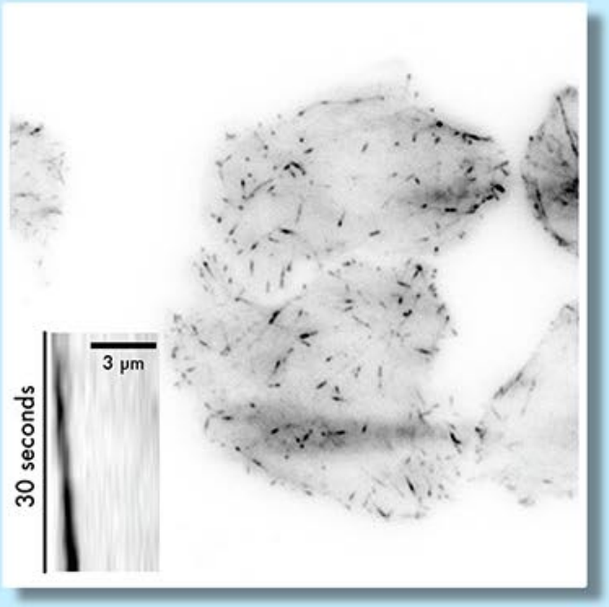
BEN LOWE

Faculty Research Mentor: Dr. Kevin Slep
Department of Biology



Fluorescently-tagged EB1 (black) Labels Growing Microtubule Plus Ends

Mini Spindles TOG1 Is Required to Promote Microtubule Polymerization and Mitotic Spindle Bipolarity

Microtubules (MTs) are dynamic polymers that regulate cellular processes including intracellular trafficking and mitotic spindle formation. MT-associated proteins (MAPs) control MT dynamics in space and time in order to ensure proper cellular function. Members of the XMAP215 protein family are conserved MAPs that utilize arrays of αβ-tubulin-binding tumor overexpressed gene (TOG) domains to promote rapid MT polymerization. A given XMAP215 protein generally possesses a pentameric array of TOG domains that are structurally different from one another despite being positionally conserved across species. It has been shown that the presence of only TOG1, TOG2, and TOG5 is sufficient to rescue reduced MT polymerization rates to wild-type rates. Furthermore, multiple studies of XMAP215 family members demonstrate that removing TOG1 and TOG2 from the pentameric array completely abrogates MT growth rates. However, the significance of TOG1 alone in regulating MT dynamics remains uncertain. We investigated the role of TOG1 using the *Drosophila melanogaster (D.m.)* XMAP215 family member mini spindles (Msps) as a model. Endogenous Msps was depleted from *D.m.* S2 cells using dsRNA and a Msps construct with TOG1 specifically deleted (ΔTOG1) from the pentameric TOG domain array was expressed. ΔTOG1 expressing cells exhibited dramatically reduced MT polymerization rates in comparison to control cells. Furthermore, ΔTOG1 expression yielded a significantly increased incidence of abnormal (non-bipolar) spindle phenotypes. These data suggest that TOG1 is critical for proper XMAP215-mediated MT dynamics and mitotic spindle formation. Together with our previous findings, the results presented here also indicate that elimination of TOG1 alone reduces MT polymerization rates nearly equivalently to removal of both TOG1 and TOG2, suggesting that either TOG1 or TOG1+2 are required for full MT polymerization activity. Future research will test which of these hypotheses is the case. Combined with studies of TOGs 3-5, a more comprehensive model of how each distinct domain contributes to XMAP215 function will serve as a paradigm for how ensembles of similar domains combine to serve functions greater than the sum of the parts.