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Alpha-1 Antitrypsin demonstrates therapeutic efficacy in a mouse model of Charcot-Marie-Tooth Disease Type 1A

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Peripheral neuropathies that are characterized by compromised myelin sheath integrity and innate Schwann cell dysfunction, such as Charcot-Marie-Tooth disease type 1A (CMT1A), lead to progressive motor and sensory deficits with debilitating consequences. Myelin sheath defects are often associated with chronic immune activation, suggesting a potential therapeutic role for anti-inflammatory and immunomodulatory agents like Alpha-1 Antitrypsin (AAT).

In this study, we conducted a detailed comparative analysis of AAT's therapeutic potential in a C3-PMP22 CMT1A mouse model. Mice (n=8) received bi-daily dose of 90mg/kg subcutaneous AAT (human plasma-derived), and outcomes were evaluated through behavioral and electrophysiological testing, nerve histology, and plasma cytokine profiling at defined time points.

AAT administration over a two week period significantly improved the nerve conduction velocity (NCV) and compound muscle action potential (CMAP) and enhanced both the axonal diameter and myelin sheath thickness (g-ratio) in CMT1A mice. Functionally, AAT-treated mice exhibited marked improvements in neuromuscular strength and coordination compared to untreated controls.

These findings reveal previously unrecognized neuroprotective and restorative effects of AAT in an animal model of an inherited demyelinating neuropathy. Our results support further investigation of AAT as a promising therapeutic strategy for CMT1A and potentially other inherited and acquired neuropathies.