

NEURODEGENERATION IN TTR AMYLOID NEUROPATHY: SCHWANN CELL HYPOTHESIS

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TTR amyloid neuropathy is characterized by extracellular amyloid deposits and peripheral nerve involvement. Sensory dominant polyneuropathy and autonomic neuropathy are usually observed as early features in the patients. Though axonal degeneration is the primary change in TTR amyloid neuropathy, segmental demyelination and Schwann cell abnormalities have also been described. We previously demonstrated that the TTR gene is significantly expressed in Schwann cells of the dorsal root ganglia (DRG) and peripheral nerves. Then, we established a spontaneously immortalized Schwann cell line, TgS1, derived from the transgenic mice expressing human TTR Met30 gene in a mouse null background (J Neurochem 2015; 134: 66-74). TgS1 cells synthesized variant TTR and secreted it into the medium. The conditioned medium (CM) derived from TgS1 cells and recombinant variant TTR inhibited neurite outgrowth from DRG sensory neurons. Immunohistochemistry revealed TTR aggregates in the cytoplasm of Schwann cells and satellite cells of the DRG of aged transgenic mice. In a few satellite cells, TTR positive inclusions were observed in the cytoplasm. TTR immunoreactivity was also detected in the cytoplasm of myelinating Schwann cells. Proteasome inhibition induced TTR aggregates as aggresomes in the TgS1 cells. Electron micrographs of the cells showed autolysosomes. These findings support the hypothesis that Schwann cells might trigger neuropathy in TTR amyloidosis.