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Potential Role of mTORC2 as a Therapeutic Target in Clear Cell Carcinoma of the Ovary

Takeshi Hisamatsu, Seiji Mabuchi, Yuki Matsumoto, Mahiru Kawano, Tomoyuki Sasano, Ryoko Takahashi, Kenjiro Sawada, Kimihiko Itó, Hirohisa Kurachi, Russell J. Schilder, Joseph R. Testa, and Tadashi Kimura

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Hypoxia can drive loss of tumor cell differentiation and elevate metastatic potential in pancreatic cancer. Inhibition of heparanase with PG545 reduced vascular function and increased hypoxia in a GEMM of pancreatic cancer; however, PG545 treatment did not enhance tumor cell EMT. Immunofluorescence was used to show that tumors from PG545-treated animals express elevated levels of membrane-associated β-catenin, a characteristic of epithelial cells. These data are consistent with observed changes in E-cadherin and other EMT-associated proteins and suggest that the proinvasive effects of hypoxia can be abrogated by inhibition of heparanase. For details, see article by Ostapoff and colleagues on page 1190.