Centre for Doctoral Training in Tissue Engineering and Regenerative Medicine – Innovation in Medical and Biological Engineering

Mechanical Properties and *in vivo* Imaging of Perineuronal Nets

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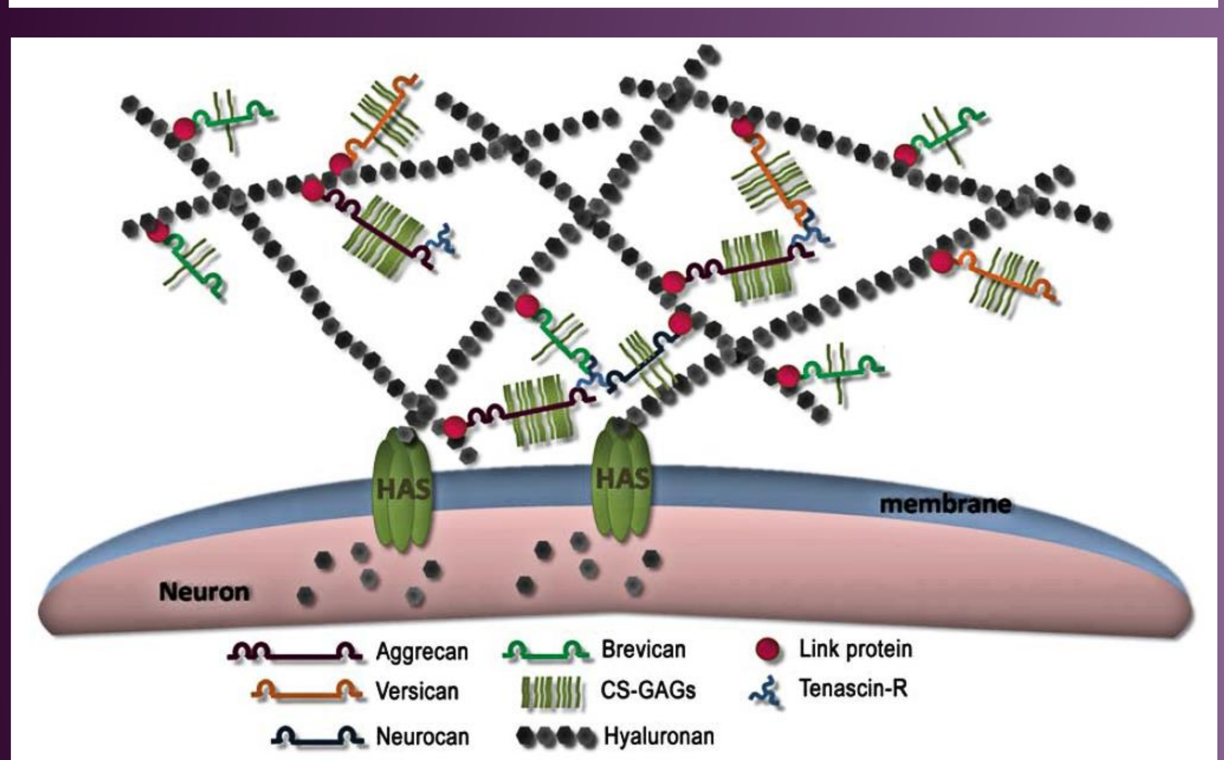
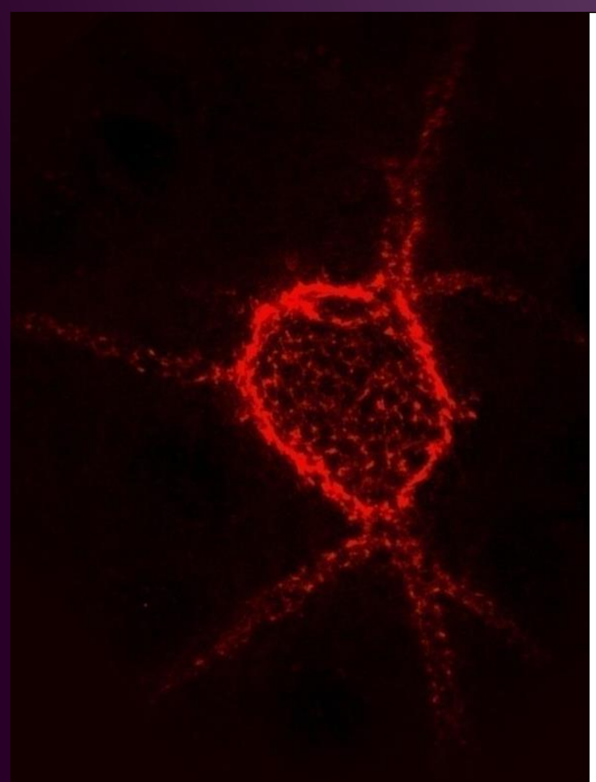
What Are Perineuronal Nets?

