IL35-Producing B Cells Promote the Development of Pancreatic Neoplasia


Précis: B cells are recruited to the pancreas during PDAC initiation and support tumor growth through IL35-mediated signaling.

See commentary, p. 230
See related article, p. 247
See related article, p. 256

Hif1α Deletion Reveals Pro-neoplastic Function of B Cells in Pancreatic Neoplasia


Précis: HIF1α prevents PDAC initiation by suppressing protumorigenic B cell recruitment to the pancreas, which is required for PDAC progression.

See commentary, p. 230
See related article, p. 247
See related article, p. 256

Bruton Tyrosine Kinase–Dependent Immune Cell Cross-talk Drives Pancreas Cancer


Précis: Inhibition of PI3Kγ/BTK signaling between B cells and FcγR-positive macrophages reactivates T cell–dependent immune responses and suppresses PDAC tumor growth in mice.

See commentary, p. 230
See related article, p. 247
See related article, p. 256

B Cells Promote Pancreatic Tumorigenesis

A. Roghanian, C. Fraser, M. Kleyman, and J. Chen

See article, p. 247
See article, p. 256
See article, p. 270

Progress on Covalent Inhibition of KRASG12C

K.D. Westover, P.A. Jänne, and N.S. Gray

See article, p. 316

miRNA Deregulation in Cancer Cells and the Tumor Microenvironment

R. Rupaimoole, G.A. Calin, G. Lopez-Berestein, and A.K. Sood

See related article, p. 247
See related article, p. 256
Application of Sequencing, Liquid Biopsies, and Patient-Derived Xenografts for Personalized Medicine in Melanoma ... 286


Précis: Next-generation sequencing of circulating tumor DNA can be used to monitor response to therapy and identify potential treatment strategies, which can be validated in patient-derived or circulating tumor cell-derived xenografts.

Oncogenic BRAF Deletions That Function as Homodimers and Are Sensitive to Inhibition by RAF Dimer Inhibitor LY3009120 ... 300


Précis: Previously unidentifiable BRAF in-frame deletions promote the formation of homodimers, which activate MAPK signaling and are sensitive to LY3009120.

Selective Inhibition of Oncogenic KRAS Output with Small Molecules Targeting the Inactive State .................................. 316


Précis: Mutant KRASG12C exhibits a dynamic nucleotide state that is responsive to upstream signaling, and its activation can be selectively and potently suppressed by small-molecule binding to the GDP-bound state.

See commentary, p. 233

Correction

Correction: Response to MET Inhibitors in Patients with Stage IV Lung Adenocarcinomas Harboring MET Mutations Causing Exon 14 Skipping ........................................... 330

Patricelli, Janes, and colleagues identified a small-molecule covalent inhibitor of mutant KRASG12C, ARS-853, that selectively bound to the GDP-bound, inactive protein and prevented formation of the GTP-bound state. ARS-853 blocked downstream mutant KRAS-driven signaling via the MAPK and PI3K pathways and inhibited the growth of KRASG12C-mutant cells. KRASG12C rapidly cycled its nucleotide state, allowing for effective binding of ARS-853, and KRASG12C–GTP levels were regulated by upstream signaling factors, suggesting that combined targeting of upstream activators may enhance the efficacy of single-agent KRASG12C inhibition. These findings indicate that ARS-853 blocks oncogenic KRASG12C signaling and has promise as a potential therapeutic for KRASG12C-mutant cancer. For details, please see the article by Patricelli, Janes, and colleagues on page 316.