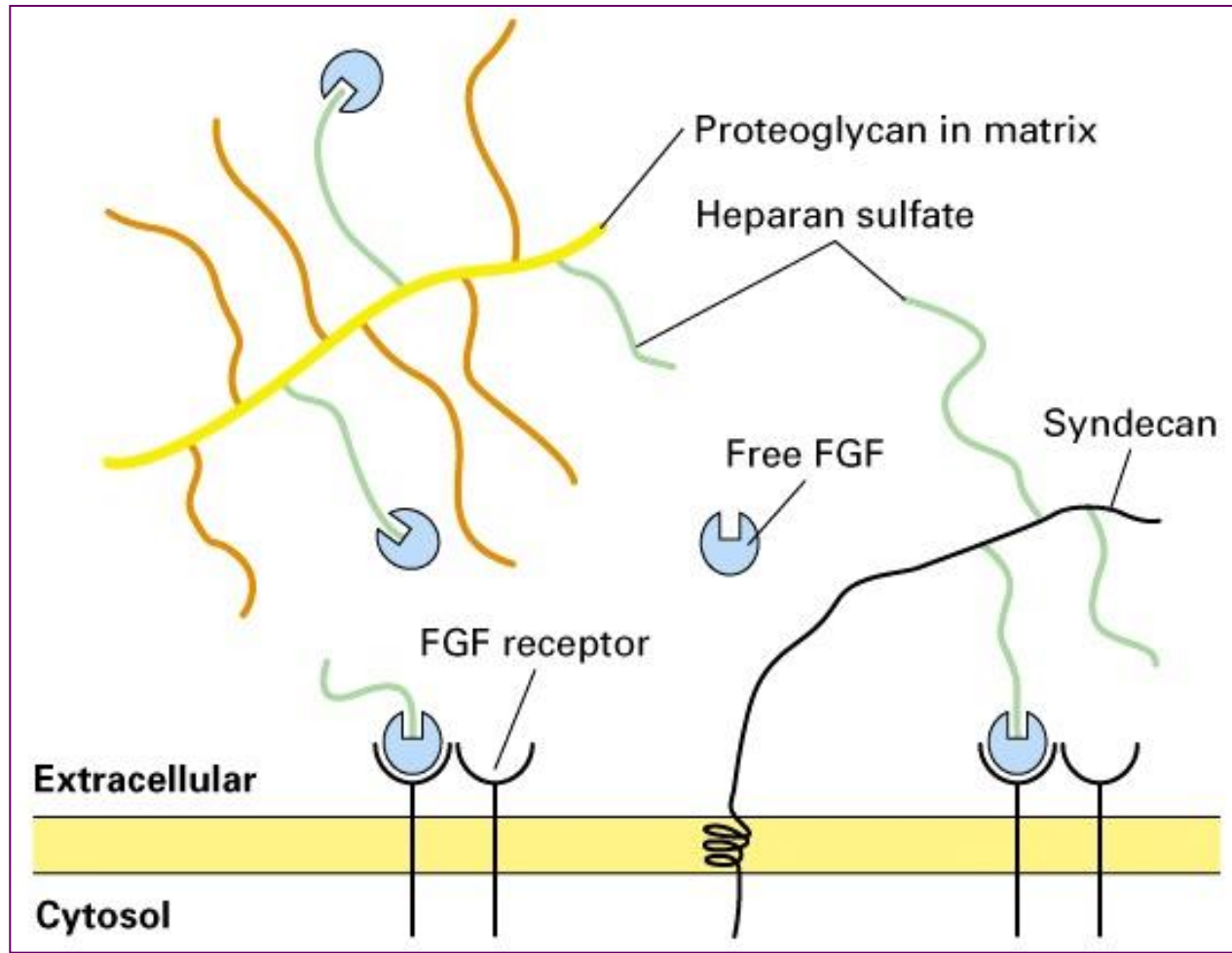
cut



C3 1 $\mu$ g/mL

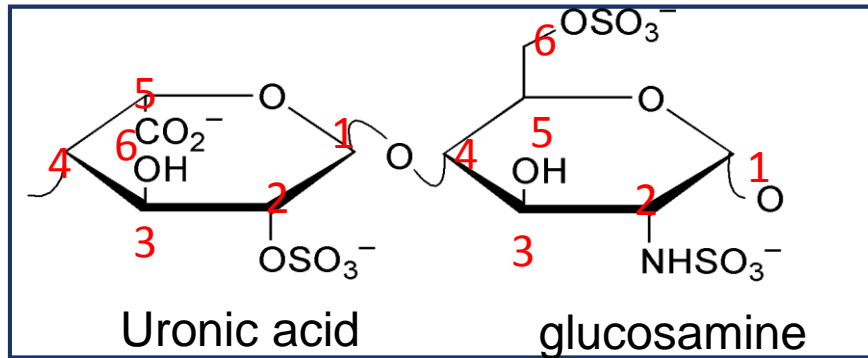
Mike Whitehead, Mike McGrath,

# Modulation of FGF Activity by Heparin Sulfate Proteoglycan (G Schultz)



Free FGF cannot bind stably to FGF-receptors. Binding of FGF or heparan sulfate chains induces a conformational change that enables FGF to bind its receptor

