Oral-facial-digital syndrome type 1 (OFD1) is a developmental disorder often associated with cystic kidney disease and is characterized by malformations of the face, oral cavity and digits. The disease results from mutations within the OFD1 gene. We have found that the OFD1 protein encoded by this gene plays an important role in formation of the primary cilium, the antenna of the cell.

The cell’s antenna

- Within a cell, there are many specialized structures, or organelles, that have a specific function.
- The centrosome (blue) is an organelle that organizes the internal cytoskeleton, which consists of a network of fibers called microtubules that contribute to cell shape, motility and trafficking. Microtubules also constitute the internal structure of the primary cilium.
- The primary cilium is a tiny hair-like projection that extends from the cell surface into the extracellular space.
- It is present on almost every cell of the human body.
- It functions as a unique antenna-like structure, sensing a wide variety of signals and coordinating numerous cellular events.

OFD1 protein localization in the cell

- Immunofluorescence microscopy reveals that the OFD1 protein localizes to the centrosome and in small aggregates in its vicinity in dividing cells.
- The OFD1 protein also localizes to the basal body and in small aggregates in ciliated cells.
- OFD1 does not localize along the stalk of the cilium.

OFD1 protein and the formation of primary cilia

- Cultured cells can be induced to form primary cilia by serum starvation.
- However, if cells are depleted of the OFD1 protein, the efficiency of cilia formation decreases.
- OFD1 depletion reduces the efficiency of cilia formation.

Conclusions and future work

- Although primary cilia were first described more than a century ago, they were long considered rudimentary and their functions remained poorly understood.
- However, recent research has shown that defects in the building of the primary cilium or in transport or function of proteins that associate with it underlie a wide range of human developmental disorders including renal cystic diseases.
- We speculate that OFD1 may be involved in the biogenesis, maintenance or signalling function of primary cilia.
- This should lead to new insights into the pathology of the OFD1 disease and, potentially, new avenues of treatment.