IN BRIEF

BREAST CANCER

Profiling the profilins

The different isoforms of profilin are known regulators of actin polymerization, and Joan Brugge and colleagues now show that profilin isoforms 1 and 2 have opposing functions in regulating cell migration and invasion. Unlike profilin 1, profilin 2 engages an ENA/VASP protein, EVL, and reduces membrane protrusion and cell migration through an actomyosin contractility mechanism. Downregulation of profilin 2 or EVL induces migration and invasion in cell lines, and reduced expression of these proteins correlates with invasive disease and a poor prognosis in patients with breast cancer.

ORIGINAL RESEARCH PAPER Mouneimne, G. *et al.* Differential remodeling of actin cytoskeleton architecture by profilin isoforms leads to distinct effects on cell migration and invasion. *Cancer Cell* **22**, 615–630 (2012)

COLORECTAL CANCER

YAP limits expansion

Yes-associated protein 1 (YAP) promotes proliferation and is oncogenic, but Barry *et al.* have shown that YAP can also limit tissue expansion. Transgenic expression of *Yap* in the mouse intestinal tract results in increased WNT signalling along with the loss of intestinal crypts. Conversely, loss of *Yap* during intestinal regeneration resulted in hypersensitivity to WNT, expansion of intestinal stem and niche cells, as well as microadenoma formation. By restricting Dishevelled (DVL) to the cytoplasm, YAP limits the nuclear activity of DVL, which promotes WNT signalling. YAP expression is lost in a subset of aggressive and undifferentiated human colorectal carcinomas.

ORIGINAL RESEARCH PAPER Barry, E. R. *et al.* Restriction of intestinal stem cell expansion and the regenerative response by YAP. *Nature* 25 Nov 2012 (doi:10.1038/nature11693)

MICROENVIRONMENT

CAFs and miRNAs

Miltra *et al.* investigated whether microRNA (miRNA) expression is altered in cancer-associated fibroblasts (CAFs) isolated from patients with ovarian cancer. They found that miR-31 and miR-214 were downregulated and that miR-155 was upregulated. Mimicking these changes in normal fibroblasts resulted in their conversion to a CAF-like phenotype, and blocking these miRNA alterations in CAFs reverted them to a normal phenotype. Gene expression profiling revealed alterations in the expression of chemokine genes, including *CCL5*, which the authors found to be a target of miR-214.

ORIGINAL RESEARCH PAPER Miltra, A. K. *et al.* MicroRNAs reprogram normal fibroblasts into cancer-associated fibroblasts in ovarian cancer. *Cancer Discov.* 21 Nov 2012 (doi: 10.1158/2159-8290.CD-12-0206)

GENOMIC INSTABILITY

A U-turn for mutagenesis?

Replication restart from collapsed replication forks can be mutagenic. Mizuno *et al.* studied replication restart in fission yeast. They found that even when replication restart occurs correctly, if the replication fork encounters a palindromic sequence within the first few kilobases, then the replication machinery occasionally makes a U-turn, generating rearranged daughter chromosomes with absent or multiple centromeres. Such a mechanism might contribute to chromosomal rearrangements and copy number alterations in cancer.

ORIGINAL RESEARCH PAPER Mizuno, K. *et al.* Recombination-restarted replication makes inverted chromosome fusions at inverted repeats. *Nature* 25 Nov 2012 (doi:10.1038/nature11676)