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LABORATORY OF

eukaryotic flagellum and cilium, flagellum construction, *Trypanosoma brucei*, biochemical approaches

In our laboratory we focus on the eukaryotic flagellum and the cilium, the organelles with motile, sensory and signalling functions. In humans the cilia are present on nearly all cell types and their malfunctions lead to pleiotropic hereditary diseases called ciliopathies. The evolutionarily conserved cytoskeletal element of the cilium, the axoneme, is a highly complex and highly organized structure. The axoneme is constructed by addition of proteins to its distal end, but how the processes of axoneme assembly are brought about is not understood. To elucidate this we take advantage of the experimental tractability of the parasitic flagellate *Trypanosoma brucei* and develop biochemical approaches for identification of proteins localizing to the distal domain of the axoneme. We study the roles of the identified proteins in the regulation of axoneme assembly and in flagellum functions, and attempt to get a mechanistic insight into their activities using in vitro reconstitution assays. Moreover, we apply the knowledge acquired studying trypanosomes to mammalian systems, such as characterizing human orthologues of the trypanosome proteins and applying the developed biochemical approaches to mammalian tissues. Understanding the processes of the axoneme assembly will help understand causes of certain ciliopathies.

Selected recent papers:

Varga V, Moreira-Leite F, Portman N, Gull K: The flagella connector of Tryponosomo brucei is a kinesin-powered junction distinct from the axonemal capping structure. Submitted.

Dean S, Moreira-Leite F, Varga V, Gull K: (2016) Cilium transition zone proteome reveals compartmentalisation and differential dynamics of ciliopathy complexes. **PNAS** 113(35):E5135-43.

Sunter J, <u>Varga V</u>, Dean S, Gull K: (2015) A dynamic coordination of flagellum and cytoplasmic cytoskeleton assembly specifies cell morphogenesis in trypanosomes. J. Cell Sci. 128(8), 1580-1594.

