TITLE: The impact of ageing on regenerative potential of glial and neuronal compartments in peripheral nerve re-myelination

THE RESEARCH TEAM:

Faculty of Biology Medicine and Health – School of Biological Sciences – Division CMBRM

Leading Early Career Researcher: Dr Alessandro Faroni (**AF**), Post Doctoral Research Associate in the Peripheral Nerve Regeneration group, Blond McIndoe Laboratories. **PI:** Dr Adam Reid (**AR**), Senior Clinical Lecturer Plastic and Reconstructive Surgery, University Hospital of South Manchester.

Faculty of Science and Engineering – School of Materials

Leading Early Career Researcher: Dr Victoria Workman (**VW**), Post Doctoral Research Associate in the Polymers & Peptides group. **PI:** Professor Alberto Saiani (**AS**), Professor of Molecular Materials

We are a multidisciplinary team combining the expertise of **nerve cell biologists** (AF/AR) and **material scientists** (AS/VW) alongside focused **clinical expertise** (AR) in the field of peripheral nerve regeneration.

BACKGROUND AND RESEARCH QUESTION:

Peripheral nerves are the "wires" that allow our bodies to communicate and interact with the external world. They carry information in form of electrical and chemical signals between the central nervous system (brain and spinal cord) to the peripheral organs (for example skin, muscles) and back. This allows us to move and to receive sensory information such as heat, pressure or pain. Similar to what happens in electric wires, this information is carried within the peripheral nerves thanks to an insulating layer called myelin. **Myelin is formed by specialized cells called Schwann cells which surround the extension of the nerve cells (neurons) ad allow fast transmission of the signals/information.** When a peripheral nerve is damaged following a traumatic injury (for example a car or a domestic accident), myelin is corrupted and this key function is lost. Although recovery following surgical repair is possible, it is **often unsatisfactory, especially in the older population** [1-3]. This is probably due to a reduction in efficiency or forming new myelin in older people, which likely affects both Schwann cells and neurons compartments. Nevertheless, the specific mechanisms on why and how this happens are not well understood [4]. Indeed, most studies are performed using *in vivo* (**whole animals**) injury models, which inevitably fail to distinguish and isolate the contribution of neurons and Schwann Cells during regeneration/re-myelination.

This project aims to study the **impact of ageing on isolated neuronal/Schwann components** influencing peripheral nerve **regeneration/re-myelination in a novel 3D *in vitro* (isolated cells) system**. Our 3D scaffold is based on self-assembling peptide hydrogels developed in the AS Polymers & Peptides lab, and tailored for application to myelinating co-cultures routinely used in the nerve regeneration lab. By using **neurons and Schwann cells derived from young and old rats on specifically tailored 3D scaffolds** we will reveal the effect of age in the separate components during re-myelination following injury. Indeed, by using peptide hydrogels in a 3D-fashion we will mimic the complexity of the *in vivo* systems and at the same time retain the versatility and simplicity of our *in vitro* cultures, allowing distinction between neuronal and Schwann cell contributions.

This work will pump-prime preliminary work towards external grant funding to study detailed mechanisms and novel interventions to address the reduced regenerative response in ageing.

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2. Pestronk, A., D.B. Drachman, and J.W. Griffin, *Effects of aging on nerve sprouting and regeneration.* Exp Neurol, 1980. **70**(1): p. 65-82.
3. Vaughan, D.W., *Effects of advancing age on peripheral nerve regeneration.* J Comp Neurol, 1992. **323**(2): p. 219-37.
4. Verdu, E., et al., *Influence of aging on peripheral nerve function and regeneration.* J Peripher Nerv Syst, 2000. **5**(4): p. 191-208.