The Role of NRBF2 in the Regulation of the ULK1 Kinase Complex

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Macroautophagy is an essential process in eukaryotic cells, involving the degradation and recycling of cytosolic components during stress conditions such as nutrient deprivation. Obtaining a greater understanding of this process is necessary as a number of diseases including neurodegenerative diseases and cancer are associated with macroautophagy malfunction. Two protein complexes are involved in controlling autophagy: the ULK1 complex and class III phosphatidylinositol-3 kinase complex I (PI3KC3-C1). NRBF2 protein has been identified as a component of PI3KC3-C1 and has been shown to interact with the ULK1 complex. The goal of this study was to identify in what way NRBF2 affects the ULK1 complex. In WT and NRBF2 knock-out mouse embryonic fibroblasts (MEF), it was observed that upstream regulators of the ULK1 complex, AMPK and mTOR, were not affected by NRBF2 depletion. Co-immunoprecipitation of WT and NRBF2 knock-out MEFs and mouse hippocampal tissue showed that NRBF2 stabilized ULK1 complex formation. Furthermore, NRBF2 expression is high in hippocampal tissue, so an Object Location Memory task was given to WT and NRBF2-KO mice to test for negative effects on the hippocampus. KO mice displayed memory impairment while WT mice did not. Thus, this study establishes the function of NRBF2 and ULK1 complex interaction and identifies a role in memory.

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