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 β1-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.