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This study characterizes a previously unexplored role of ncNATs in regulation of isoform expression of associated sense genes, highlighting a mechanism of alternative promoter usage in cancer.

5904 The HNF4 α -BC200-FMR1-Positive Feedback Loop Promotes Growth and Metastasis in Invasive Mucinous Lung Adenocarcinoma

Xiong Chen, Yujie Zhao, Daxuan Wang, Ying Lin, Jihuan Hou, Xiaolin Xu, Jianben Wu, Linhai Zhong, Yitong Zhou, Jinying Shen, Wenqing Zhang, Hanwei Cao, Xiaoting Hong, Tianhui Hu, and Yan-yan Zhan

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This study identifies a bioactive pool of carbon-bound exogenous compounds in patient tissues associated with several tumor biological features, contributing to an improved understanding of drivers of lung cancer pathophysiology.

5919 ALDH1A1 Activity in Tumor-Initiating Cells Remodels Myeloid-Derived Suppressor Cells to Promote Breast Cancer Progression

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This study uncovers mechanisms by which radiotherapy can promote GBM recurrence by inducing senescence in non-neoplastic brain cells, suggesting that senolytic therapy can blunt recurrent GBM growth and aggressiveness.

5948 Supraphysiologic Testosterone Induces Ferroptosis and Activates Immune Pathways through Nucleophagy in Prostate Cancer

Rajendra Kumar, Janet Mendonca, Olutosin Owoyemi, Kavya Boyapati, Naiju Thomas, Suthicha Kanacharoen, Max Coffey, Deven Topiwala, Carolina Gomes, Busra Ozbek, Tracy Jones, Marc Rosen, Liang Dong, Sadie Wiens, W. Nathaniel Brennen, John T. Isaacs, Angelo M. De Marzo, Mark C. Markowski, Emmanuel S. Antonarakis, David Z. Qian, Kenneth J. Pienta, Drew M. Pardoll, Michael A. Carducci, Samuel R. Denmeade, and Sushant K. Kachhap

This study demonstrates that supraphysiologic testosterone induces two parallel autophagy-mediated processes, ferritinophagy and nucleophagy, which then activate nucleic acid sensors to drive immune signaling pathways in prostate cancer.

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- 6044 Specific Activation of the CD271 Intracellular Domain in Combination with Chemotherapy or Targeted Therapy Inhibits Melanoma Progression**
Annalisa Saltari, Andreas Dzung, Marika Quadri, Natascia Tiso, Nicola Facchinello, Alberto Hernández-Barranco, Susana Garcia-Silva, Laura Nogués, Corinne Isabelle Stoffel, Phil F. Cheng, Patrick Turko, Ossia M. Eichhoff, Francesca Truzzi, Alessandra Marconi, Carlo Pincelli, Héctor Peinado, Reinhard Dummer, and Mitchell P. Levesque
The discovery of a means to specifically activate the CD271 death domain reveals unknown pathways mediated by the receptor and highlights new treatment possibilities for melanoma.

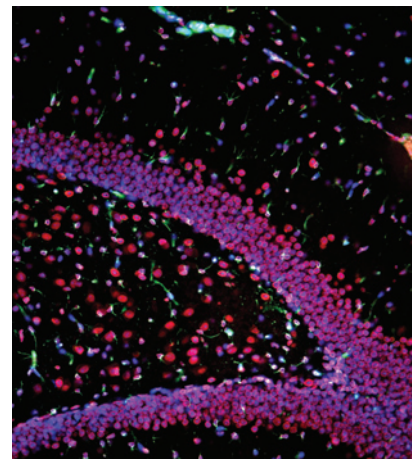
TRANSLATIONAL SCIENCE

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ABOUT THE COVER

Glioblastomas are routinely treated with ionizing radiation. During treatment, the tissue surrounding tumors is also irradiated, which can induce senescence of normal brain cells including astrocytes. Senescent astrocytes promote glioblastoma aggressiveness and recurrence via release of SASP factors, and this can be ameliorated by senolytic therapy. The cover shows an image of a mouse brain stained for nuclei (blue), GFAP (green; marker for astrocytes), and Lamin B1 (red; loss of which is a marker for senescence). For details, see the article by Fletcher-Sananikone and colleagues on page 5935.

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