EXTRACELLULAR MATRICES IN PERIPHERAL NERVE INJURY AND REGENERATION

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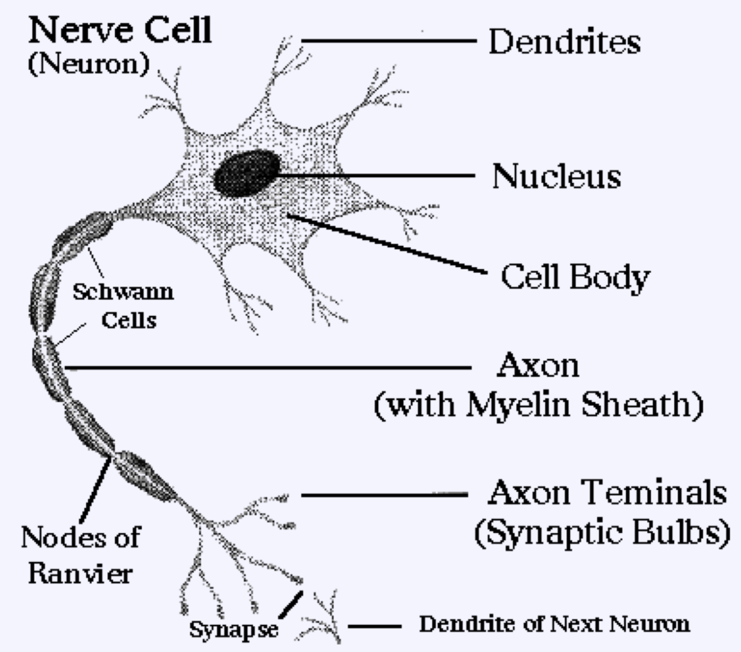
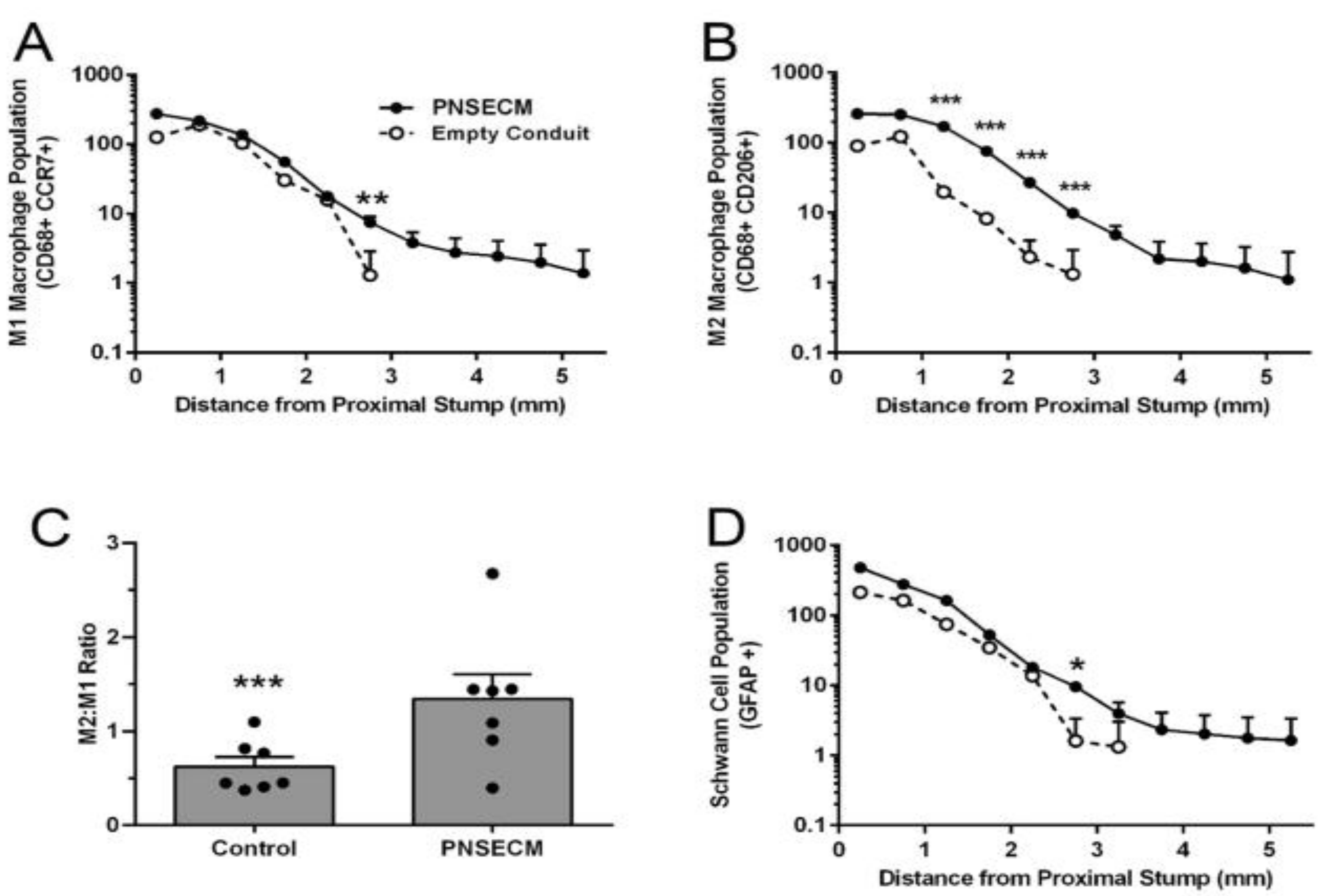
Peripheral Nerve Injury and Regeneration

305,496 surgeries were performed to repair injured nerves in 2009 alone. Peripheral nerves are nerves that are not a part of the central nervous system (brain and spinal cord). Nerve injuries that affect the cell body are permanent and the nerve cannot be regenerated. However, if the axon or terminal end of the nerve is damaged, it will grow back at a rate estimated to be about 1mm a day.



