# Enabling nerve regeneration means evicting the cleanup crew

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Macrophages are the immune cells that engulf and destroy the debris of damaged tissue to enable the healing process to begin. Their presence at the scene of damage is critical, but once their task is complete, it is just as critical that macrophages exit rapidly, ending the inflammatory process and making way for regrowth. In fact, the continued presence of macrophages could damage tissue, compromising repair.

While researchers know a great deal about the molecular machinery that launches this cellular cleanup crew into action, little has been known about the just-as-critical exit process.

Now, researchers have identified a key process by which macrophages are cleared from sites of peripheral nerve injury. The scientists say their findings could also have implications for understanding the same fundamental mechanism in spinal cord injury, stroke and multiple sclerosis.

Samuel David and colleagues published their findings in the March 1, 2007 issue of the journal *Neuron*, published by Cell Press.

The researchers concentrated on a family of cell receptors known as Nogo receptors, already known to be present on nerve cells and to play a role in nerve growth. Specifically, David and colleagues explored the role of one such Nogo receptor, NgR1. Receptors such as NgR1 are protein switches that nestle in the membranes of cells, and which induce a cellular response when triggered by a specific chemical signal, or

ligand.

In the researchers' experiments, they induced damage in the sciatic nerve in the thigh of rats and mice and analyzed the role of NgR1 in the repair process.

They found that macrophages showed the presence of NgR1 on their surface once they arrive at the injury site and began their cleanup. Further experiments revealed that as the healing nerve began to form the protein myelin—the insulating sheath around nerves—this receptor not only caused a reduction in the macrophages' binding to myelin, but also an outright repulsion from the forming myelin. In fact, when the researchers created nerve injury such that new myelin would not be formed, the macrophages continued to lurk around the injury site. The researchers' experiments also identified specific molecules on myelin that triggered such repulsion.

The findings could also apply to nerves other than peripheral nerves, because macrophages activated during stroke, multiple sclerosis injury, and spinal cord injury also express NgR1 on their surface, pointed out the researchers.

"Our discovery of this novel (to our knowledge) role for NgRs in mediating the efflux of macrophages from inflamed neural tissue via interactions with myelin could therefore have broader implications for the regulation of inflammatory responses not only in other peripheral nerve pathologies, but also in [central nervous system] inflammation such as in spinal cord injuries, stroke, and multiple sclerosis," they concluded.

Source: Cell Press