

Intramuscular Adipose Tissue: A Therapeutic Target to Preserve Muscle Mass and Function in Neurodegenerative Disease

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Muscle atrophy and degeneration are hallmark features of neurodegenerative diseases such as amyotrophic lateral sclerosis (ALS) and Parkinson's disease. In these conditions, denervation leads to the progressive loss of skeletal muscle mass, which is frequently replaced by intramuscular adipose tissue (IMAT) and fibrotic scar tissue. This fatty fibrosis not only compromises muscle function but also contributes to irreversible motor disability. Despite its clinical significance, the molecular drivers of IMAT accumulation remain poorly understood, and therapeutic strategies to prevent or reverse this process are lacking. Our lab focuses on developing novel strategies to block the formation of intramuscular adipocytes. Using genetic and pharmacologic approaches in murine models, we demonstrated that targeting a specific population of fibro-adipogenic progenitors (FAPs)—cells that contribute to fat infiltration after injury or denervation—can effectively reduce IMAT formation, thereby promoting muscle regeneration. Furthermore, we identified key signaling pathways that regulate FAP differentiation, offering promising therapeutic entry points. Given that ALS and Parkinson's patients experience progressive denervation, our findings have critical implications for preserving muscle integrity in these populations. By inhibiting the conversion of FAPs into adipocytes, we may be able to slow or prevent the fatty degeneration of skeletal muscle that exacerbates functional decline. Ongoing work in our lab aims to translate these findings into models of neurodegenerative disease and assess their impact on disease progression and quality of life.

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