Structural Basis of Tubulin Recruitment and Assembly by Microtubule Polymerases

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XMAP215/Stu2/Alp14 proteins accelerate microtubule plus-end polymerization by recruiting tubulins via arrays of Tumor Overexpressed Gene (TOG) domains. The underlying mechanism of these arrays as microtubule polymerases remains unknown. Here, we describe the biochemical and structural basis for TOG domain arrays in recruiting and polymerizing tubulins. Alp14 binds four tubulins via dimeric TOG1-TOG2 arrays, each with distinct exchange rates. X-ray structures reveal pseudo-dimeric square-shaped assemblies in which four TOG domains position four unpolymerized tubulins in a polarized wheel-like configuration. Crosslinking confirms square assemblies form in solution, and inactivation of their interfaces destabilizes square organizations without influencing tubulin binding. Using an approach to modulate tubulin polymerization, we determined a X-ray structure showing an unfurled assembly in which TOG1 and TOG2 uniquely bind two polymerized tubulins. Our findings suggest a new microtubule polymerase model in which TOG arrays recruit tubulins by forming square assemblies, which then unfurl facilitating their concerted polymerization into protofilaments [1,2].

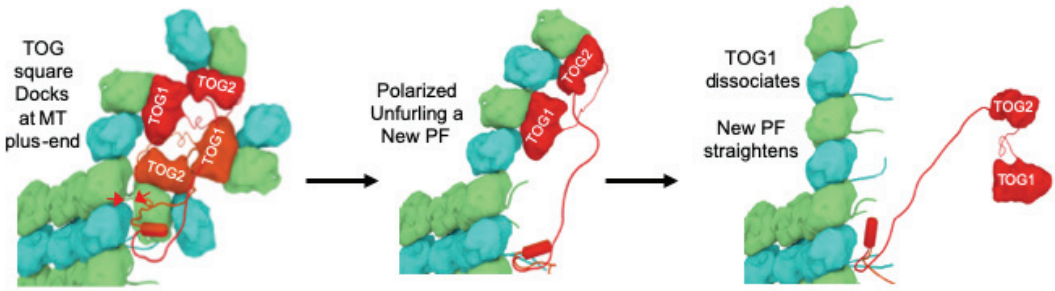

Fig. 1. A new microtubule polymerase model (MT, microtubule; PF, protofilament).

References
[1] Nithianantham, S. *et al.* (2018). *eLife*, **13**:e38922.
[2] Cook, B. D. *et al.* (2019). Mol Biol Cell, **10**: in press.