### IN THIS ISSUE
Highlighted research articles .................................. 1047

### NEWS IN BRIEF
Important news stories affecting the community ............ 1052

### RESEARCH WATCH
Selected highlights of recent articles of exceptional significance from the cancer literature ............ 1057

### ONLINE
For more News and Research Watch, visit Cancer Discovery online at http://cancerdiscovery.aacrjournals.org/content/early/by/section.

### VIEWS
In The Spotlight

**More T Cells versus Better T Cells in Patients with Breast Cancer** .... 1062
D.E. Speiser and G. Verdeil
See article, p. 1098

**Targeting the Noncoding Genome: Superenhancers Meet Their Kryptonite** ............... 1065
E. Wang and I. Aifantis
See article, p. 1136

**Soils and Seeds That Initiate Pancreatic Cancer Metastasis** .. 1067
C.R. Vakoc and D.A. Tuveson
See article, p. 1184

### REVIEW
How Ribosomes Translate Cancer .................................. 1069
S.O. Sulima, I.J.F. Hofman, K. De Keersmaecker, and J.D. Dinman

### RESEARCH BRIEF
TCR Repertoire Intratumor Heterogeneity in Localized Lung Adenocarcinomas: An Association with Predicted Neoantigen Heterogeneity and Postsurgical Recurrence .............. 1088
A. Reuben, R. Gittelman, J. Gao, J. Zhang, E.C. Yusko, C.-J. Wu, R. Emerson, J. Zhang

---


**Précis:** T-cell receptor sequencing of 45 tumor regions from 11 patients with NSCLC found T-cell repertoire intratumor heterogeneity that was associated with disease relapse and reduced disease-free survival.

---

### RESEARCH ARTICLES

**Immune Escape in Breast Cancer During In Situ to Invasive Carcinoma Transition** ............ 1098

**Précis:** Progression from ductal carcinoma in situ to invasive ductal carcinoma is characterized by a switch to a more suppressive immune microenvironment.

See commentary, p. 1062

**Whole-Genome and Epigenomic Landscapes of Etiologically Distinct Subtypes of Cholangiocarcinoma** ............. 1116

---

In The Spotlight

**More T Cells versus Better T Cells in Patients with Breast Cancer** .... 1062
D.E. Speiser and G. Verdeil
See article, p. 1098

**Targeting the Noncoding Genome: Superenhancers Meet Their Kryptonite** ............... 1065
E. Wang and I. Aifantis
See article, p. 1136

**Soils and Seeds That Initiate Pancreatic Cancer Metastasis** .. 1067
C.R. Vakoc and D.A. Tuveson
See article, p. 1184

---

**How Ribosomes Translate Cancer** .................................. 1069
S.O. Sulima, I.J.F. Hofman, K. De Keersmaecker, and J.D. Dinman

---

**TCR Repertoire Intratumor Heterogeneity in Localized Lung Adenocarcinomas: An Association with Predicted Neoantigen Heterogeneity and Postsurgical Recurrence** .............. 1088
A. Reuben, R. Gittelman, J. Gao, J. Zhang, E.C. Yusko, C.-J. Wu, R. Emerson, J. Zhang

---

In The Spotlight

**More T Cells versus Better T Cells in Patients with Breast Cancer** .... 1062
D.E. Speiser and G. Verdeil
See article, p. 1098

**Targeting the Noncoding Genome: Superenhancers Meet Their Kryptonite** ............... 1065
E. Wang and I. Aifantis
See article, p. 1136

**Soils and Seeds That Initiate Pancreatic Cancer Metastasis** .. 1067
C.R. Vakoc and D.A. Tuveson
See article, p. 1184

---

**How Ribosomes Translate Cancer** .................................. 1069
S.O. Sulima, I.J.F. Hofman, K. De Keersmaecker, and J.D. Dinman

---

**TCR Repertoire Intratumor Heterogeneity in Localized Lung Adenocarcinomas: An Association with Predicted Neoantigen Heterogeneity and Postsurgical Recurrence** .............. 1088
A. Reuben, R. Gittelman, J. Gao, J. Zhang, E.C. Yusko, C.-J. Wu, R. Emerson, J. Zhang
In-depth genetic characterization defines cholangiocarcinoma subtypes and identifies previously undescribed drivers, noncoding promoter mutations, and structural variants.

Superenhancer Analysis Defines Novel Epigenomic Subtypes of Non-APL AML, Including an RARα Dependency Targetable by SY-1425, a Potent and Selective RARα Agonist .............. 1136

Characterization of enhancer landscapes in patients with AML identified a subset of non-APL AML with an RARA superenhancer that confers sensitivity to treatment with the selective RARα agonist SY-1425.

See commentary, p. 1065

Overcoming the Immunosuppressive Tumor Microenvironment of Hodgkin Lymphoma Using Chimeric Antigen Receptor T Cells .................. 1154

Anti-CD123 chimeric antigen receptor T cells overcome the immunosuppressive tumor microenvironment in Hodgkin lymphoma by targeting both malignant cells and tumor-associated macrophages.

Loss of MutL Disrupts CHK2-Dependent Cell-Cycle Control through CDK4/6 to Promote Intrinsic Endocrine Therapy Resistance in Primary Breast Cancer .......................... 1168

Dysregulation of the mismatch repair complex MutL promotes intrinsic resistance to endocrine therapy in ER+ breast cancer model systems and patients and may confer sensitivity to CDK4/6 inhibitors.

BLIMP1 Induces Transient Metastatic Heterogeneity in Pancreatic Cancer .............. 1184

Pancreatic ductal adenocarcinoma metastasis is promoted by hypoxia and HIF-driven upregulation of the prometastatic transcription factor BLIMP1.

See commentary, p. 1067

To determine how intratumor heterogeneity in the T-cell landscape correlates with the genomic landscape and with patient outcome in non–small cell lung cancer (NSCLC), Reuben and colleagues characterized the T-cell repertoire in a cohort of 11 patients with NSCLC who had previously been subject to whole-exome sequencing. T-cell receptor (TCR) sequencing profiled 45 tumor regions across the 11 tumors and revealed a high level of intratumor heterogeneity, with differences in T-cell density, clonality, and repertoire. TCR intratumor heterogeneity was linked to neoantigen heterogeneity and was correlated with disease relapse and reduced disease-free survival in patients with NSCLC. These findings link T-cell repertoire heterogeneity to genomic intratumor heterogeneity and relapse in NSCLC. For details, please see the article by Reuben and colleagues on page 1088.