IN BRIEF

TELOMERES

A template trigger for translocation

The telomerase ribonucleoprotein enzyme maintains eukaryotic chromosomes through unique means. Its telomerase reverse transcriptase (TERT) enzymatic subunit synthesizes telomeric DNA repeats from the template RNA subunit (TER) by 'repeat addition processivity'. How telomerase recycles this internal template, and how the template progresses through the TERT active site, was unclear. Berman *et al.* addressed these questions in *Tetrahymena thermophila*. They used biochemical assays to assess which regions of TER are important for enzyme activity and assayed changes in RNA conformation during the enzymatic cycle using single molecule fluorescence resonance energy transfer. They propose that the RNA template actively drives translocation through the TERT active site by an 'accordion' movement, in which the RNA sequences that flank the template ensure its correct position and translocation.

ORIGINAL RESEARCH PAPER Berman, A. J. *et al.* The RNA accordion model for template positioning by telomerase RNA during telomeric DNA synthesis. *Nature Struct. Mol. Biol.* 20 Nov 2011 (doi:10.1038/nsmb.2174)

CELL POLARITY

A scaffolding spindle guide

During asymmetric cell division in *Drosophila melanogaster* neuroblasts, Partner of Inscuteable (PINS) at the apical cortex mediates spindle orientation through two pathways, one of which requires MUD (Mushroom body defect). Wee *et al.* reveal that the scaffolding protein Canoe (called afadin or AF6 in mammals), which also regulates spindle orientation, does so by directly interacting with PINS and MUD. They show that, in *D. melanogaster* S2 cells, Canoe binds directly to RAN·GTP; this interaction is important for the localization of MUD to the cortex, where it interacts with PINS to mediate spindle orientation. Canoe also binds the tetratricopeptide (TPR) domain of PINS, which promotes recruitment of Canoe to the cortex, where it can activate the PINS–MUD-mediated spindle orientation pathway. Wee *et al.* speculate that RAN·GTP may release MUD from importins to allow its interaction with PINS. This mechanism might have broad significance, given that many of these pathway components are conserved in mammals.

ORIGINAL RESEARCH PAPER Wee, B. *et al.* Canoe binds RanGTP to promote PinsTPR/Mud-mediated spindle orientation. *J. Cell Biol.* **195**, 369–376 (2011)

MECHANISMS OF DISEASE

p53 puts a damper on WNT signalling

Kim *et al.* reveal why loss of the p53 tumour suppressor protein correlates with the activation of WNT signalling in cancer. During WNT signalling, WNT stabilizes β-catenin, which forms a complex with T cell factor and lymphoid enhancer factor (TCF/LEF)-family transcription factors. Here, the authors found that p53, as well as the microRNA miR-34 family, which are transcriptional targets of p53, inhibited WNT signalling. Genes in the WNT pathway, including the genes encoding WNT1 and β-catenin, were identified as direct miR-34 targets, and knockdown of p53 reduced miR-34 levels and increased WNT signalling output. Furthermore, analysis of breast cancer samples showed that genes predicted to be increased when miR-34 activity is low correlated with signatures of high β-catenin–TCF/LEF activity and mutant p53. Thus, p53 negatively regulates WNT signalling through miR-34. This helps to explain why WNT signalling is activated in tumours lacking functional p53.

ORIGINAL RESEARCH PAPER Kim, N. H. *et al.* p53 and microRNA-34 are suppressors of canonical Wnt signaling. *Sci. Signal.* **4**, ra71 (2011)