CELL POLARITY

APC throws the anchor

Although RNA localization is known to be important for establishing and maintaining cell polarity, there have been few comprehensive studies of RNA localization in mammalian cells. As reported in *Nature*, Ian Macara and colleagues have now identified the RNAs that accumulate at cell protrusions through an unanticipated mechanism involving the adenomatous polyposis coli (APC) tumour suppressor protein.

Using a fractionation method combined with Affymetrix GeneChip arrays, the authors identified approximately 50 RNAs that preferentially localized to the pseudopodial protrusions of fibroblasts exposed to migratory stimuli. Two of these mRNAs — *Rab13* and *Pkp4* (plakophilin 4) — were chosen to study the mechanism of localization. *Rab13* mRNAs containing the open reading frame and the 3'-untranslated region (3'-UTR) were enriched in pseudopodia, but lost this localization when the 3'-UTR was replaced with that of another non-pseudopodial localized gene. Moreover, fusion of the *Rab13* 3'-UTR to the non-localized β -globin mRNA resulted in β -globin being recruited to pseudopodia, showing that *Rab13* 3'-UTR is necessary and sufficient to direct RNA accumulation in pseudopodia. To analyse this localization in live cells, the authors inserted 24 repeats of the MS2 phage coat protein-binding sites between the β -globin region and the *Rab13* 3'-UTR. This reporter RNA could be indirectly visualized on co-expression with an MS2-green fluorescent protein (GFP) fusion that binds to the 24 repeats, and thus accompanied the RNA to the cytoplasm. The authors observed that the GFP signal concentrated in granules at the tips of protrusions and that the *Pkp4* 3'-UTR conferred a similar localization. Fluorescence recovery after photobleaching experiments indicated that the RNAs were stably sequestered in these granules.

But what are the cellular structures that anchor transcripts at pseudopodial tips? Expression of fluorescently tagged markers for various structures revealed that the granules were attached to microtubule plus ends. This association was specific for stable microtubules that did not exhibit dynamic instability, a finding consistent with the granules being relatively stationary.

The APC tumour suppressor is known to bind to plus ends of stable microtubules that grow into migrating cell protrusions. The authors found that APC co-localized with the RNA granules, and that both *Rab13* and *Pkp4* transcripts associated with endogenous APC. Furthermore, APC knockdown reduced the number of these transcripts in pseudopodia, showing that APC mediates RNA accumulation and anchoring in protrusions.

This work identifies — on a genome-wide scale — the RNAs that are asymmetrically distributed in migrating cells, and shows that APC anchors RNAs with specific 3'-UTRs to microtubule plus ends at pseudopodial tips. However, whether the effects of APC on cell polarization and migration are due to its RNA-anchoring function remains to be determined.

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[Cell Migration Gateway](#)

ORIGINAL RESEARCH PAPER Mili, S., Moissoglu, K. & Macara, I. G. Genome-wide screen reveals APC-associated RNAs enriched in cell protrusions. *Nature* 453, 115–119 (2008)