Life Sciences Seminar

A reconstituted mammalian mRNA transport system selectively transports defined amounts of axonal mRNAs

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Cytoplasmic mRNA transport on microtubules and local translation are essential for the spatial control of gene expression. In mammalian neurons, mRNA localization is required for essential processes as axonal growth-cone steering, cell migration and synaptic plasticity underlying long-term memory formation. Decades of research revealed several components involved in mammalian mRNA transport processes. However, which factors are essential and how they act in concert to produce the required mRNA distributions is not clear. Using biochemical in vitro reconstitutions in combination with fast, single-molecule sensitivity fluorescent imaging we show that the tumor suppressor adenomatous polyposis coli (APC) functions as adaptor linking the axonally localized beta-actin and beta-tubulin mRNAs to the heterotrimeric kinesin-2 KIF3A/B/KAP3. We demonstrate that the kinesin-2 cargo-adaptor KAP3 is required to couple APC-RNA complexes to the motor protein, while APC activates transport by recruiting the kinesin to microtubules. Remarkably, our minimal in vitro system shows that two proteins are sufficient for processive mRNA transport and also to generate key-characteristics of neuronal mRNA transport as mRNA-cargo specificity and transport of defined numbers of mRNAs. We further demonstrate that guanine-rich sequences increase mRNA transport efficiency and balance the access of different mRNAs to the transport system to compensate for relative mRNA abundance. Our results reveal for the first time a minimal set of proteins sufficient to drive kinesin-based, mammalian mRNA transport.

Tuesday, July 16, 2019 02:00pm - 03:00pm
Mondi Seminar Room 2, Central Building

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