Wallerian degeneration occurs when the terminal end is separated from the rest of the cell and the axon and myelin breaks down. This process is highly dependent on the presence of macrophages and Schwann cells. These cells are the bodies first response to a nerve injury. They begin the signaling processes that are required for the full immune system response. These signaling processes are also dependent on the extracellular matrix.

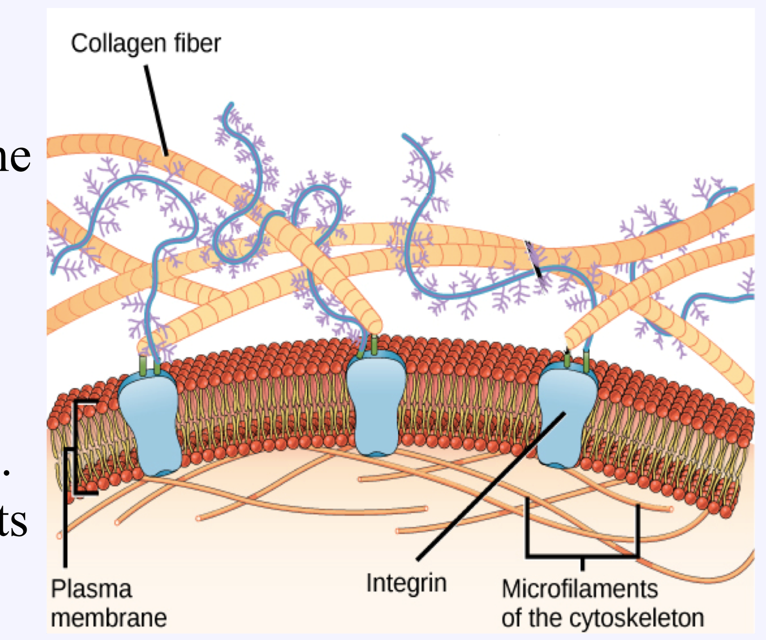
The macrophages (immune system cells), clear the area of damage cells and other debris. Schwann cells aide regeneration of the axon itself and increases the efficiency of the process. If regeneration does not occur fast enough, the muscles can atrophy due to a lack of stimulation. The speed of regeneration is directly related to the concentration of macrophages, Schwann cells and other signaling proteins present in the extracellular matrix (ECM). The ECM technology investigated here increases the rate and efficiency of axon regeneration



The Extra Cellular Matrix

The ECM is a complex network of macromolecules that reside outside of the cell. These macromolecules include proteoglycans and fibrous proteins such as collagens, elastins, fibronectins and laminins. These components interact with cellular components such as transmembrane proteins and cytoskeletons.

The ECM interacts with cells on the biophysical and biochemical level. The ECM preforms mechanical functions for the cell and acts as a scaffold that connects cells together. It is also responsible for much of the signaling and communication between the cells. The ECM is the structure that connects cells and allows them to work as a cohesive unit.



The Hydrogel

The ECM can be extracted from animals and injected into the cite of nerve injury. Inserting a nerve ECM promotes the migration of macrophages and Schwann cells, which are key factors in nerve regrowth and repair.

The ECM is obtained by extracting nerve tissue from an animal (usually pigs) and treating the tissue with multiple chemical washes until there is little to no unique genetic material present and the ECM is isolated. This process is known as decellularization. After decellularization occurs, the ECM can be made into a gel and inserted during surgery.

Decellularization of a rat heart

The Experiment

The graph to the left shows evidence that inserting an ECM increases the concentration of macrophages and Schwann cells, thus promoting nerve regeneration. This experiment involves inserting a peripheral nerve specific extracellular matrix (PNSECM) during a surgery treating a rat sciatic nerve injury. Graph A, B, and C shows that there are more M1 macrophages, M2 macrophages, and Schwann cells present when the PNSECM was used during the surgery versus when there was no ECM used. Graph C depicts that there is a higher M2:M1 macrophage ratio when using the PNECM. This is important because the M2 macrophages are anti-inflammatory which promote regrowth more than the pro-inflammatory M2 macrophages.

Sustainability

Quality of Life	• The ECM technology allows peripheral nerve injuries to heal faster and more fully than a nerve grafting procedure would. • Grafting is currently the most prominent treatment for certain types of peripheral nerve injuries.
Accessibility	• ECM technologies are derived from animal nerve tissue, which is more abundant than the human nerve tissue that is required for grafting. • Grafting also has extra restrictions involving nerve length, shape, and cross sectional area.
Equity	• The ECM technology simplifies the surgery required to treat peripheral nerve injuries. • The surgery is less invasive because it does not require the harvesting of a healthy nerve from the patient, like some grafting procedures call for.
Environmental	• Because the ECM technology is derived from natural materials, it is more environmentally friendly than a synthetic biomaterial. • The ECM does not need to be disposed of because it is incorporated to the biology of the host itself and is decomposed by the bodies natural methods. • The chemicals used in the decellularization of the nerve tissue can be harmful to the environment. Thus, it is imperative that the chemical waste is disposed of correctly.
Economic	• Many ECM technologies are still in the human trial phase, thus there is no evidence to determine weather or not the ECM technology will be more cost effective than other peripheral nerve injury treatments.