Clinical Cancer Research
Highlights
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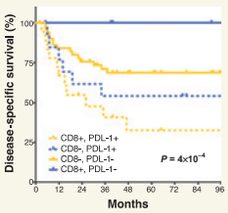
Selected Articles from This Issue

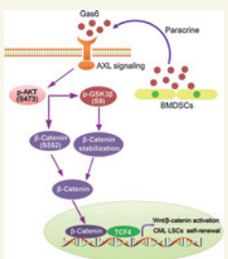
PD-L1 and Radiation Resistance



As novel immunotherapeutics enter the clinic, understanding the dynamic relationship between standard therapy and immune response becomes increasingly important. Skinner and colleagues perform a comprehensive proteomic and transcriptomic analysis of multiple cohorts of head and neck squamous cell carcinoma (HNSCC) patients and identify PD-L1 as highly associated with treatment failure following radiation. Moreover, integrating this analysis with *in vitro* data reveals a potential Axl-PI3 kinase-PD-L1 signaling axis modulating response to radiation in HNSCC. Targeting this pathway may allow for both direct tumor effects as well as indirect effects on tumor immune response. ■

See article by Skinner et al., p. 2713

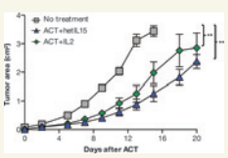
Disruption of Gas6/AXL Axis Eliminates LSCs in CML



Leukemia stem cells (LSCs) can cause resistance to imatinib in chronic myelogenous leukemia (CML). To validate druggable targets of LSCs, Jin and colleagues identified that the axis of receptor tyrosine kinase AXL and its ligand Gas6 derived from microenvironment was required for survival and self-renewal of CML LSCs. *AXL* knockdown and pharmacologic inhibition of AXL eliminated LSCs and prolonged survival of *BCR-ABL*-driven CML mice. Gas6/AXL ligation stabilized β-catenin in LSCs. These findings imply that disruption of Gas6/AXL axis is a promising approach to eliminate LSCs, which may facilitate curing the subset of CML patients with AXL overexpressed. ■

See article by Jin et al., p. 2842

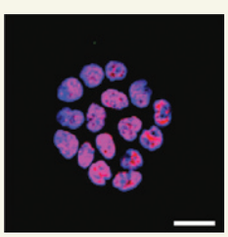
hetIL15 Enhances Efficacy of ACT for Cancer Immunotherapy



Heterodimeric IL15 (hetIL15) is an important lymphocyte growth and activation factor. Ng and colleagues show that hetIL15 administration induces lymphocyte entry into tumors and activation of intratumoral $CD8^+$ T cells. hetIL15 induces enrichment of antigen-specific lymphocytes in the tumor and increases $CD8^+$/Treg cell ratio. hetIL15 administration may be a general method to enhance T-cell tumor entry, increasing the success rate of immunotherapy interventions. hetIL15 increases total body lymphocytes and replaces the need for lymphodepletion prior to adoptive cell transfer for cancer therapy. Elimination of the need for lymphodepletion could make more patients eligible for cell-transfer protocols. ■

See article by Ng et al., p. 2817

ADNP Represses WNT in Colorectal Cancer



Constitutive over activation of WNT signaling is a typical feature of colorectal cancers. Therefore, targeting WNT signaling in this malignancy may be promising for therapeutic intervention. By using transcriptome, proteome, and cell biology approaches, Blaj and colleagues identify ADNP as a repressor of WNT signaling that can be pharmacologically induced by treatment with low-dose ketamine. Ketamine treatment significantly reduced WNT activity and slowed tumor growth in a preclinical colon cancer xenograft model. WNT repression through ADNP induction may be a new therapeutic strategy for colorectal cancer patients. ■

See article by Blaj et al., p. 2769

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