Finding clues for nerve cell repair

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A new study at the Montreal Neurological Institute at McGill University identifies a key mechanism for the normal development of motor nerve cells (motor neurons) - cells that control muscles. This finding is crucial to understanding and treating a range of conditions involving nerve cell loss or damage, from spinal cord injury to neurodegenerative diseases such as ALS, also known as Lou Gehrig's disease.

Nerve cell regeneration is a complex process. Not only do nerve cells have to regenerate, but just as importantly, their specific and individual connections need to be regenerated also. The study, published recently in the *Proceedings of the National Academy of Sciences*, provides invaluable insight into these vital processes by understanding the mechanisms involved in normal development of selected types of spinal cord motor nerve cells.

Motor neurons are highly specialized. They have distinct characteristics and connect to specific muscle types in specific regions of the body. "These highly targeted nerve cell-to-muscle connections are determined in part by specific patterns of gene expression during embryonic development. More specifically, certain genes are expressed which tell the neuron what its properties will be, where to settle and which particular muscle to connect with," says Dr. Stefano Stifani, neuroscientist at the Montreal Neurological Institute and lead investigator in the study.

When nerve cells develop they require characteristic patterns of gene expression in order to become motor neurons or another type of nerve

cell called interneurons. Dr. Stifani and colleagues show that during development, motor nerve cells have to express certain genes that continually suppress interneuron developmental characteristics.

"We have identified a key factor, called Runx1, which controls the correct development of motor neurons in the upper part of the spinal cord. Runx1, a factor that controls gene expression, helps motor neurons to maintain their status by regulating the expression of specific genes. In doing so, it might also help motor neurons find their target muscles."

Understanding the normal development and the highly specialized nature of nerve cells has important implications for understanding diseased or damaged nerve cells. For example, in ALS, the motor nerve cells that are involved in swallowing and controlling the tongue are often the first to degenerate. Knowing the specific patterns of gene expression of different motor nerve cells may help to explain why certain motor neurons are more susceptible to degeneration and help identify new targets for treatments.

Source: Montreal Neurological Institute and Hospital