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Combining radiation therapy and immunomodulatory microRNAs: Preclinical assessment and translational approaches

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herapeutic resistance is the primary factor that limits the effectiveness of current therapies for solid tumors. Strategies for vercoming this resistance should readily translate into improved outcomes. This concept is particularly relevant for overcoming resistance to ionizing radiation, which is currently the only potentially curative nonsurgical approach for most solid tumors. Therapeutic delivery of synthetic microRNAs (miRNAs) that mimic endogenous tumor suppressor miRNAs has emerged as a promising approach for treating cancer. MiRNAs target multiple cellular processes and thus in theory can have broader effects beyond current approaches that are limited to targeting single aspects of a cellular pathway. The ability to inhibit oncogenic miRNAs or replace them with tumor suppressor miRNAs may complement traditional treatments such as chemotherapy and radiation. However, the role of miRNAs in mediating resistance to radiotherapy is poorly understood. Therefore, the ultimate goal is to assess the potential applicability of miRNA delivery in combination with radiation therapy. Furthermore, the immune-modulating effects of radiation therapy have recently gained considerable interest and there have been multiple reports of synergy between radiation and immunotherapy. We previously found that immunomodulatory miRNAs, such as miR-200 and miR-34a, can overcome resistance to radiation. We next generated a preclinical tumor model resistant to radiation and immunotherapy and identified upregulation of miRNAs as an underlying mechanism by which some tumors do not respond to immunotherapy. Our future goal is to validate these findings on our ongoing clinical studies.

Biography:

Maria Angelica received her master's and Ph.D degree from University of Sao Paulo, Brazil, in 2009. She completed part of her thesis at Dr. George Calin laboratory at MD Anderson, where she devoted her thesis to understanding the roles of noncoding RNAs, including microRNAs, in the molecular mechanisms underlying tumor progression. She joined Dr. Welsh's lab as a postdoctoral fellow in 2011 and was appointed Instructor at the Department of Radiation Oncology in 2015. Dr. Cortez's long-term career goal is to discovery novel therapeutic strategies to target immunotherapy resistant lung and breast cancer cells. Her current projects include: 1) understanding the mechanisms by which tumors evade the immune system, and 2) exploring the interaction between radiation and immunotherapies for the treatment of lung cancer.