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WRAPPING UP

Weizmann Institute Scientists reveal a mechanism for healthy nerve development, which may lead to new treatments for neurodegenerative diseases

In a host of neurological diseases, including multiple sclerosis (MS) and several neuropathies, the protective covering surrounding the nerves – an insulating material called myelin – is damaged. Scientists at the Weizmann Institute of Science have now discovered an important new line of communication between nervous system cells that is crucial to the development of myelinated nerves – a discovery that may aid in restoring the normal function of the affected nerve fibers.

Nerve cells (neurons) have long, thin extensions called axons that can reach up to a meter and or more in length. Often, these extensions are covered by myelin, which is formed by a group of specialized cells called glia. Glial cells revolve around the axon, laying down the myelin sheath in segments, leaving small nodes of exposed nerve in between. More than just protection for the delicate axons, the myelin covering allows nerve signals to jump instantaneously between nodes, making the transfer of these signals quick and efficient. When myelin is missing or damaged, the nerve signals can't skip properly down the axons, leading to abnormal function of the affected nerve and often to its degeneration.

In research published recently in *Nature Neuroscience*, Weizmann Institute scientists Prof. Elinor Peles, graduate student Ivo Spiegel and their colleagues in the Molecular Cell Biology Department and in the United States, have now provided a vital insight into the mechanism by which glial cells recognize and myelinate axons.

How do the glial cells and the axon coordinate this process? The Weizmann Institute team found a pair of proteins that pass messages from axons to glial cells. These proteins, called Necl1 and Necl4, belong to a larger family of cell adhesion molecules, so called because they sit on the outer membranes of cells and help them to stick together. Peles and his team discovered that even when removed from their cells, Necl1, normally found on the axon surface, and Necl4, which is found on the glial cell membrane, adhere tightly together. When these molecules are in their natural places, they not only create physical contact between axon and glial cell, but also serve to transfer signals to the cell interior, initiating changes needed to undertake myelination.

The scientists found that production of Necl4 in the glial cells rises when they come into close contact with an unmyelinated axon, and as the process of myelination begins. They observed that if Necl4 is absent in the glial cells, or if they blocked the attachment of Necl4 to Necl1, the axons that were contacted by glial cells did not myelinate. In the same time period, myelin wrapping was already well under way

around most of the axons in the control group.

“What we’ve discovered is a completely new means of communication between these nervous system cells,” says Peles. “The drugs now used to treat MS and other degenerative diseases in which myelin is affected, can only slow the disease, but not stop or cure it. Today, we can’t reverse the nerve damage caused by these disorders. But if we can understand the mechanisms that control the process of wrapping the axons by their protective sheath, we might be able to recreate that process in patients.”

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The Weizmann Institute of Science in Rehovot, Israel, is one of the world's top-ranking multidisciplinary research institutions. Noted for its wide-ranging exploration of the natural and exact sciences, the Institute is home to 2,600 scientists, students, technicians and supporting staff. Institute research efforts include the search for new ways of fighting disease and hunger, examining leading questions in mathematics and computer science, probing the physics of matter and the universe, creating novel materials and developing new strategies for protecting the environment.

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