LABORATORY OF

CELL MOTILITY

Flagellum/cilium, microtubule-based cytoskeleton, kinetoplastid parasites, mammalian cells, advanced light and electron microscopy

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In the Laboratory of Cell Motility, we study the eukaryotic flagellum and cilium (the terms are interchangeable), a fascinating organelle with motile, signalling and sensory roles. The flagellum/cilium is evolutionarily well conserved and is present on surfaces of many eukaryotic cells, including important parasitic protists and most mammalian cell types. In humans, malfunction of cilia causes severe hereditary disorders called ciliopathies.

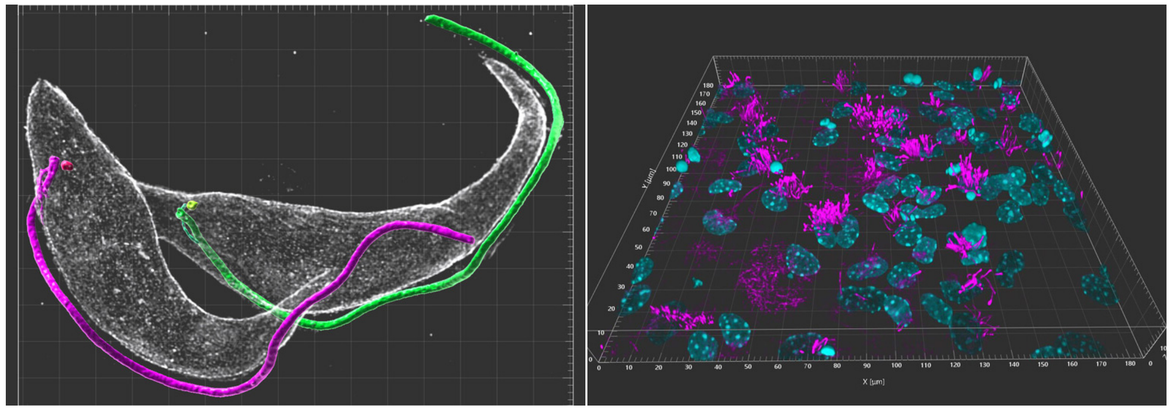
The principal structural and force-generating component of the flagellum/cilium is the microtubule-based axoneme. The axoneme consists of several hundred protein species organized in a highly defined manner. How does the cell form such a complex yet highly organized structure?

Using the highly experimentally tractable flagellated protist *Trypanosoma brucei*, the causative agent of human African trypanosomiasis, we have developed and optimized biochemical, cell biology, and imaging techniques to identify proteins critical for the processes of axonemal construction and length regulation.

Importantly, due to the high evolutionary conservation of the organelle, we were able to identify mammalian orthologues of some of these proteins and assess their roles in mammalian cells.

Finally, to reveal intrinsic activities of these newly identified proteins, we study their behaviour by in vitro biochemical assays. In particular, we employ microscopy-based single-molecule assays, which provide deep mechanistic insights into the activities of individual molecules.

We believe that integrating these approaches will provide a comprehensive understanding of the processes orchestrating the axonemal growth and will give insights into the causes of certain ciliopathies.



Left: The microtubule-based cytoskeleton of a *Trypanosoma brucei* cell. Flagella and structures associated with their base are highlighted in colour. The cell was imaged using the expansion microscopy approach. Right: Cell culture of mouse multiciliated ependymal cells. This type of cells is found of the surface of the ventricular system in the brain, and the ciliary beating contributes to generation of the cerebrospinal fluid flow. The cilia are in magenta, cell nuclei in cyan.

Selected publications:

1. Gorilak P, Pružincová M, Vachova H, Olšinová M, Schmidt Cernohorska M, Varga V*: Expansion microscopy facilitates quantitative super-resolution studies of cytoskeletal structures in kinetoplastid parasites. Open Biol 2021 11(9): 210131.
2. Kiesel P, Alvarez Viar G, Tsoy N, Maraspini R, Gorilak P, Varga V, Honigmann A, Pigino G: The molecular structure of mammalian primary cilia revealed by cryo-electron tomography. Nat Struct Mol Biol 2020 Dec;27(12):1115-1124.
3. Vachova H, Alquicer G, Sedinova M, Sachova J, Hradilova M, Varga V*: A rapid approach for in locus overexpression of *Trypanosoma brucei* proteins. Mol Biochem Parasitol 2020 239: 111300.