The Cilium and Centrosome Associated Protein CCDC11 Is Required for Cytokinesis via Midbody Recruitment of the ESCRT-III Membrane Scission Complex

Parker, Jillian (School: Half Hollow Hills High School West)
Lee, Jiachen (School: Half Hollow Hills High School East)
Ahmed, Arooba (School: Half Hollow Hills High School East)

Abscission is the final stage of cytokinesis, the division of the cytoplasm between daughter cells, in which cells are physically separated by severing the intercellular bridge on either side of the midbody structure. Components of the Endosomal Sorting Complex Required for Transport (ESCRT-III) machinery are utilized to accomplish this internal membrane fission mechanism. Based on a prior observation that the cilium-associated protein CCDC11 localized adjacent to the midbody during abscission in dividing retinal pigment epithelial cells (RPE1), a series of experiments were conducted to elucidate a potential cytokinetic role for CCDC11. Localization of both endogenous and ectopically expressed CCDC11 to midbody structures was validated in HeLa and U2OS cell lines through immunofluorescence microscopy. Additionally, two N-terminal coiled-coil domains (CCDs) present in CCDC11 were required for its midbody recruitment. Transient siRNA knockdown (KD) of CCDC11 in U2OS demonstrated significant increases in binucleated cells, indicative of cytokinetic defect. Furthermore, CCDC11 KD in U2OS cells demonstrate a depletion of CHMP2A at the midbody as compared to control, strongly suggesting the CCDC11 cytokinetic defect is attributed to a failure to recruit the ESCRT-III machinery to the midbody prior to abscission. This data provides for a novel, previously uncharacterized function for CCDC11 that may well encompass all cellular membrane scission events. Considering that synaptic pruning is also mediated by the ESCRT-III complex, the functional role of CCDC11 may be critical in combating neurodegenerative disorders including Alzheimer's disease as well as neurological disorders including autism and schizophrenia.

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