

Abstract

Glycogen synthase kinase-3 β (GSK-3 β) is a serine/threonine protein kinase involved in a number of signaling processes. Pharmacological inhibition of GSK-3 β has been shown to have neuroprotective effects, and its dysregulation is present in a variety of neurodegenerative, neuromuscular, developmental, and psychiatric disorders. GSK-3 β is an essential component of the canonical Wnt pathway, which is involved in nervous system development. Notch signaling, like Wnt, plays a key role in development, but its relationship to GSK-3 β remains unclear. The existing literature indicates that GSK-3 phosphorylates Notch intracellular domain but contradicts whether GSK-3 β affects Notch positively or negatively. Thus, such molecular "cross-talk" is highly complex and interactions may exist at multiple levels beyond simple phosphorylation with other components being involved. Myotonic dystrophy is a genetic neuromuscular disease that causes dysregulated protein expression of many proteins, including GSK-3 β , and features developmental, muscle, and neurological symptoms. Studying molecular interactions in the context of myotonic dystrophy may help uncover effects that GSK-3 β and Notch have on development and disease of nervous and muscular systems.

This thesis presents a review of previous studies concerning the relationship between GSK-3 and Notch and reports my attempts to expand on past research using a different approach. VDAC1, a protein reportedly interacting with both GSK-3 β and N1ICD was selected from GSK-3 β interactome in myotonic dystrophy muscle cells (unpublished mass spectrometry results provided Laboratory of Structural Biology and Cell Signaling) and the molecular "toolset" for further studies was prepared. GSK-3 β , N1ICD and VDAC1 were visualized experimentally using immunocytochemistry and *in silico* using modern Alphafold-based techniques.

Keywords: GSK-3, Glycogen synthase kinase 3, Notch signaling, crosstalk, neurodegeneration, myotonic dystrophy, signal transduction, protein-protein interactio