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CELL CYCLE

Achieving entry

Whereas the accumulation of cyclins triggers mitotic entry in embryonic cells, the trigger in somatic cells has been elusive. Reporting in *Science*, Guowei Fang and colleagues now show that Bora, a protein that participates in asymmetric cell division, and the kinase Aurora A synergistically activate Polo-like kinase-1 (PLK1) and thereby induce mitotic entry in somatic cells.

Several studies have suggested that activation of PLK1, which results in downstream activation of cyclin-dependent kinase-1 (CDK1), probably initiates mitotic entry in somatic cells. In support of this model, Fang and colleagues found that PLK1 accumulates in early G2 phase, but is only phosphorylated on Thr210, and thereby activated, in late G2, immediately before mitosis.

To determine how PLK1 activation is controlled, the authors suppressed the expression of genes that are upregulated during G2. Notably, they found that Bora is an important regulator of the G2–M transition, and depletion of Bora delayed PLK1 phosphorylation and activation. As the conserved sequence around Thr210 of PLK1 matches the consensus site that is phosphorylated by Aurora A, the authors examined the effects of Bora and Aurora A on PLK1 activity *in vitro*. Whereas Bora alone had no effect on PLK1 activity and Aurora A alone had only a minimal effect, Bora and Aurora A together increased the activation of PLK1 by seven- to ninefold.

Analysis of the structural relationship between Bora and PLK1 indicated that Bora probably controls the accessibility of Thr210, allowing the authors to propose a mechanism for the synergistic activation of PLK1 by Bora and Aurora A. During interphase, they propose, PLK1 is locked in an unphosphorylated, inactive state. Induction of Bora expression and binding between Bora and PLK1 during G2 results in a structural change that makes Thr210 accessible for phosphorylation by Aurora A. Active PLK1 then initiates a positive-feedback loop, also involving CDC25 and CDK1, that results in mitotic entry.

Notably, this Bora- and Aurora-A-dependent regulatory circuit appears to be evolutionary conserved, as the authors show that Plx1, the *Xenopus laevis* homologue of PLK1, also requires both Bora and Aurora A for activation.

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ORIGINAL RESEARCH PAPER Seki, A. *et al.* Bora and the kinase Aurora A cooperatively activate the kinase Plk1 and control mitotic entry. *Science* **320**, 1655–1658 (2008)