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.
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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.
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Bruton Tyrosine Kinase–Dependent Immune Cell Cross-talk Drives Pancreas Cancer
Précis: Inhibition of PI3Kγ/BTK signaling between B cells and FcγRI-positive macrophages reactivates T cell–dependent immune responses and suppresses PDAC tumor growth in mice.
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B Cells Promote Pancreatic Tumorigenesis
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Progress on Covalent Inhibition of KRASG12C
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Application of Sequencing, Liquid Biopsies, and Patient-Derived Xenografts for Personalized Medicine in Melanoma


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


Précis: Previously unidentified 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


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.

Correction

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

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.