Perineuronal nets are structures that primarily surround the cell body of subpopulations of neurons in the central nervous system (CNS). They form a compact, lattice-like matrix layer on the surface of neurons. The composition and structure of perineuronal nets is summarised below[1].



The mechanism that causes extracellular matrix molecules to form perineuronal nets on the surface of neurons is still unknown[2].



An image of perineuronal nets (left): the red structure is a stained perineuronal net surrounding the cell body of a CNS neuron. They have been observed in the brain and spinal cord.

Why are Perineuronal Nets Important?

Recovery from spinal cord injuries, as well as memory retention in mice with Alzheimer's disease has been enhanced when perineuronal nets are removed. This suggests perineuronal nets block new connection from forming, therefore removing them may enhance the formation of new neuronal connections.

Regulating perineuronal net formation could present a promising therapeutic target. The benefit will go beyond spinal cord injury and Alzheimer's disease, as it may also provide potential therapies to overcome addiction.

Currently, studies have removed perineuronal nets by digesting chondroitin sulfate using an enzyme.

Research Challenges & Questions

Perineuronal nets are compact and dense. Similar matrices in the body are soft and thick. We want to understand the factors that contribute to these differences in matrix properties.

Could the formation of perineuronal nets on the neuronal surface influence neuronal behaviour?

Considering the importance of perineuronal nets in plasticity, is it possible to design a probe that can specifically target perineuronal nets *in vivo*?

Methodology 1

Regional differences in biochemistry will be characterised. This will involve glycan isolation and size exclusion chromatography.

Regional differences in biophysical properties will be characterised, involving measuring stiffness, thickness, viscosity and elasticity.

Timeframe: 1.5 years

The results from above will be correlated to understand the relationship between the biochemical composition and biophysical properties of perineuronal nets.

