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Comment on "A Centrosome-Independent Role for γ-TuRC Proteins in the Spindle Assembly Checkpoint"

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Abstract

Müller *et al.* (Reports, 27 October 2006, p. 654) showed that inhibition of the γ-tubulin ring complex (γ-TuRC) activates the spindle assembly checkpoint (SAC), which led them to suggest that γ-TuRC proteins play molecular roles in SAC activation. Because γ-TuRC inhibition leads to pleiotropic spindle defects, which are well known to activate kinetochore-derived checkpoint signaling, we believe that this conclusion is premature.

The spindle assembly checkpoint (SAC) is an inhibitory signaling network that delays anaphase onset until all the chromosomes are stably attached to spindle microtubules (MTs) by their kinetochores (1–3). Recently, Müller *et al.* (4) proposed that, in addition to kinetochores, the SAC is regulated by the γ-tubulin ring complex (γ-TuRC), which is required for MT nucleation at centrosomes and within the spindle (5,6). They showed that RNA interference-mediated inhibition of γ-TuRC has pleiotropic effects on spindle assembly, yielding monopolar spindles or bipolar spindles lacking centrosomes, consistent with previous observations (7,8). This in turn delays mitotic progression in a SAC-dependent manner. The simplest explanation for SAC activation is that inhibition of γ-TuRC induces spindle defects that prevent kinetochores from achieving full MT occupancy and/or coming under tension. However, the authors argue that this simple explanation is not sufficient to explain their observations, stating that γ-TuRC–deficient cells show "abundant microtubule arrays with amphitelic-like chromosome microtubule attachment." Instead, they hypothesize that γ-tubulin is part of a signaling complex that triggers the SAC when γ-TuRC proteins are abrogated. SAC activation in γ-TuRC–deficient cells argues against the hypothesis that γ-tubulin is an activator of the SAC, although in a formal sense, γ-TuRC proteins act as negative regulators of the SAC, as is true of other structural proteins required for spindle assembly. The fact that the SAC is not activated after repression of centrosomin (cnn), which removes γ-tubulin from spindle poles, is consistent with the notion that centrosome integrity is not essential for spindle assembly or timely anaphase onset (9,

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10). However, in contrast to the authors' conclusion that γ-tubulin plays a direct role in the SAC, we favor the simple explanation, for two reasons. First, the presence of abundant microtubule arrays is not sufficient to inactivate the SAC. Second, although chromosomes may appear "amphitelic-like," this does not guarantee that all the kinetochores are stably attached to MTs. The following example illustrates these latter two points. Meta-phase cells treated with low doses of taxol or cooled to 23°C display normal bipolar MT arrays in which almost all the kinetochores are attached to microtubules from opposite spindle poles (i.e., "amphitelic-like"), yet in both cases, a SAC-dependent mitotic delay ensues (11,12). Indeed, because a single unattached kinetochore is sufficient to activate the SAC (13), the simplest explanation for the observations of Müller *et al.* is that inhibition of γ-TuRC perturbs spindle assembly and/or MT dynamics, which in turn results in inadequate levels of MT attachment and/or tension at all kinetochores, thereby activating the SAC and delaying mitotic progression.

References

1. Cleveland DW, Mao Y, Sullivan KF. Cell 2003;112:407. [PubMed: 12600307]
2. Musacchio A, Hardwick KG. Nat Rev Mol Cell Biol 2002;3:731. [PubMed: 12360190]
3. Taylor SS, Scott MI, Holland AJ. Chromosome Res 2004;12:599. [PubMed: 15289666]
4. Müller H, Fogeron ML, Lehmann V, Lehrach H, Lange BMH. Science 2006;314:654. [PubMed: 17068266]
5. Luders J, Patel UK, Stearns T. Nat Cell Biol 2006;8:137. [PubMed: 16378099]
6. Mahoney NM, Goshima G, Douglass AD, Vale RD. Curr Biol 2006;16:564. [PubMed: 16546079]
7. Colombie N, et al. Mol Biol Cell 2006;17:272. [PubMed: 16236791]
8. Raynaud-Messina B, Mazzolini L, Moisand A, Cirinesi AM, Wright M. J Cell Sci 2004;117:5497. [PubMed: 15479719]
9. Khodjakov A, Cole RW, Oakley BR, Rieder CL. Curr Biol 2000;10:59. [PubMed: 10662665]
10. Megraw TL, Kao LR, Kaufman TC. Curr Biol 2001;11:116. [PubMed: 11231128]
11. Shannon KB, Canman JC, Salmon ED. Mol Biol Cell 2002;13:3706. [PubMed: 12388768]
12. Waters JC, Chen RH, Murray AW, Salmon ED. J Cell Biol 1998;141:1181. [PubMed: 9606210]
13. Rieder CL, Cole RW, Khodjakov A, Sluder G. J Cell Biol 1995;130:941. [PubMed: 7642709]