# Syngeneic Immunocompetent Mouse Ovarian Cancer Models

The study of ovarian carcinogenesis has been limited by the lack of appropriate immuno-competent syngeneic mouse models that recapitulate genetic changes in human ovarian carcinoma. The Orsulic Laboratory has engineered multiple mouse ovarian cancer cell lines with defined genetic alterations that are frequently present in human high-grade serous ovarian cancer. One example is the FVB-syngeneic mouse ovarian cancer cell line BR5-Luc with combinations of genetic alterations in p53, Brca1, myc, and Akt. The tumors in this model are infiltrated with the host stromal cells while the luciferase and HA tags allow for convenient visualization and quantification of cancer cells by whole animal imaging and immunohistochemistry. Several features of this model make it suitable for studying microenvironment dynamics during ovarian cancer progression, such as:

1) the intact immune system

2) tumors form with 100% penetrance and predictable latency

3) the main genetic and pathologic aspects of human ovarian cancer are represented
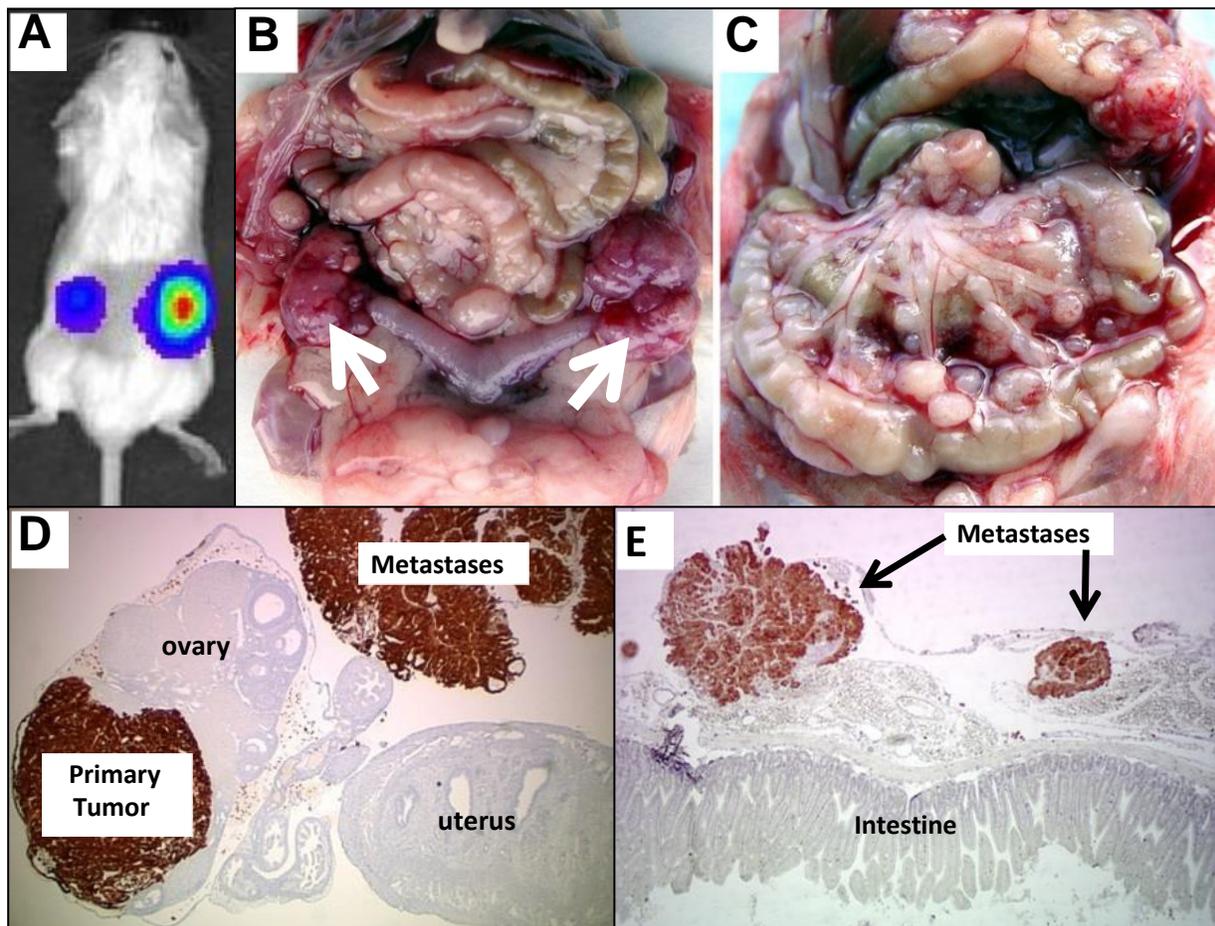
A mouse syngeneic ovarian cancer model. (A) Small animal imaging visualization of luciferase-tagged cells 10 days after orthotopic implantation of mouse ovarian cancer cells. **(B)** Tumor growth in ovaries. **(C)** Peritoneal metastatic spread. **(D**, **E)** Visualization of HA-tagged cancer cells with immunohistochemistry in paraffin sections.

We have shown that this ovarian cancer model recapitulates human serous histology, pattern of metastatic spread, and response to standard and targeted therapies [1-14]. In collaboration, we have analyzed immune cell infiltrates, including CD4$^+$ and CD8$^+$ T cells, B cells, NK cells, CD4$^+$ T$_{reg}$ cells, tumor-associated macrophages, and MDSCs, and demonstrated the utility of this model in studying the effects of therapies on the composition of major immune cell types [9, 11-14]. For example, we have shown that targeting the CXCL12/CXCR4 axis results in the selective reduction of intratumoral FoxP3$^+$ T$_{reg}$ cells and a marked increase in T-cell-mediated antitumor immune response [9]. We have also demonstrated that the efficacy of anti-CTLA-4 therapy is greatly potentiated in combination with decitabine, which promotes the differentiation of naïve T cells into effector T cells and prolongs cytotoxic lymphocyte responses [14]. In addition to this FVB-syngeneic model, we have recently developed a C57BL/6-syngeneic mouse ovarian cancer model.

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