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TRANSLATIONAL SCIENCE

5606  Cancers from Novel Pole-Mutant Mouse Models Provide Insights into Polymerase-Mediated Hypermutagenesis and Immune Checkpoint Blockade

Two mouse models of polymerase exonuclease deficiency shed light on mechanisms of mutation accumulation and considerations for immunotherapy.

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5619  The Functional Landscape of Patient-Derived RNF43 Mutations Predicts Sensitivity to Wnt Inhibition
      Jia Yu, Permeen A. Mohamed Yusoff, Danielle T.J. Woutersen, Pamela Geh, Nathan Harman, Ron Smits, David M. Epstein, David M. Virshup, and Babita Madan

Systematic examination of patient-derived RNF43 mutations identifies rules to guide patient selection, including that truncation or point mutations in well-defined functional domains sensitize cancers to PORCN inhibitors.

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RIG-I–Like Receptor LGP2 Is Required for Tumor Control by Radiotherapy

Wenxin Zheng, Diana Rose E. Ranoa, Xiaona Huang, Yuzhu Hou, Kaiting Yang, Elizabeth C. Poli, Michael A. Beckett, Yang-Xin Fu, and Ralph R. Weichselbaum

These findings reveal an essential role of LGP2 in promoting antitumor immunity after radiotherapy and provides a new strategy to enhance radiotherapy.

STAT3-Mediated Astrocyte Reactivity Associated with Brain Metastasis Contributes to Neurovascular Dysfunction

Manuel Sarmiento Soto, James R. Larkin, Chris Martin, Alexandre A. Khrapitchev, Melissa Maczka, Vasiliki Economopoulos, Helen Scott, Carole Escartin, Gilles Bonvento, Sébastien Serres, and Nicola R. Sibson

These findings demonstrate that selectively targeting STAT3-mediated astrocyte reactivity ameliorates the cerebrovascular dysfunction associated with brain metastasis, providing a potential therapeutic avenue for improved patient outcome.

ABOUT THE COVER

Ovarian cancer cells rely on differential signaling of EGFR/ERBB2- or FOXM1-activated pathways when cancer cells become spheroids or when they attach to the mesothelium on distant organs, respectively. Using immunofluorescence, the authors photographed GFP-labeled ovarian cancer cells (green) that were grown on the RFP-labeled mesothelial cells (red). Ovarian cancer cells were then sorted, and gene expression signatures for both adherent and nonadherent cells were determined. The authors further identified that ZEB1 is an important regulator of EGFR, ERBB2, and FOXM1, which are critical for the transition between adherent and nonadherent forms of cells. For details, see the article by Parashar and colleagues on page 5554.