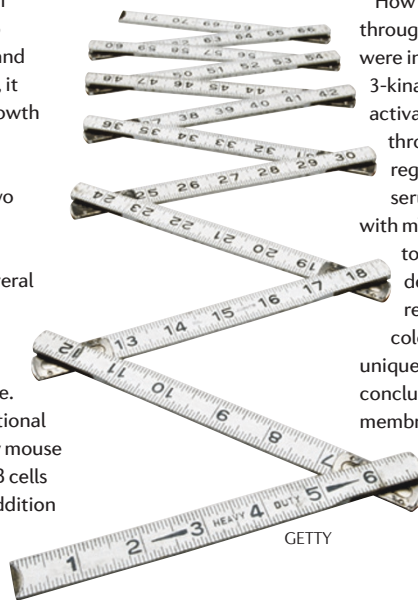


CELL GROWTH

RAC1 sizes up mTOR

RAC RhoGTPases are factors of many talents when it comes to choreographing cytoskeletal and adhesion dynamics. But RAC1, it seems, can also control cell growth through mammalian target of rapamycin (mTOR) signalling.

The mTOR kinase works in two complexes, mTOR complex 1 (mTORC1) and mTORC2, to regulate cell size; although several factors that mediate signalling through mTORC1 have been characterized, the control of mTORC2 has been more elusive. Saci *et al.* observed that conditional deletion of RAC1 from primary mouse embryonic fibroblasts (MEFs), B cells or T cells reduced cell size in addition to its expected effects on the



actin cytoskeleton. This reduced cell size in the absence of RAC1 correlated with disrupted mTOR signalling: RAC1 deletion inhibited the mTORC1- and mTORC2-mediated phosphorylation of key substrates in several cell types.

How does RAC1 affect signalling through both mTORCs? Its effects were independent of phosphoinositide 3-kinase (a known regulator of mTOR activation) and of RAC1 activation through GTP binding. Instead, RAC1 regulated mTOR localization: upon serum stimulation, RAC1 relocalized with mTOR from the perinuclear region to the plasma membrane, and deletion of RAC1 disrupted mTOR relocalization. By assessing the colocalization of subunits that are unique to each complex, the authors concluded that RAC1 promotes the membrane localization of both mTORC1 and mTORC2. Consistent with the observation that RACGTP binding is not important for this role, the effects of RAC1

on mTOR membrane localization were independent of its ability to promote actin polymerization. Furthermore, the authors showed that RAC1 associated with both common and distinct components of mTORC1 and mTORC2, and that this did not require GTP binding by RAC1. Instead, this relied on an intact carboxyl terminus of RAC1 that bound directly to mTOR itself.

RAC1 is the first common regulator of mTORC1 and mTORC2 to be identified, and it will be important to work out how it cooperates with other regulators of mTOR signalling and how this role in growth signalling is integrated with its many other roles.

Alison Schuldt

ORIGINAL RESEARCH PAPER Saci, A., Cantley, L. C. & Carpenter, C. L. Rac1 regulates the activity of mTORC1 and mTORC2 and controls cellular size. *Mol. Cell* **42**, 50–61 (2011)

FURTHER READING Zoncu, R., Efeyan, A. & Sabatini, D. M. mTOR: from growth signal integration to cancer, diabetes and ageing. *Nature Rev. Mol. Cell Biol.* **12**, 21–35 (2011)