New insight into human ciliopathy

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In the September 1st issue of *G&D*, Dr. Karen Oegema (UCSD) and colleagues identify the molecular basis of the lethal developmental disorder, hydrolethalus syndrome, and reveal that hydrolethalus syndrome actually belongs to the emerging class of human ciliopathy diseases.

"5 years ago a human genetics study linked Hydrolethalus syndrome to a mutation in a protein named HYLS1. Since this discovery the function of HYLS1 has remained unknown. Our work solves this mystery, showing that HYLS1 is a centriolar protein required for the formation of cilia, small hair-like cellular projections that execute a variety of essential motile and sensory functions," explains Dr. Oegema.

Hydrolethalus syndrome is a rare genetic disorder characterized by severe birth defects (hydrocephalus, polydactyly, cardio/pulmonary malformations) that result in stillbirth or early neonatal death. The majority of cases affect people of Finnish ancestry, where the incidence is roughly 1 in 20,000. Ten years ago it was discovered that hydrolethalus syndrome results from mutations in the HYLS1 gene, located on the long arm of chromosome #11.

Dr. Oegema and colleagues now show that the evolutionarily conserved HYLS1 protein is, in fact, a centriolar protein that is specifically required for cilia formation in both *C. elegans* and vertebrates. The researchers demonstrated that HYLS-1 stably incorporates into centrioles during their assembly, and plays a crucial role in the early step steps of the ciliogenesis pathway. Interestingly, however, HYLS-1 is

dispensable for centriole assembly and centrosome function during cell division.

Their work expands the range of previously recognized human ciliopathies - which vary from polycystic kidney disease to male infertility and obesity - and establish hydrolethalus syndrome as one of the most severe ciliopathies identified to date.

Source: Cold Spring Harbor Laboratory (news : web)