CELL CYCLE

# ARPC1B — a regulator of regulators

> “the cytoskeletal remodelling protein ARPC1B … binds and activates Aurora A and is a novel regulator of centrosome integrity”

The Aurora family of cell cycle kinases regulates centrosome stability and thus influences cell cycle progression. Cytoskeletal remodelling proteins such as p21-activated kinase 1 (PAK1) have been predicted to regulate mitosis by activating Aurora A, although it has been unclear how. In the *Journal of Cell Biology*, Molli *et al.* provide evidence that the cytoskeletal remodelling protein ARPC1B, a component of the actin-related protein 2/3 (ARP2/3) complex, binds and activates Aurora A and is a novel regulator of centrosome integrity.

Having previously identified ARPC1B as a substrate of PAK1 during mitosis, the authors tested the hypothesis that ARPC1B is involved in cell cycle regulation. They discovered that overexpression of ARPC1B in breast cancer cells increased their tumorigenicity and resulted in centrosome amplification, a classic hallmark of Aurora A activity. Indeed, ARPC1B was found to localize to centrosomes and interact directly with Aurora A. Several lines of evidence suggest that the association between the proteins occurred independently of the full ARP2/3 complex.

Next, the authors investigated whether ARPC1B stimulates the activity of Aurora A. Using *in vitro* kinase assays, they established that ARPC1B stimulates Aurora A activity through phosphorylation of its autoregulatory site, Thr288, and that knockdown of ARPC1B inhibits Aurora A activity in cells. Mutation of Thr21 to Ala in ARPC1B reduced the binding and activation of Aurora A, suggesting that this site is important in mediating the ARPC1B–Aurora A association. Small interfering RNA-mediated depletion of ARPC1B impaired G2–M phase cell cycle progression and resulted in reduced activation of Aurora A on the centrosome compared with cells in which ARPC1A and ARP3 were depleted. Knockdown of Aurora A similarly reduced the number of cells in G2–M phase. Collectively, these results suggest that inhibition of G2–M progression on ARPC1B depletion may be due to reduced activation of Aurora A.

Interestingly, the authors found that in addition to activating Aurora A, ARPC1B is a substrate of this kinase. Aurora A phosphorylated ARPC1B on Thr21, the regulatory residue phosphorylated by PAK1 and required for Aurora A binding. Depletion of Aurora A in *PAK1*$^{-/-}$ mouse embryonic fibroblasts led to reduced phosphorylation of ARPC1B and disruption of the ARP2/3 complex, suggesting that Aurora A and ARPC1B are intimately linked in a feedback mechanism.

These findings identify a new regulator of centrosome homeostasis and show that ARPC1B is both an activator and a substrate of Aurora A, and is thus a new player in the complex regulatory network that maintains centrosome integrity during mitosis.

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**ORIGINAL RESEARCH PAPER** Molli, P. R. *et al.* Arpc1b, a centrosomal protein, is both an activator and substrate of Aurora A. *J. Cell. Biol.* **190**, 101–114 (2010)