# Level of sulphation affects CNS repair in vitro



Major repeating disaccharide of

- CNS and PNS myelination are regulated differently by levels of sulphation
- Modified Heps maybe a novel strategy to promote CNS and PNS repair

Collaboration: Prof J Turnbull, (University of Liverpool)

Mike Whitehead, Mike McGrath, HSPGs (Glycomar, Charlie Bavington)

# Modification of sulphation around SCI can promote repair

Collaborate (Riddell) on in vivo models on MS and SCI, use levels of sulphation, astrocytes status and stem cells as a therapeutic approach

SC have low sulfatase expression secrete sulphated HS

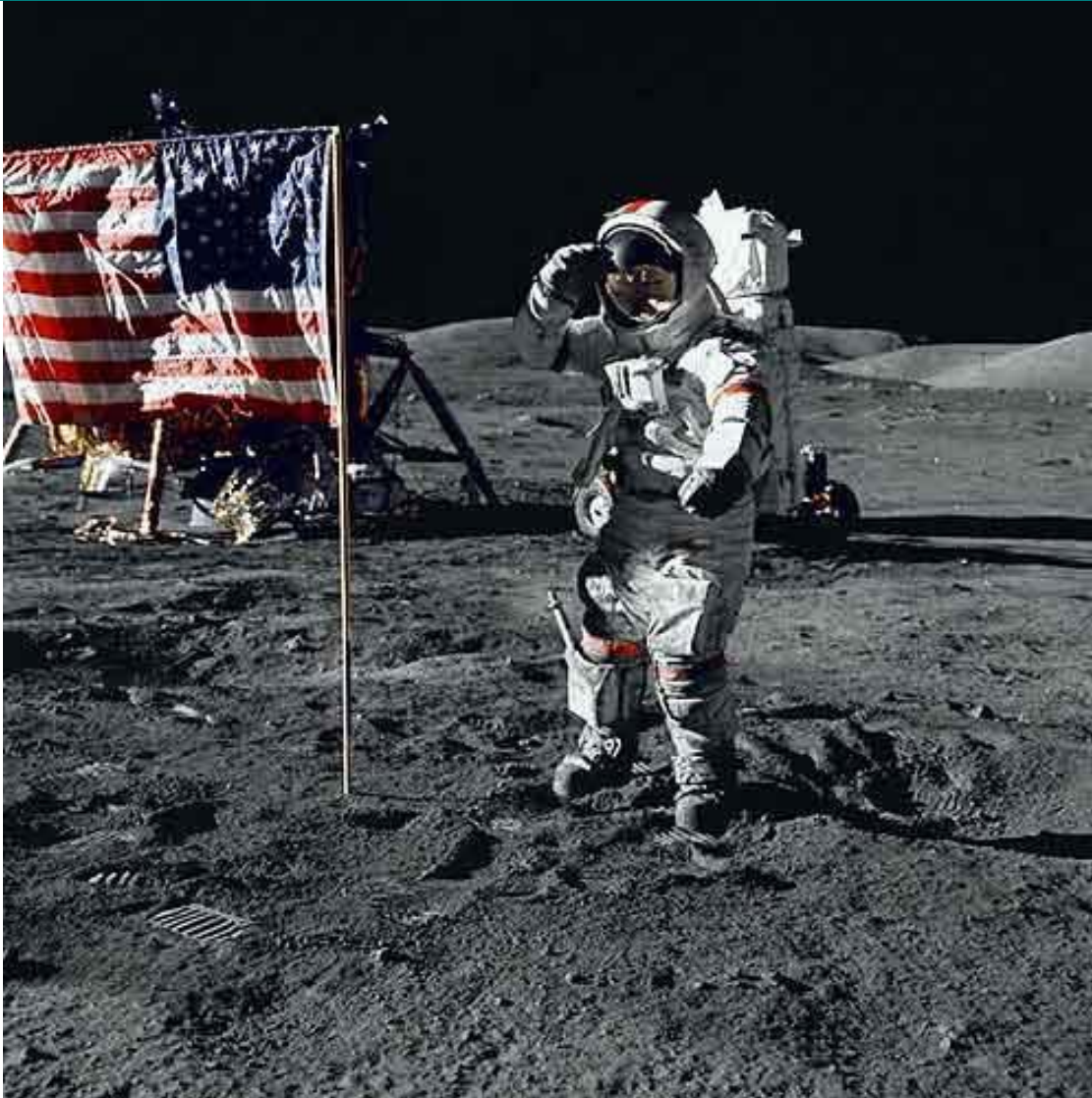
OECs contain high levels of sulphatase so secrete less sulphated moieties

