CCDC11 Regulates Efficient Midbody Recruitment of Ist1 Suggesting Impaired Organization of ESCRT Machinery

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Abscission, the final stage of cytokinesis, is characterized by the separation of cells through the severing of the intercellular bridge at the midbody. Components of the Endosomal Sorting Complex Required for Transport(ESCRT-III) are utilized to accomplish this internal membrane fission event. Based on a prior observation that the centrosome and cilium-associated protein CCDC11 localized adjacent to the midbody during abscission and that CCDC11 KD demonstrated a reduction of ESCRT-III subunit CHMP2A, a series of experiments were conducted to elucidate possible interactions of CCDC11 and midbody proteins. Transient siRNA knockdown(KD) CCDC11 HeLa cells were co-immunostained with IST1, Alix, Tsg101, and VPS4. Depletion of CCDC11 led to a substantial reduction in IST1 and VPS4 as compared to control. This further narrows the time frame to which CCDC11 functions and establishes a possible interaction between CCDC11 and IST1. To expand upon the possible overlap between CCDC11's role in ciliogenesis and cytokinesis, immunofluorescence microscopy was utilized to observe centrosome and midbody localization of CCDC11 expressing the R158G mutation. There appeared to be no effect on efficient cytokinesis, demonstrating that CCDC11's cytokinetic role is likely distinct from that in ciliogenesis. Aggregate mutant domains throughout the cytoplasm were observed to co-localize with CHMP2A and IST1 as was seen in the full length plasmids, suggesting that CCDC11 R158G mutants are capable of recruiting ESCRT-III proteins. In addition, L-leucyl-L-leucine methyl ester (LLOMe) was used to induce endolysosomal rupturing, but CCDC11 was observed to not be physically present on damaged structures, suggesting it may not be involved in endolysosomal repair.

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