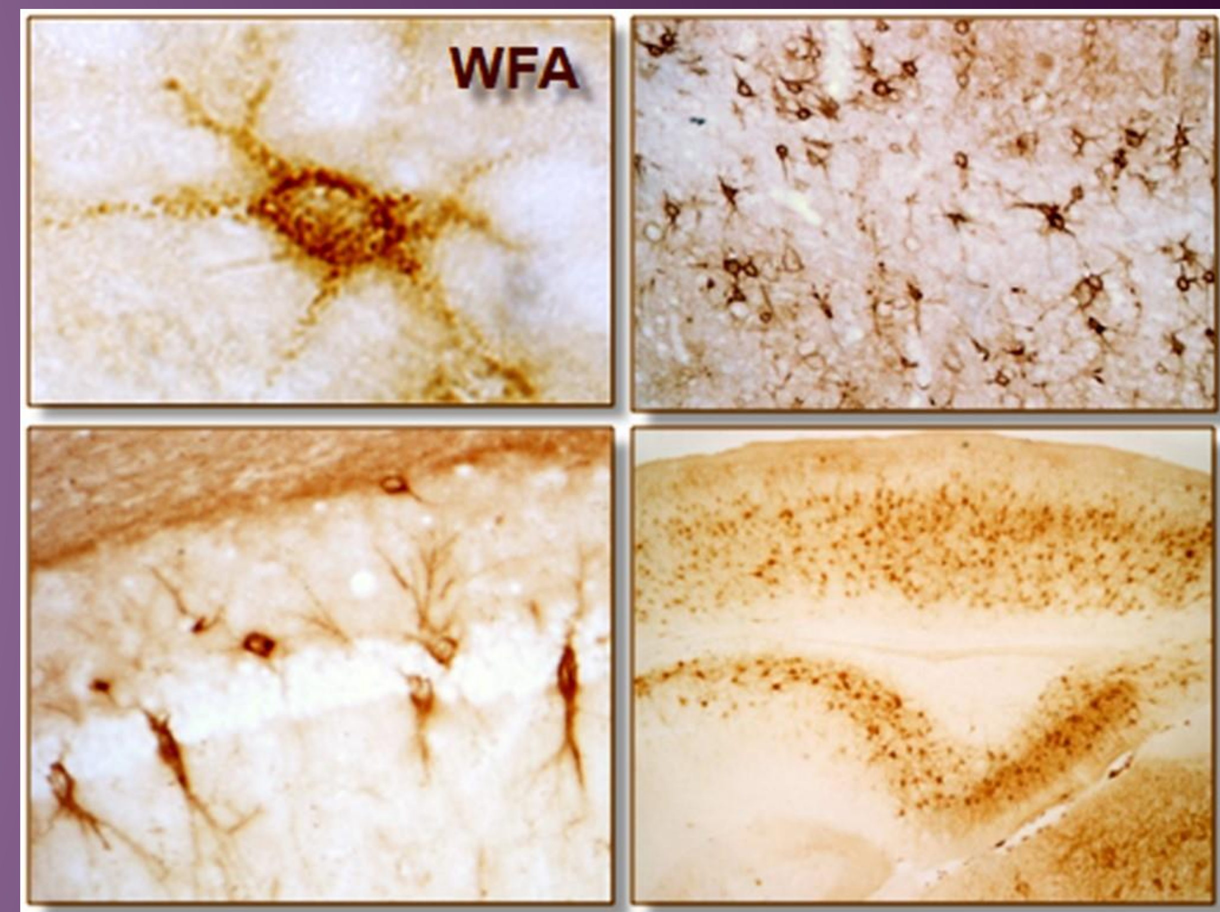
Timeframe: 1 year

The information collected will allow the fabrication of an artificial biomimetic surface that simulates perineuronal nets.

By changing the biophysical properties of the material, we can study the neuronal behaviour in relation to biophysical properties in a highly controlled environment. This will allow us to tease out the important components in controlling synapse formation.

Methodology 2

Running alongside methodology 1 is the aim of designing a probe that would allow for *in vivo* imaging of perineuronal nets. This will involve modifying *Wisteria floribunda* agglutinin (WFA), a protein which attaches to perineuronal nets as demonstrated in the image below. We hope to modify it to allow *in vivo* imaging using MRI.



Expected Outcomes

The results will provide valuable information for the design of new therapeutic targets to monitor changes in perineuronal nets.

Understanding how to manipulate perineuronal nets may allow for therapies to be produced to help recovery following spinal cord injury.

Novel insights into how biophysical properties of a neural matrix can affect neuronal behaviour will be gained.

References

1) Kwok JC, Dick G, Wang D, Fawcett JW. (2011) Extracellular matrix and perineuronal nets in CNS repair. Dev Neurobiol. 71:1073-89.

2) Kwok JC, Carulli D, Fawcett JW. (2010) In vitro modeling of perineuronal nets: hyaluronan synthase and link protein are necessary for their formation and integrity. J Neurochem. 114:1447-59.

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