"Novel Approaches to Target High Grade Ovarian Cancers"

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Abstract: Despite recent progress, we lack effective therapies for patients with advanced ovarian cancer. This deficiency exists in part because: (1) we still lack a comprehensive view of the genetic alterations responsible for ovarian cancer pathogenesis, (2) current experimental models do not reflect the subtypes of ovarian cancers, and (3) we do not have the means to target many classes of potential targets. We propose a novel approach to targeting ovarian cancer that combines the discovery of novel targets, the development and application of innovative therapeutic modalities and newly discovered, physiologically relevant ovarian models. The co-investigators of this application each bring a unique perspective and expertise to this project, whose overarching goal is to develop strategies to target currently undruggable oncogenes. Specifically, we will perform integrative genome scale profiling for genes essential for high grade ovarian cancers in both cancer cell lines and innovative new models of ovarian tumor initiating cells derived from patients. We will then validate candidates identified by these approaches in animal models using two novel delivery systems: chimeric peptide conjugated antisense oligonucleotides and tumor-penetrating nanoparticles. Together this project will integrate patient derived experimental models, genome scale molecular profiling and novel delivery technology to create a new platform for identifying and validating potential therapeutic targets in ovarian cancer.