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Therapeutic targeting of ovarian cancer stem cells

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Ovarian cancer is the fifth leading cause of cancer death in women. An exciting hypothesis emerging in cancer biology is that cancer cells with stem cell properties are a major driving force for both tumor development and chemoresistance to therapy based on their propensity to divide indefinitely and survive standard cancer chemotherapy. This could explain the high rate of therapeutic failure and tumor relapse seen in patients. Our research group has recently generated animal models of ovarian cancer that recapitulate the human disease with great accuracy. Our animal models constitute invaluable tools that will help identify, characterize, and define the key roles of ovarian cancer stem cells in tumor metastasis and resistance to chemotherapy. Furthermore, they provide us with unique, relevant systems in which to screen new and exciting therapies specifically targeting ovarian cancer stem cells. Our current investigation focuses on whether ovarian cancer stem cells contribute to platinum chemoresistance and tumor relapse. In addition, we are examining whether key stem cell markers constitute good markers for predicting chemoresistance to platinum and doxorubicin in ovarian cancer. Finally, we plan to test a nanotechnology-based strategy for therapeutic delivery, which will selectively target and sensitize cancer stem cells in a spatiotemporal fashion. This constitutes a novel paradigm in the strategies towards developing effective therapies and a cure for ovarian cancer. It is well established that the chemotherapeutic options used today are of limited value in ovarian cancer patients who relapse. The addition of a front-line therapeutic agent specifically targeting cancer stem cells have the potential to greatly improve the high rate of therapeutic failure and tumor relapse currently seen in ovarian cancer patients and especially platinum resistant or refractory patients worldwide. Our studies aim to reduce cancer mortality rates and improve the quality of life of cancer patients through more efficient and less toxic therapies. Data collected from these key preclinical studies will be instrumental in the design of new human clinical trials for ovarian cancer therapy selectively targeting cancer stem cells.

Biography

Daniela Dinulescu is an Assistant Professor at Harvard Medical School. She received her PhD from Oregon Health and Science University and completed her Postdoctoral studies in the field of Cancer Genetics at MIT. Her 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.

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