

Cilia are tiny cellular extensions playing many important roles in humans. Motile cilia appear as multiple structures at the surface of ciliated epithelia lining respiratory tracts, brain ventricles, Fallopian tubes (oviducts) and efferent ductules of testicles (short part in male reproductive system, between testicle and epididymis) and are formed by sperm cells (known as flagella). Motile cilia shift mucus and fluids along the surface of epithelia (e.g. removal of bacteria and pollutants from respiratory tracts, circulation of cerebrospinal fluid in brain ventricles and central canal of spinal cord, picking of oocyte from ovary into Fallopian tube and sperm from testis to epididymis) and enable the motility of sperm cells. Cilia of the second type, so-called primary cilia, are immotile, sensory structures. The sensory cilia receive extracellular signals and thus regulate intracellular processes and enable cell's reaction to changes in its environment. These structures play a crucial role during organism development, for example are involved in the formation of the left-right asymmetry, and brain development. Equally important are functions of primary cilia in the mature organism. These tiny extensions are present at the surface of cells of nearly all types and allow co-operation of cells, tissues, and organs.

Because cilia play so many and important roles, their dysfunction leads to development of severe disorders, known as ciliopathies, characterized by broad spectrum of symptoms, including chronic respiratory infections, hydrocephalus, infertility, polycystic kidney and liver, blindness, obesity and intellectual disability.

Cilia are very complex structures, composed of at least few hundred of proteins, and nearly 180 of these proteins were connected to human diseases. However, in the case of large group of patients with ciliopathy symptoms, the causing mutation is unknown. For this, research concerning cilia formation and functioning is so important.

A ciliary tip is particularly poorly characterized part of the cilium. This segment is a place of cilium growth and accumulation of external signal receptors. Currently, only few proteins that build up ciliary tip are known and their mutations were identified in patients with Joubert syndrome, a type of ciliopathy. Therefore, our goal is to characterize a cilia tip composition and better understand its participation in cilia-related processes.

To identify novel cilia tip proteins, we will use a ciliate *Tetrahymena thermophila*, an appreciated model in research concerning cilia structure and functions' regulation. Using this model will allow us to collect bulk amount of the material for biochemistry and microscopic assays. Obtained results will allow us to prepare approximate map of protein-protein interactions, and probably also a 3D map of cilium tip. Using commercially available antibodies, we will verify if newly identified proteins are present also in tips of primary and motile cilia formed by mammalian cells. Proteins forming cilia tip in different organisms will be subjected to further analysis. We will check how their depletion or mutations influence cilia functioning, especially during cilia growth, length regulation and motile cilia beating. Our findings can discover till-now unknown proteins whose mutation is linked with ciliopathies. Therefore, we hope to provide data that could be helpful in ciliopathies diagnostic and in targeted therapy.