ARMC2: a multifaceted protein involved in both flagella and cilia formation and function.

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In humans and mice, the absence of the ARMC2 protein is linked to Multiple Morphological Abnormalities of the Flagellum (MMAF), characterized by the absence or abnormality (coiled, short, irregular shape) of spermatozoa flagella. Patients with this condition exhibit disorganization of flagellar axonemal microtubules and the absence of the axonemal central pair. Recently, knockout (KO) animals also displayed signs of ciliopathies, such as hydrocephalus and situs inversus, indicating a potential role of ARMC2 in cilia formation and function.

To unravel ARMC2's involvement in cilia formation, we examined the ultrastructure and morphology of two multiciliated epithelia expressing Armc2: the trachea and the oviduct. Unlike spermatozoa, no apparent morphological abnormalities were observed at the tissue level in either tissue. However, transmission electron microscopy of the trachea revealed two major defects: disorganization of basal bodies at the plasma membrane and loss of cilia axonemal symmetry. Additionally, scanning electron microscopy showed shorter tracheal cilia in KO mice. Oviductal cilia exhibited no obvious ultrastructural defects, but KO females showed subfertility with a decrease in the number of pups compared to wild-type counterparts. Ongoing experiments analyzing beat frequency and infundibulum cilia pattern, along with cumulus-oocyte complexes collection, will further elucidate the observed female subfertility. Furthermore, histological analysis of Armc2-deleted mouse brains indicated cerebral ventricular dilatation associated with the observed hydrocephaly phenotype.

In conclusion, our findings highlight that the ARMC2 protein not only plays a role in flagella formation but also contributes to cilia formation and function, shedding new light on the investigation of ciliopathies.