Ovarian Cancer Cell Lines for Testing PARP Inhibitors in Mice

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Introduction

Ovarian cancer is the leading cause of death from gynecological malignancies, with an overall mortality of 60%. Molecular targeted agents, such as Poly (ADP-ribose) polymerase (PARP) inhibitors, represent an exciting new avenue of clinical investigation. Preclinical studies on a reliable disease model play a key role in this drug discovery process.

Description

- The Mouse Ovarian Cancer Cell Lines developed by Dr. Sandra Orsulic are the only BRCA1-proficient and BRCA1-deficient isogenic pair of ovarian cancer cell lines that grow tumors upon intraperitoneal injection into immunocompetent mice.
- The tumors recapitulate human ovarian cancer biology (serous histology; intraperitoneal carcinomatosis + ascites) and genetic alterations (BRCA1-/- or wt; p53-/-; myc, Kras, Akt).
- This pair of cell lines is useful for testing PARP inhibitors and other DNA damage-targeted therapies in immunocompetent mice. Luciferase transduced versions of cell lines are available for Ivis small animal imaging.

Publications

References using earlier versions of the mouse ovarian cancer cell lines for testing BRCA-targeted therapies:

The PARP1 inhibitor BMN 673 exhibits immunoregulatory effects in a Brca1(-/-) murine model of ovarian cancer. Huang J, Wang L, Cong Z, Amoozgar Z, Kiner E, Xing D, Orsulic S, Matulonis U, Goldberg MS. Biochem Biophys Res Commun. 2015 Aug 7;463(4):551-6. [*Link*]

The immunomodulatory effects of pegylated liposomal doxorubicin are amplified in BRCA1-deficient ovarian tumors and can be exploited to improve treatment response in a mouse model. Mantia-Smaldone G, Ronner L, Blair A, Gamerman V, Morse C, Orsulic S, Rubin S, Gimotty P, Adams S. Gynecol Oncol. 2014 Jun;133(3):584-90. [*Link*]

Nanoparticle-mediated delivery of siRNA targeting Parp1 extends survival of mice bearing tumors derived from Brca1-deficient ovarian cancer cells. Goldberg MS, Xing D, Ren Y, Orsulic S, Bhatia SN, Sharp PA. Proc Natl Acad Sci U S A. 2011 Jan 11;108(2):745-50. [*Link*]

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