# Microtubule dynamics: 50 years after the discovery of tubulin and still going strong

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The Minisymposium "Microtubule Dynamics" featured speakers ranging from a founding member of the microtubule field to graduate students embarking on their scientific journeys. The session spanned a broad range of topics, from fundamental questions about the structure and dynamics of microtubules, to the behavior of molecular motors in reconstituted systems, to the therapeutic potential of microtubule regulators in neuroregeneration. Fifty years after the discovery of tubulin by Borisy and Taylor, this session was proof that microtubules still have many secrets.

**Dick McIntosh** (University of Colorado, Boulder) kicked off the session by showing that the growing tips of microtubules, as seen by electron tomography, displayed protofilaments that curled out from the polymer axis both in vitro and in vivo. Curvatures were greatest at the protofilament tips and low enough near the wall of a growing microtubule to allow attractive forces between dimers to drive protofilament straightening. This mechanism of microtubule growth differs from several published models and will certainly catalyze a new look at the tubulin polymerization pathway. **Annapurna Vemu** (Roll-Mecak laboratory, National Institute of Neurological Disorders and Stroke, National Institutes of Health) tackled an old problem in microtubule biology of how tubulin isoform composition influences microtubule dynamics. By performing label-free in vitro dynamic assays with tubulin purified from different cell types as well as recombinantly expressed single-isoform human tubulin, Vemu showed that different tubulin isoforms have dramatically different dynamic parameters and that microtubule dynamics can vary proportionally with isoform composition. **Anne Straube** (University of Warwick, Coventry, United Kingdom) uncovered a differential positioning of the three mammalian microtubule end-binding proteins (EB1, EB2, and EB3) from the growing microtubule tip. Straube's team found that behind the tip-binding specificities is the ability of EBs to bind between two protofilaments and sense the specific nucleotide state of both flanking β-tubulins.

Two talks focused on microtubule nucleation. **Garrett Greenan** (Ron Vale and David Agard laboratories, University of California, San Francisco) presented electron cryotomography reconstructions of centrioles from *Drosophila* and mammalian cell lines, which contain doublet and triplet microtubules, respectively. Although their overall ninefold symmetrical architecture is conserved, the reconstructions showed that in the absence of the C-tubule, *Drosophila* centriole doublets are connected via an A/A-linker, distinct from the A/C-linker seen in mammalian centrioles in both position and structure. Greenan postulated that this difference in architecture maintains the ability of the *Drosophila* centriole to recruit pericentriolar material and nucleate microtubules. **Jan Brugués** (Max Planck Institute for Molecular Cell Biology and Genetics, Dresden, Germany) examined what sets the upper size limit in spindles by measuring microtubule nucleation. Through a combination of laser ablation to measure minus ends with depletion experiments and mathematical modeling, Brugués presented evidence that the amount of active nucleators sets the size and mass of spindles through microtubule-stimulated microtubule nucleation.

The session then switched gears to microtubule-based motors. **Stephen Norris** (Ohi and Zanic laboratories, Vanderbilt University) focused on the microtubule minus end, specifically the role of kinesin-14 (HSET/KIFC1 in humans) in focusing supernumerary centrosomes to the two poles. Using single-molecule fluorescence based assays, he showed that soluble tubulin activated HSET minus end–directed motility through a clustering mechanism that also protected microtubule minus ends from depolymerization, suggesting an updated model for microtubule minus-end organization in mitotic cells. **Tomohiro Shima** (Riken QBiC, Osaka, Japan) overturned the conventional view that microtubules serve only as passive tracks for kinesin-1 by showing that KIF5C, a kinesin-1 family member, changes microtubule conformation into a high-affinity form. Shima proposed a positive feedback between KIF5C binding and microtubule conformation that accelerates successive kinesin binding. **Anand Rao** (Baas laboratory, Drexel University, Philadelphia) showed that in cerebellar migratory neurons, the sliding of a small pool of centrosome-unattached microtubules ensures proper trajectory of migration. In postmigratory neurons, where all microtubules are believed to be centrosome unattached, sliding is the means by which axonal microtubules achieve their hallmark plus-end-out polarity pattern. Rao uncovered a dynein-based mechanism responsible for "polarity sorting" of microtubules by sliding them into and out of the axon with their plus ends leading.

The final two talks focused on proteins that stabilize or sever microtubules. Microtubules of motile cilia experience strong

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mechanical stress. **Mayukh Guha** (Gaertig laboratory, University of Georgia, Athens, GA) showed that the swimming velocity of *Tetrahymena* cells is greatly reduced after knockout of SPEF1, a microtubule-binding protein conserved in species with motile cilia. The loss of SPEF1 induces defects to the central pair microtubules, which are prone to breakage under mechanical stress, revealing a role of SPEF1 in stabilizing microtubules. **Lisa Baker** (Sharp laboratory, Albert Einstein College of Medicine, Bronx, NY) revealed a role of fidgetin-like 2 (FL2), a microtubule-severing enzyme, as negative regulator of neuronal growth cone motility. In vivo knockdown of FL2 promotes striking nerve regeneration in rodents with nerve injuries. Baker showed that FL2 is a promising therapeutic target for enhancing axon regeneration after nerve injury in both adult central and peripheral nervous systems.