Video Article

Development of an orthotopic model of serous ovarian cancer in immunocompetent mice for in vivo tumor imaging and monitoring of tumor immune responses

Selene Nunez-Cruz[1], Denise Connolly[1], Nathalie Scholler[1]
[1]

Correspondence to: Selene Nunez-Cruz at selene@mail.med.upenn.edu

URL: http://www.jove.com/video/2276
DOI: doi:10.3791/2276

Keywords: Ovarian cancer, syngeneic, orthotopic, katushka (TurboFP635), in vivo imaging.

Date Published: 6/15/2015

Citation: Nunez-Cruz, S., Connolly, D., Scholler, N. Development of an orthotopic model of serous ovarian cancer in immunocompetent mice for in vivo tumor imaging and monitoring of tumor immune responses. *J. Vis. Exp.* (), e2276, doi:10.3791/2276 (2015).

Abstract

Background: Ovarian cancer is generally diagnosed at an advanced stage where the case/fatality ratio is high and thus remains the most lethal of all gynecologic malignancies among US women 1,2,3. Serous tumors are the most widespread forms of ovarian cancer and 4,5 the Tg-MISIIR-TAg transgenic represents the only mouse model that spontaneously develops this type of tumors. Tg-MISIIR-TAg mice express SV40 transforming region under control of the Mullerian Inhibitory Substance type II Receptor (MISIIR) gene promoter 6. Two strains of Tg-MISIIR-TAg mice were developed with differential expression of TAg. DR26 females express high levels of TAg and spontaneously develop bilateral serous ovarian tumors 6, while EE73 females express lower levels and do not develop cancer. Consequently, EE73 females can serve as syngeneic recipients for ovarian tumor cells originating from DR26 Tg-MISIIR-TAg tumors. Objective: Although tumor imaging is possible 7, early detection of deep tumors is challenging in small living animals. To enable preclinical studies in an immunologically intact animal model for serous ovarian cancer, we developed a syngeneic mouse model for this type of ovarian cancer that permits in vivo imaging, studies of the tumor microenvironment and tumor immune responses. Methods: We first derived a TAg+ mouse cancer cell line (MOV1) from a spontaneous ovarian tumor harvested in a 26 week-old DR26 Tg-MISIIR-TAg female. Then, we stably transduced MOV1 cells with TurboFP635 Lentivirus mammalian vector that encodes Katushka, a far-red mutant of the red fluorescent protein from sea anemone Entacmaea quadricolor with excitation/emission maxima at 588/635 nm 8,9,10. We orthotopically implanted MOV1Kat in the ovarian bursa of EE73 Tg-MISIIR-TAg females. Tumor progression was followed by in vivo optical imaging and tumor microenvironment was analyzed by immunohistochemistry. Results: Orthotopically implanted MOV1Kat cells developed serous ovarian tumors. MOV1Kat tumors could be visualized by in vivo imaging up to three weeks after implantation (fig. 1) and were infiltrated with leukocytes, as observed in human ovarian cancers 11 (fig. 2). Conclusions: We successfully developed an orthotopic model of ovarian cancer suitable for in vivo imaging of early tumors due to the high pH-stability and photostability of Katushka in deep tissues. We propose the use of this novel syngeneic model of serous ovarian cancer for in vivo imaging studies and monitoring of tumor immune responses and immunotherapies.

Disclosures

No conflicts of interest declared.