



## Alternative Splicing Associated with Metastatic Colonization

Lu *et al.* \_\_\_\_\_ Page 305

Alternative pre-mRNA splicing plays a critical role in cancer development, progression, and metastasis. To elucidate alternative splicing events associated with cancer metastasis, Lu and colleagues carried out comprehensive transcriptome analyses of cancer cells derived from *in vitro* and *in vivo* models of metastatic colonization. Deep RNA sequencing revealed an extensive splicing regulatory network involving multiple splicing factors and their downstream targets that affect the invasiveness and metastatic behavior of cancer cells. These findings underscore the importance of alternative splicing in cancer metastasis, and suggest possible molecular biomarkers and therapeutic targets.

## A Mechanism That Produces Slowly Proliferating Cancer Cells

Dey-Guha *et al.* \_\_\_\_\_ Page 223

The proliferative heterogeneity within human tumors complicates the diagnosis and treatment of cancer patients because slow proliferators are hard to eradicate, can be difficult to detect, and may cause disease relapse sometimes years after apparently curative treatment. Here, Dey-Guha and colleagues identify a novel  $\beta$ 1-integrin-associated signaling pathway that rapidly proliferating cancer cells occasionally trigger to divide asymmetrically and produce a slowly proliferating daughter cell. These findings reveal a targetable mechanism for reducing the proliferative heterogeneity within cancer cell populations and have broad implications for understanding cancer progression, dormancy, and therapeutic resistance.

## TRIML2 Enhances p53-Mediated Apoptosis

Kung *et al.* \_\_\_\_\_ Page 250

Over 30 years after the discovery of p53, the critical regulators of its "life versus death" decision still remain unclear. Whereas clear data indicate that a common polymorphism in p53 (proline 72 or arginine 72) influences this decision, the underlying basis is not understood. Kung and colleagues identify *TRIML2* as a gene that is preferentially induced by the arginine 72 variant of p53. Furthermore, *TRIML2* interacts with p53 and induces SUMOylation of this protein. This facilitates the ability of p53 to transactivate specific proapoptotic target genes, thus revealing a novel mediator of p53-mediated apoptosis.

## ERG Inhibits ANXA2 Expression and Function in CaP

Griner *et al.* \_\_\_\_\_ Page 368

Annexin A2 (*ANXA2*) expression is high in normal prostate glands, becomes lost in low-grade tumors, but reemerges in advanced tumors. Examination of primary prostate cancer specimens by Griner and colleagues, using immunocytochemistry and gene expression analysis, revealed a reciprocal relationship of *ANXA2* and *ERG*. In a majority of cases, *ANXA2* was absent or reduced in well-differentiated *ERG*-positive tumors but was expressed at moderate to high levels in *ERG*-negative tumors with poorly differentiated features. This reciprocal association is demonstrated by mechanistic studies to be mediated by the transcriptional repression of *ANXA2* by *ERG* and will be helpful for the stratification of patients.