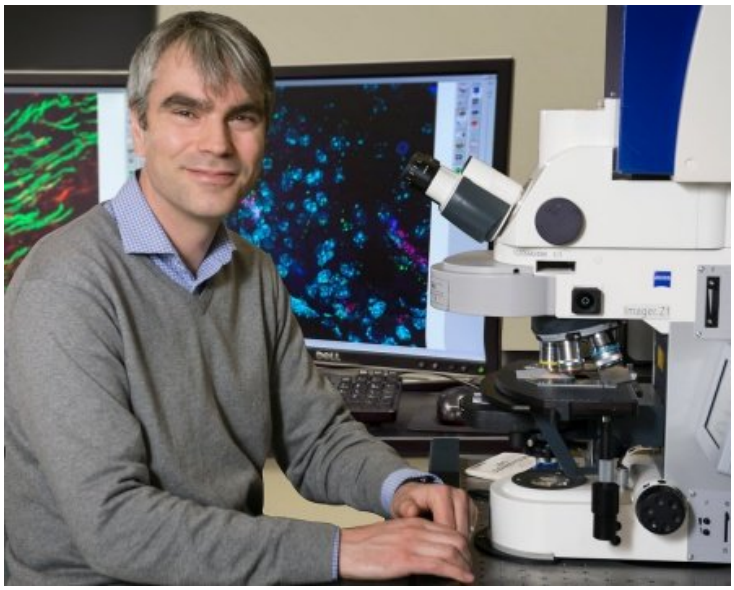
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New stem cell research has identified novel therapeutic targets for MS treatment

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The study defines the role of the previously undescribed transcription factor known as PRRX1 in human oligodendrocyte progenitor cells, the cells that generate myelin-forming oligodendrocytes.



The preclinical findings published in Cell Reports reveal that activation of a specific transcription factor induces a phenomenon called pathological quiescence — when adult stem cells are rendered incapable of responding to injury by producing myelin-forming oligodendrocytes. The failure to remyelinate is the key feature of MS.

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Providing a New Direction in MS Research

Current MS research focuses largely on drugs that induce the differentiation of human oligodendrocyte progenitors. In contrast, the Jacobs School of Medicine and Biomedical Sciences research presents a novel concept for the development of new drugs based on blocking the pathological quiescence of progenitors.

“The idea that pathological quiescence of progenitors could prevent regeneration in MS is distinct from the current preclinical strategies making their way into trial,” explains Sim, senior author on the paper.

“We found that switching this gene on could cause problems in myelin repair by blocking the proliferation of the oligodendrocyte progenitor cell, the stem cell-like precursor that is responsible for all myelin regeneration in the adult brain,” says Sim, who is a faculty member in the neuroscience program.

The research demonstrated that PRRX1 expression results in the cell cycle arrest and quiescence of oligodendrocyte progenitors, which disabled the production of myelin.

In an animal model of leukodystrophy — the group of genetic disorders in which myelin fails to form or is destroyed in children — Sim says that pathological quiescence induced by PRRX1 prevented cell colonization of white matter and effective myelin regeneration by transplanted human oligodendrocyte progenitors.

Findings Identify Novel Therapeutic Targets

The researchers also found that blocking expression of this transcription factor prevented the negative effects of proinflammatory cytokines, such as interferon-?, which regulates its expression.

“We found that blockade of PRRX1 expression prevents the negative effects of interferon-?, suggesting that PRRX1 expression might be a viable target in inflammatory diseases, such as multiple sclerosis, where interferon-? may prevent successful myelin regeneration,” Sim notes.

This suggests new targets for therapeutic intervention and how the disease environment in MS may prevent effective myelin repair and regeneration.

The finding that pathological quiescence is key to the inability to repair and regenerate myelin in MS and similar diseases provides a novel direction for the team’s research.

“We plan to pursue the idea that perhaps we could identify treatments for MS that work by overcoming pathological quiescence of oligodendrocyte precursors in demyelinating lesions that characterize this disease,” Sim says.