Effect of NDR2 overexpression on neuronal autophagy

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Abstract:
NDR2 is a Serine Threonine kinase involved in neuronal development, cell cycle control & neurite growth. Recently, we have explored the possibility that it might act as a major autophagy regulator in the brain. Neuronal Autophagy, which is under circadian regulation, is involved in extensive functions such as protein homeostasis, organelle turnover memory formation, and learning, moreover, impairments in autophagy have been implicated in the etiology of many neurodegenerative diseases and aging. Unpublished data from our group showed an effect of NDR2 overexpression on the circadian fluctuation of LC3. Those findings point towards a critical role of NDR2 in autophagy regulation, even though the mechanism and result of the interaction are not yet known. Hence, the project aims to determine the effect of NDR2 overexpression on neuronal autophagic flux and if this relates to the circadian regulation of autophagy. To confirm changes in autophagy, protein levels of LC3, p62, and other autophagy related proteins like cEBPβ, Beclin-1, mTOR, and ULK1 from hippocampi taken at different time points will be quantified. Alongside mRNA and protein levels of NDR2 will be quantified to look into a possible circadian regulation of the protein. Further hippocampal cell culture will be performed and treated with rapamycin and or chloroquine to analyze the effect of NDR2 on autophagy activation, through LC3/p62 puncta quantification and live-cell imaging. Lastly, a battery of behavioral tasks will be used to analyze effects on spatial navigation, open field exploration, and active avoidance in mice undergoing circadian manipulation.