Janus Kinase 3–Activating Mutations Identified in Natural Killer/T-cell Lymphoma


Précis: The presence of activating JAK3 mutations in 35.4% of natural killer/T-cell lymphomas suggests that JAK inhibition may be an effective therapeutic strategy.

Chimeric Transcript Generated by cis-Splicing of Adjacent Genes Regulates Prostate Cancer Cell Proliferation

Y. Zhang, M. Gong, H. Yuan, H.G. Park, H.F. Frierson, and H. Li

Précis: RNA transcription across the SLC45A3–ELK4 gene boundary results in a putative oncogenic fusion product in the absence of chromosomal rearrangements.

The HIF-1α Hypoxia Response in Tumor-Infiltrating T Lymphocytes Induces Functional CD137 (4-1BB) for Immunotherapy


Précis: Selective expression of CD137 by tumor-infiltrating lymphocytes in response to hypoxia can be targeted with anti-CD137 immunotherapy.
A Bioluminescent Transposon Reporter-Trap Identifies Tumor-Specific Microenvironment-Induced Promoters in Salmonella for Conditional Bacterial-Based Tumor Therapy .......... 624
Précis: Tumor colonization by Salmonella and activation of Salmonella genes in response to the tumor microenvironment can be exploited for tumor-specific expression of toxic transgenes.

The Transcription Factor ZNF217 Is a Prognostic Biomarker and Therapeutic Target during Breast Cancer Progression ................. 638
Précis: ZNF217 overexpression in breast cancer is associated with poor survival and response to neoadjuvant chemotherapy but may be a predictor of triciribine efficacy.

Zhang and colleagues observed that transcription occurs across the boundary of 2 adjacent genes, solute carrier family 45, member 3 (SLC45A3) and ETS-domain protein SRF accessory protein 1 (ELK4), in prostate cancers in association with decreased CCCTC-binding factor (CTCF) occupancy at intergenic insulator sequences. Multiple prostate cancer cell lines were dependent on SLC45A3-ELK4 expression, and chimeric SLC45A3-ELK4 RNA levels correlated with Gleason score. These findings establish cis-splicing as a mechanism by which oncogenic gene fusions can potentially occur and implicate SLC45A3-ELK4 as a putative driver of prostate cancer development. For details, please see the article by Zhang and colleagues on page 598.

For more News and Research Watch, visit Cancer Discovery online at http://CDnews.aacrjournals.org. Online-only News stories include the following:
• T-DM1 "Smart Bomb" Hits Breast Cancer Targets
• Neoadjuvant Drug Combination Eliminates Some Prostate Tumors
• BRAF and MEK Inhibitors Offer Good News in Melanoma
• Anti-PD-1 Drug Shows Strong Promise
• Pushing the Science of Prostate Screening
• Aggressive Pediatric Cancers Respond to ALK Inhibitor

ON THE COVER
Zhang and colleagues observed that transcription occurs across the boundary of 2 adjacent genes, solute carrier family 45, member 3 (SLC45A3) and ETS-domain protein SRF accessory protein 1 (ELK4), in prostate cancers in association with decreased CCCTC-binding factor (CTCF) occupancy at intergenic insulator sequences. Multiple prostate cancer cell lines were dependent on SLC45A3-ELK4 expression, and chimeric SLC45A3-ELK4 RNA levels correlated with Gleason score. These findings establish cis-splicing as a mechanism by which oncogenic gene fusions can potentially occur and implicate SLC45A3-ELK4 as a putative driver of prostate cancer development. For details, please see the article by Zhang and colleagues on page 598.