

Journal club



LOCALIZING CELLULAR HOUSEKEEPING

It is now well established that cellular 'housekeeping' activities, such as protein synthesis, take place at specific sites to control local signalling. Indeed, when I was working on my Ph.D., the first reports of mRNA transport to the distant ends of neurons, allowing protein synthesis far away from the cell body, were published. With respect to cell migration, almost 20 years ago the Singer laboratory showed that β -actin mRNA is targeted to the leading edge of fibroblasts to enable local actin synthesis. Later, the idea of targeted protein synthesis in cell migration was expanded by Mingle *et al.* They showed that the mRNAs encoding the seven proteins constituting the actin-related protein 2/3 (ARP2/3) complex, which drives actin polymerization, are targeted to

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cellular protrusions in fibroblasts, precisely where these proteins are needed for motility.

Conversely, the breakdown of signalling proteins also occurs at defined locations. In a 2003 landmark paper by Wang *et al.*, this was demonstrated for the RHO GTPase RHOA, one of the key regulators of cell polarity, cell division and chemotaxis. The authors showed that RHOA is targeted for ubiquitylation and degradation by the E3 ubiquitin ligase SMAD ubiquitylation regulatory factor 1 (SMURF1), and that loss of SMURF1 leads to a marked accumulation of RHOA in cellular protrusions. Moreover, the CDC42-partitioning defective 6-protein kinase C ζ polarity complex recruits SMURF1 to filopodia and lamellipodia, linking protein degradation to the control of cell polarity.

In general, RHO GTPases are depicted as being recycling on-off switches that are inactivated upon GTP hydrolysis. Extending this

'dogma', the SMURF1 story was the first in a growing number of papers underscoring the notion that local ubiquitylation and degradation represents an additional way to terminate GTPase signalling. So, just as we have specific places to wash our dishes, our cars and even ourselves, a cell does its housekeeping at just the right site.

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The author declares no competing financial interests.

ORIGINAL RESEARCH PAPERS Kislauskis, E. H., Zhu, X. & Singer, R. H. Sequences responsible for intracellular localization of β -actin messenger RNA also affect cell phenotype. *J. Cell Biol.* **127**, 441–451 (1994) | Mingle, L. A. *et al.* Localization of all seven messenger RNAs for the actin-polymerization nucleator Arp2/3 complex in the protrusions of fibroblasts. *J. Cell Sci.* **118**, 2425–2433 (2005) | Wang, H. R. *et al.* Regulation of cell polarity and protrusion formation by targeting RhoA for degradation. *Science* **302**, 1775–1779 (2003)