Single-Cell Analysis of the Multicellular Ecosystem in Viral Carcinogenesis by HTLV-1


Précis: High-dimensional single-cell landscape of immune alterations during HTLV-1 infection and leukemogenesis identifies hallmarks of premalignant and malignant T-cell states and the accompanying shift of systemic immune state toward myeloid and immunosuppressive.

Bortezomib Induces Anti–Multiple Myeloma Immune Response Mediated by cGAS/STING Pathway Activation


Précis: Robust antitumor immune response contributes to bortezomib clinical efficacy in myeloma. Induction of immunogenic cell demise and viral mimicry response via the STING pathway identifies a novel therapeutically targetable vulnerability.

See commentary, p. 405

Mutation Signatures of Pediatric Acute Myeloid Leukemia and Normal Blood Progenitors Associated with Differential Patient Outcomes


Précis: A subset of pediatric AML cases harbors more somatic mutations in their genomes compared to normal blood progenitors. This subset displays expression profiles that resemble more committed progenitors and associates with better patient survival.

Inhibition of MET Signaling with Ficlatuzumab in Combination with Chemotherapy in Refractory AML: Clinical Outcomes and High-Dimensional Analysis


Précis: A phase Ib trial of ficlatuzumab and cytarabine in high-risk AML reports a favorable safety profile and promising clinical activity. Multidimensional single-cell analyses collected before and after therapy identify several candidate prospective and pharmacodynamic biomarkers of response.

In The Spotlight

Bortezomib Induces Immunogenic Cell Death in Multiple Myeloma

L. Zitvogel and G. Kroemer

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Scalable Manufacturing of CAR T Cells for Cancer Immunotherapy

M. Abou-el-Enein, M. Elsallab, S.A. Feldman, A.D. Fesnak, H.E. Hesp, P. Marks, B.G. Till, G. Bauer, and B. Savoldo

Bispecific Antibodies in Multiple Myeloma: Present and Future


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Précis: Plasma protein binding reduces potency of stauroporine-derived tyrosine kinase inhibitors against Flt3-mutant AML. “Decoy” drugs interfering with the binding, including mifepristone, can be harnessed to restore the antileukemia activity.

ON THE COVER In this issue, Keisuke Kataoka and colleagues map the trajectory of adult T-cell leukemia/lymphoma (ATL) development driven by HTLV-1 infection in a large cohort of ATL patients, asymptomatic HTLV-1 carriers, and healthy controls. The study maps at single-cell resolution the cellular ecosystem populating the systemic immune landscape. It identifies biologically and clinically relevant cues to navigate this high-dimensional space, including phenotypic hallmark of premalignant clonal expansion. By tracking clonal evolution of the infected T cells toward malignancy, the authors reveal that the neoplastic transformation develops hand in hand with alterations in the noninfected lymphoid and myeloid compartments, including PD-L1 protein transfer from malignant T cells to their neighbors. For details, please see the article on page 450.

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