Human WIPI β-Propeller Function in Autophagy and Neurodegeneration

Human WIPI beta-propellers function as PI3P effectors in autophagy, with WIPI4 and WIPI3, both mutated in human neurodegenerative diseases, being able to link autophagy control by AMPK and TORC1 to autophagosome formation. WIPI4 is considered to play an important role in the formation of autophagosomal membranes together with its distinct protein interaction partner ATG2. De novo mutations in WDR45, the gene encoding human WIPI4, are causative of beta-propeller-associated neurodegeneration (BPAN) hallmarked by high brain iron accumulation. The underlying mechanism how WDR45 mutations cause BPAN are unknown. We discuss a role for WIPI4 in lysosomal ferritin degradation, and how this function may be altered in the pathophysiological context of BPAN.