Molecular motors

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The "Molecular Motors" Minisymposium focused mainly on the microtubule-based motors kinesin and dynein and a class V myosin. A common feature of all these motors is that they move processively on their track, meaning that the motor can take multiple steps without dissociating. A common theme of the Minisymposium was motor function in a complex intracellular environment.

Kathy Trybus (University of Vermont) reconstituted mRNA transport in vitro, using a class V myosin from budding yeast (Myo4p), and synthesized *ASH1* mRNA, the most well-studied localizing mRNA in budding yeast. Myo4p is single-headed, but the mRNA-binding protein She2p recruits two single-headed motors to form a processive complex. Importantly, the mRNA cargo itself is essential to stabilize the complex at physiological ionic strength, providing a checkpoint to ensure that only cargo-bound motors move processively. The most efficient transport was achieved when motor complexes were bound at more than one of the four localization elements ("zip codes") in *ASH1* mRNA, and when the mRNP (messenger ribonucleoprotein complex) walked on bundles of actin filaments, conditions closest to those found in the cell. By building complexity in vitro, one can begin to mimic cellular processes in a controlled way.

Paul Selvin (University of Illinois) tackled the question of how kinesin and dynein, which move in opposite directions on the microtubule, interact when bound to a common cargo. When kinesin walks toward the plus end of the microtubule, dynein walks backward, and thus both motors are engaged. Selvin argued that this scenario is beneficial when a dual motor–bound cargo encounters a roadblock. Kinesin detaches at an obstacle, allowing the dynein to back up, switch tracks, and allow kinesin to reengage and continue forward motion. He termed this a "synergistic tug-of-war." Based on a comparison of in vivo and in vitro directional stall forces using an optical trap, a similar situation prevails in the cell. A broad range of stall forces is observed for plus end–directed motion (stall force of kinesin minus a variable number of engaged dyneins). For minus end–directed motion, stall forces are multiples of the stall force of dynein, consistent with kinesin not being engaged with the microtubule.

Roop Mallik (Tata Institute of Fundamental Research) used optical trapping within cells to show that part of the reason why dynein is so complex may be to allow multiple dyneins to work efficiently together as a team. This complexity appears to encode a gear-like behavior, which results in a high sensitivity of dynein to load compared with kinesin. This causes the lead dynein on a cargo to slow down, while the lagging dyneins move relatively faster. As a result, dyneins in a team tend to cluster and therefore share load more efficiently. The ability of dynein to vary step size (and therefore velocity) with load and to then catch-bond to the microtubule at high load are key components of the dyneins ability to function as a team.

Vaishnavi Ananthanarayanan (Max Planck Institute of Molecular Cell Biology and Genetics), from I. Tolic-Norrelykke's laboratory, used single-dynein imaging in fission yeast to understand how dynein finds its cortical anchoring spots. A surprising finding was that once dynein initially binds to the microtubule, rather than undergoing directed motion, it diffuses along the microtubule. The switch to directed motion occurs when dynein binds to the cortex. For substantiation of this finding, the pleckstrin homology domain of the anchor was deleted, but its binding to dynein was still sufficient to switch motion from diffusive to processive. The diffusive ability of dynein on microtubules and its switch to processive motion upon finding its cortical anchor is critical for its ability to generate large-scale cellular movements.

Marvin Bentley (Oregon Health and Science University), from Gary Banker's laboratory, described a novel "split-kinesin" assay that will be extremely useful for identifying the kinesins that move specific vesicle populations. The approach is to use separate constructs that encode only the motor domain or only the tail domain of kinesin. The tail will target its native vesicle but will be unable to affect the distribution of vesicles. Likewise, the motor domain will move on microtubules, but will carry no cargo. When the two domains are joined via chemical dimerization, there will be a large change in distribution of that particular vesicle. Several examples using this strategy were shown. In principle, this strategy should be useful in many cell types and for different classes of motors.

Wen Lu (Northwestern University Feinberg School of Medicine), from Vladimir Gelfand's laboratory, studied the role of kinesin in generation of cell polarity. She demonstrated that kinesin-1 induces sliding of microtubules against each other in *Drosophila* neurons, and that this "telescoping" movement is both necessary and sufficient to drive the initial axon's extension. Thus, in addition to cargo transport, the new major function of conventional kinesin is formation of cellular processes by microtubule–microtubule sliding.

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