RESEARCH HIGHLIGHTS

Stem and cancer cells Wnt long telomeres

Stem cells, similarly to cancer cells, possess long telomeres. Although telomerase (TERT) is known to control telomere length, the mechanisms regulating its expression have not been fully elucidated. Kemler and colleagues reveal that the Wnt–β-catenin pathway — which regulates pluripotency in stem cells and is commonly dysregulated in cancers — directly promotes *TERT* expression in both of these biological contexts (*Science* **336,** 1549–1554; 2012).

The authors found that β-catenin activity directly correlated with *Tert* expression in mouse embryonic stem cells. Chromatin immunoprecipitation assays revealed that β-catenin bound to the *Tert* promoter and recruited chromatin remodelling factors and active RNA polymerase II. Wnt3a enhanced this interaction. Interestingly, the transcription factor Klf4, which regulates both pluripotency and tumorigenesis, was necessary for efficient β-catenin accumulation at the *Tert* promoter. β-catenin was also identified at the *Tert* promoter in adult intestinal stem cells and primary neurospheres.

In a mouse model of β-catenin-driven intestinal hyperplasia, β-catenin was shown to accumulate at the *Tert* promoter, along with RNA Pol II. This accumulation was also seen in human embryonal carcinoma and colorectal carcinoma cell lines. However, β-catenin depletion decreased h*TERT* levels in these cells. These results offer direct evidence that β-catenin promotes *TERT* expression in stem and cancer cells, revealing an intriguing mechanistic link between tumorigenesis and pluripotency. EJC

Synchronizing actin and microtubules for axonal branching

Sprouting of axon branches from the axonal shaft involves the formation of F-actin-based filopodia that are invaded by microtubules. Spiliotis and colleagues show that septins, proteins known to interact with both actin and microtubules, coordinate these two networks to achieve such collateral axonal branching (*Curr. Biol.* **22,** 1109–1115; 2012).

Septins 6 and 7 (SEPT6 and SEPT7) were previously implicated in dendritic morphogenesis. By manipulating SEPT6 and SEPT7 levels in chick embryo dorsal root ganglia neurons, the authors established that they are both required for collateral axon branching. However, further analyses demonstrated that SEPT6 and SEPT7 have distinct axonal localizations and functions. SEPT6 accumulates at axonal F-actin patches, the regions of filopodia and axonal branching initiation, where it regulates filopodia formation by increasing the recruitment of cortactin, an activator of Arp2/3-dependent actin polymerization. In contrast, SEPT7 alters the organization of the axonal cytoskeleton to mediate the entry of microtubules into filopodia. Although the precise mechanisms through which SEPT6 and SEPT7 achieve these effects remain to be elucidated, these findings highlight septins as cytoskeletal regulators that are able modulate both the actin and microtubule cytoskeletons for formation of collateral axon branches. AIZ

BRCA2 in abscission

The tumour suppressor BRCA2 functions in DNA repair but has also been suggested to regulate cytokinesis. This role, however, as well as its localization at the midbody, has remained controversial. Couch and colleagues demonstrate that BRCA2 recruits regulators of abscission to the midbody (*Dev. Cell* **23,** 137–152; 2012).

Using several antibodies, siRNAs (small interfering RNAs) and cells from BRCA2-knockout mice, the authors confirm that BRCA2 localizes to the central spindle and midbody, and that its loss causes cytokinesis failure. The midbody localization of BRCA2 is dependent on a previously identified interaction with the actin-binding protein filamin A. In the absence of BRCA2, cytokinesis regulators (such as MKLP1, MKLP2, PRC1, Alix, Tsg101 and endobrevin) are mislocalized, and biochemical analyses reveal that BRCA2 promotes the formation of complexes of the abscission-regulator CEP55 with ESCRT-associated proteins Alix and Tsg101 in mitosis. The authors thus propose that BRCA2 acts as a scaffold to assemble part of the cytokinesis machinery at the midbody. Importantly, a BRCA2 deletion mutant lacking DNA repair function is able to rescue cytokinesis defects induced by BRCA2 loss. The authors also identify a missense mutation in BRCA2 that disrupts filamin A binding and midbody localization but retains DNA repair capacity, showing that the functions are separable. Whether specific disruption of the cytokinesis function of BRCA2 plays a role in cancer is an interesting question for the future. CKR

Watching hair grow

Following cell behaviour *in vivo* should help unravel the ways in which tissues regenerate. Greco and colleagues use intravital two-photon imaging to examine hair follicle regeneration, and observe a combination of oriented divisions and migrations of stem cell progeny that accompany hair growth (*Nature* http://doi.org/h3n; 2012). They follow, over time, the epithelial nuclei in skin of anesthetized transgenic mice expressing histone H2B–GFP driven by the keratin-14 promoter. Hair follicle stem cells are located in the bulge at the base of the follicles, and their immediate progeny are found below the bulge and above the mesenchymal dermal papilla. The authors find that, during hair regeneration, the stem cell progeny are the first to proliferate, with their mitotic spindles globally oriented along the long axis of the hair follicle, whereas stem cells themselves divide at lower rates and in random orientation. They also observe that the stem cell progeny extend downwards, as distance between their nuclei increases, and that the cells closer to the mesenchyme realign in a synchronized fashion to encircle each individual dermal papilla. Signals from the dermal papilla are known to activate the bulge stem cell progeny at each hair regeneration cycle, and the authors show that laser-mediated ablation of a dermal papilla impairs hair growth. Further studies using this live imaging system will allow a better understanding of how the dermal papilla influences the division, orientation and movement of stem cell progeny. NLB

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