SC-sulf secrete similar levels of OECs.

Modifying sulphation  
around an injury may  
reduce astrocytosis



# Olfactory cells and the repair of SCI



Olfactory glia do not appear to promote SCI repair alone

Olfactory mucosa contains many cell types

MSC from human olfactory mucosa promote CNS myelination in vitro

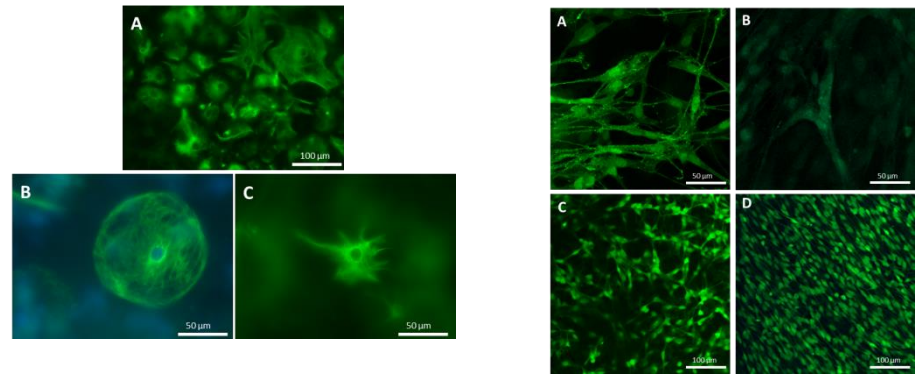
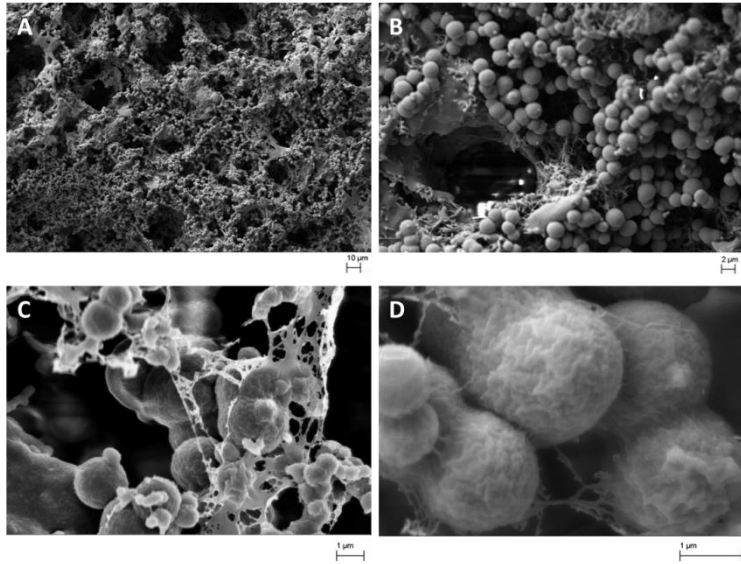


# MSCs transplantation enhances endogenous SC myelination

next studies

How do MSCs effect  
myelination in the EAE model

# Scaffolds/ compounds for CNS repair



Collaborate on biomaterials for CNS repair, macroporous compounds and marine Oligosaccharrides;

Sara Hosseinzadeh, Mathis Reihle, Don Wellings (Spirotech), Charlie Bavington (GlycoMar)

## What I need now -

- in vivo models of myelination, EAE expertise,
- Chemical manipulations of sulphation, generate transgenic mice,
- Sugar chemistry

# Future collaborations

- Charlie Bavington, GlycoMar
- Jerry Turnbull, University of Liverpool
- Ronaldo Ichiyama, University of Leeds
- John Riddell
- Carl Goodyear
- Manuel Salmeron-Sanchez
- Mathis Riehle
- Hugh Willison
- And continue to collaborate with Julia, Chris and 3Is...