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# Stem cell models in ovarian cancer

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Ovarian cancer has a high mortality rate and despite initially robust clinical responses to platinum and taxane-based chemotherapy, most patients will relapse within 2 years following diagnosis. Drug-resistant self-renewing cancer stem cells, which evade the anti-cancer effects of systemic chemotherapy, have emerged as a key player responsible for tumor recurrence. Identifying the chemoresistance signatures of cancer stem cells is an important step for designing new strategies for therapeutic intervention in recurrent tumors. Multiple studies have now defined cancer stem cells (CSCs) as having an increased tumorigenic ability in serial transplantation experiments conducted in tumor xenografts. This assay, however, may not be entirely accurate in clearly identifying CSCs. Nevertheless, there is enough evidence to support the idea that CSCs are necessary to initiate and propagate tumor diversity. In addition, CSCs are studied in multiple solid tumors, including ovarian cancer, due to their intrinsic chemoresistance properties. Thus, while non-CSCs have been shown to be sensitive to available therapies, CSCs are enriched in response to treatment and regenerate an increasingly platinum resistant tumor. Furthermore, similar to normal stem cells, CSCs are likely shielded from damage and injury by the tumor niche microenvironment, which makes it difficult to target them therapeutically.

The cellular origin of ovarian cancer stem cells has been difficult to identify. Multiple stem cell models have been proposed. One model proposes that CSCs can originate either from somatic adult stem cells or from progenitor non-stem cells. The ovarian surface epithelium and distal fallopian tube, which are tumor initiation sites, consist of both adult stem cells and also progenitor cells that are relatively undifferentiated and capable of differentiating into distinct morphological subtypes. We have recently found that ovarian cancer and somatic stem cells share common molecular pathways and markers, which is consistent with the model that some cancer stem cells may either arise from adult stem cells or most likely evolve to mimic somatic stem cell properties. Clearly, the identification of key CSC markers and pathways and their efficient use in the design of targeted therapies are necessary before such treatments can be meaningfully implemented in the clinic. Our research presentation will detail key aspects of CSC-driven tumor chemoresistance in ovarian cancer, outline methods of efficiently targeting CSCs, and discuss the implications of using these novel therapies in the clinical setting.

**Biography:**

Dr. Dinulescu is an Assistant Professor at Harvard Medical School. She received her Ph.D. from Oregon Health and Science University and completed her postdoctoral studies in the field of Cancer Genetics at MIT. Dr. Dinulescu's research interests focus on cancer biology, malignancies of the gonads and reproductive tract, with a special emphasis on ovarian cancer research and endometriosis. Our laboratory is actively investigating the key contribution of cancer stem cells (CSCs) to tumor chemoresistance. Our current studies focus on better understanding the mechanism of stem cell signaling in the maintenance of the CSC niche and ovarian tumorigenesis. The aim is to harness the power of nanotechnology to develop improved "homing" technologies for the delivery of therapeutic agents specifically targeting and sensitizing ovarian cancer cells, including CSCs, in a spatio-temporal fashion.