In Focus
Harnessing CAR T-cell Insights to Develop Treatments for Hyperinflammatory Responses in Patients with COVID-19 .... 775
S. Agarwal and C.H. June

TMPRSS2 and COVID-19: Serendipity or Opportunity for Intervention? .......... 779

Patients with Cancer Appear More Vulnerable to SARS-CoV-2: A Multicenter Study during the COVID-19 Outbreak ............ 783

Précis: In a study of 105 patients with cancer and 536 without, all with confirmed COVID-19, cancer was predictive of more severe disease, with stage IV cancer, hematologic cancer, and lung cancer being associated with worse outcomes.

The Evolutionary Origins of Recurrent Pancreatic Cancer .... 792

Précis: Sequencing of primary and recurrent stage I or II pancreatic ductal adenocarcinomas revealed that the genetic origins of recurrence were diverse; interestingly, one patient thought to have recurrence had a second primary tumor.

Mutations in the RNA Splicing Factor SF3B1 Promote Tumorigenesis through MYC Stabilization ............ 806
Z. Liu, A. Yoshimi, J. Wang, H. Cho, S-C.-W. Lee, M. Ki, L. Bitner, T. Chu, H. Shah, B. Liu,

Précis: Cancer-associated mutations in SF3B1, encoding an RNA splicing factor, cause aberrant splicing of the PP2A component PPP2R5A, leading to stabilization of the PP2A target and proto-oncogene MYC.

See commentary, p. 765

Golgi Acidification by NHE7 Regulates Cytosolic pH Homeostasis in Pancreatic Cancer Cells


Précis: Pancreatic ductal adenocarcinoma cells use the sodium–hydrogen exchanger NHE7 to acidify the Golgi apparatus, helping them maintain their intracellular pH even as glycolysis generates excess acid.

See commentary, p. 768

Combined Cohesin–RUNX1 Deficiency Synergistically Perturbs Chromatin Looping and Causes Myelodysplastic Syndromes


Précis: Mutations in the cohesin subunit STAG2 and the transcription factor RUNX1 synergize to disrupt chromatin loops, downregulate transcription of genes with high basal pausing, and promote myelodysplastic syndromes.

Global Regulation of the Histone Mark H3K36me2 Underlies Epithelial Plasticity and Metastatic Progression


Précis: The histone methyltransferase NSD2 and the histone demethylase KDM2A emerged as opposing enzymes that modulate histone 3 lysine residue 36 dimethylation to influence cell plasticity and, consequently, metastasis.

Repression of the Type I Interferon Pathway Underlies MYC- and KRAS-Dependent Evasion of NK and B Cells in Pancreatic Ductal Adenocarcinoma


Précis: Modest overexpression of human MYC plus expression of KrasG12D drove rapid pancreatic ductal adenocarcinoma development in mice, suppressing the type I interferon response and preventing NK- and B-cell infiltration.

ON THE COVER

The COVID-19 pandemic has raised questions about the impact of the disease on patients with cancer, who are generally more susceptible to infections. Dai and colleagues report the results of a multicenter study in Wuhan, China, comparing patients with cancer to age-matched controls, all diagnosed with COVID-19. Substantial differences in prognosis based on cancer stage and type emerged: Stage IV cancer conferred a much worse prognosis than non-metastatic cancer, and patients with hematologic or lung malignancies were most at risk for severe complications of COVID-19. For details, please see the article by Dai and colleagues on page 783. Additional coverage of the relationship between COVID-19 and cancer can be found in the News and In Focus sections of this issue.