



# Antagonism of muscarinic receptors drives peripheral nerve repair to reverse neuropathic disease in rodents and humans

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## NEUROSCIENCE GRAND ROUNDS

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### DATE

Friday, March 14th, 2025

9:00 AM - 10:00 AM

### LOCATION

Psychiatry Bldg. 2nd Floor Rm PX236/238

### SPEAKER

Paul Fernyhough , PhD

Professor, Dept of Pharmacology & Therapeutics and Director, Division of Neurodegenerative and Neurodevelopmental Disorders, University of Manitoba.

### BIO

Professor in Pharmacology & Therapeutics at University of Manitoba and Director of DNND at St Boniface

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### ABSTRACT

Distal dying-back of nerve fibers is observed in many diseases including diabetic neuropathy, chemotherapy-induced peripheral neuropathy (CIPN) and human immunodeficiency virus (HIV)-associated neuropathy. The impact on human health is significant and rising. There are no therapies for any of these neuropathies. Our recent studies have revealed a novel therapeutic target for preventing and even reversing neuropathy-induced nerve loss. We have found that muscarinic acetylcholine type 1 receptors (M1Rs) regulate sensory axonal plasticity. We have discovered that antimuscarinic drugs selective or specific for the M1R can drive axonal outgrowth and prevent/reverse neurodegeneration in rodent models of peripheral nerve disease. I will present recent phase 2 clinical trial data in persons with diabetic neuropathy revealing improved nerve fiber levels in skin in response to such drugs. I will also discuss the multiple mechanisms triggered by antimuscarinic drug action at the M1R to modulate ion channel function and enhance neuronal metabolism and axonal outgrowth.

### OBJECTIVES

1. Inform about muscarinic receptor signaling in sensory neurons.
2. Provide update on mechanisms of nerve repair in peripheral neuropathy.
3. Describe latest findings in phase 2 clinical trials in humans with diabetic neuropathy.