

P008 The LCA associated protein AIPL1 modulates NUB1
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Mutations in the aryl hydrocarbon receptor interacting protein-like 1 (AIPL1) cause the blinding disease Leber's congenital amaurosis (LCA). AIPL1 is a tetratricopeptide repeat (TPR) protein homologous to the aryl hydrocarbon receptor interacting protein (AIP) and immunophilin FKBP51/52 TPR co-chaperones. AIPL1 interacts with the cell cycle regulator NUB1. We investigated the functional significance of the AIPL1-NUB1 interaction through immunofluorescent confocal microscopy of transfected SK-N-SH neuronal cells. AIPL1 was predominantly cytoplasmic, whereas NUB1 was predominantly nuclear due to a functional NLS located near its C-terminus. In contrast, fragments of NUB1 formed inclusions. NUB1-N (residues 1 to 306) formed inclusions that decorated the periphery of the nucleus, whilst NUB1-C (residues 347 to 684) formed intranuclear inclusions. Co-transfection of AIPL1 with NUB1 resulted in a concentration-dependent modulation of NUB1 subcellular distribution towards the cytoplasm. Furthermore, co-transfection of AIPL1 with NUB1-N and NUB1-C showed a concentration-dependent suppression of NUB1 inclusion formation and redistribution of these fragments in the cytoplasm. This chaperone function of AIPL1 was specific for NUB1, since AIPL1 was unable to suppress the aggregation of a number of aggregation-prone proteins. AIPL1 C-terminal truncation mutants abolished the effect on NUB1 inclusion formation. Hence, the effect of AIPL1 on NUB1 requires the C-terminal region of AIPL1 and maps to a region outside of the central TPR domain. This study identifies AIPL1 as a potential important modulator of NUB1 cellular function.