The role of dynein in nuclear migration

Dynein is a fascinating molecular motor that transports a diverse range of cargos along microtubules. The dynein multi protein complex has a molecular weight of around 1.2 MDa. Within the complex, the motor domain is responsible for force generation. Recent years have seen progress in our understanding of how ATP hydrolysis in its ring of AAA+ modules powers movement (1-2). At the moment the field is moving towards the question of how dynein interacts with and is regulated by its cargos. The part of the dynein complex that binds to the cargo is the tail, which extends from the linker. It dimerizes and interacts with the other components of the dynein complex to provide a platform for cargo binding. Furthermore, cargo transport requires adaptors, which establish the connection between the tail and the cargo, and often also the ubiquitous dynein activator dynactin.

Among the plethora of dynein cargos, nuclei have attracted a lot of attention. It has been demonstrated that nuclear transport processes involving dynein are important for nuclear positioning and development (3). Prominent examples include the nuclear movements during hypodermal syncytium hyp7 formation in *C. elegans*, the movement of the female pro-nuclei towards the male pro-nuclei after fertilization and the interkinetic nuclear migration in radial glial progenitor cells, a crucial step during brain development. To get insights into how dynein participates in these exciting processes, we will express recombinant dynein complexes in insect cells, purify these complexes by chromatography and determine their structures using a combination of cryoEM and X-ray crystallography. We will evaluate mechanistic models about dynein driven nuclear movements by single molecule fluorescence microscopy. Together with external collaboration partners, there will be also the opportunity to test these hypotheses in *in-vivo* systems.

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