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See commentary, p. 1018
### CDKN2B Loss Promotes Progression from Benign Melanocytic Nevus to Melanoma


**Précis:** The BRAFV600E-induced, TGFβ-dependent upregulation of p15 causes growth arrest of melanocytic nevi, which can(488,1336),(545,1363) be reversed by p15 loss to drive melanomagenesis both in vitro and in vivo.

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### Pancreatic Cancer Metastases Harbor Evidence of Polyclonality

R. Maddipati and B.Z. Stanger

**Précis:** Lineage tracing experiments in an autochthonous mouse model implicate polyclonal seeding and metastatic site–specific clonal outgrowth in PDAC progression.

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### Regulatory T-cell Response to Enterotoxigenic Bacteroides fragilis Colonization Triggers IL17-Dependent Colon Carcinogenesis


**Précis:** Regulatory T cells drive differentiation of procarcinogenic Th17 cells and promote the early stages of colon tumorigenesis in response to bacterial infection.

See commentary, p. 1021

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**Regulatory T-cell Response to Enterotoxigenic Bacteroides fragilis Colonization Triggers IL17-Dependent Colon Carcinogenesis**


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See commentary, p. 1021

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**ON THE COVER**

Geis and colleagues found that depletion of regulatory T cells (Treg) unexpectedly impaired early microadenoma formation in multiple intestinal neoplasia mice colonized by the bacterium enterotoxigenic Bacteroides fragilis (ETBF). This reduction in neoplastic growth was accompanied by a decrease in Th17 cells and IL17 production and an increase in the IFNγ-producing Th1 cell population, suggesting that Tregs modulate the balance of Th1/Th17 cells. Treg consumption of IL2 resulted in an increase in Th17 polarization and a subsequent decrease in the Th1 population following ETBF colonization, consistent with a cell-extrinsic role for Tregs in promoting Th17 differentiation. These results demonstrate that Tregs drive Th17 polarization to establish pro-tumorigenic colitis and are necessary for the early stages of tumorigenesis in colitis-associated colorectal cancer. For details, please see the article by Geis and colleagues on page 1098.