The Relationship between Tumor Suppressor Genes LZTR1 and SMARCB1 in Schwannomatosis Pain

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Schwannomatosis is a rare genetic disease characterized by pain and the development of peripheral nerve sheath tumors called schwannomas. Schwannoma in patients have mutations in the NF2 gene. In addition, these tumors have mutations in either the SMARCB1 gene or the LZTR1 gene. Patients with SMARCB1 and LZTR1 mutations both experience pain but may have different degrees or types of pain. Recent findings indicate that Schwann cells with SMARCB1 mutations secrete proteins that induce increased pain sensitivity in sensory neurons. However, the role of LZTR1 in the development of chronic pain in schwannomatosis remains unclear. The goal of this study was to test the hypothesis that mutations in SMARCB1, a transcriptional regulator, might influence LZTR1 expression. Wild type and SMARCB1-null mouse Schwann cells as well as a SMARCB1-null cell line (RTM) with and without SMARCB1 were grown in vitro then analyzed for changes in LZTR1 transcription and protein expression. No direct change in LZTR1 gene expression was observed, indicating that SMARCB1 does not directly regulate LZTR1 transcription. Yet, LZTR1 protein levels increased in the absence of SMARCB1. These findings suggest that SMARCB1 may indirectly affect LZTR1 translation, possibly linking changes in SMARCB1 and LZTR1 to the pain experienced by schwannomatosis patients.