NIH Award from the National Cancer Institute

Principal investigator: Jindan Yu, medicine: hematology-oncology, Feinberg School of Medicine

- **Project:** The Role of beta-adrenergic Signaling in Prostate Cancer
- **Start Date:** September 1, 2009
- **Total Award Amount:** $53,162

**How the results of this project will benefit society:**
Prostate Cancer (PCa) is a leading cause of cancer-related death in American men. Like other cancers, PCa develops in the background of intrinsic cues and extrinsic factors. Distinct sets of genes and proteins dictate progression from precursor lesion of the prostate, to localized PCa, and finally to metastatic disease. Clinically localized PCa can be effectively ablated using surgical or radiation treatments. Hormone-refractory metastatic disease, however, is invariably incurable and leads to death. Therefore, characterizing the genes that regulate the growth of metastatic PCa are of particular relevance to prostate cancer research and may offer novel targets for therapeutic intervention.

**The problem the project is trying to solve:**
One of these genes we identified was EZH2, a Polycomb group protein that is up-regulated in aggressive cancers. Dysregulation of EZH2 promotes tumor progression through the repression of a key set of tumor suppressor genes, including ADRB2, a critical regulator of the beta-adrenergic signaling pathway. ADRB2 is a direct target of EZH2-mediated transcriptional repression and may serve as a prognostic biomarker in PCa. However, ADRB2 function and its downstream cellular signaling cascade in PCa remain unclear. My long-term goal is to understand the molecular machineries regulating cancer progression.

**How the project will work:**
The objective of this application is to characterize the role of ADRB2 in regulating prostate cancer growth and development. Specific Aim 3: Understand the mechanism of ADRB2 as a tumor suppressor in prostate cancer. In summary, this proposal addresses the expression, functional roles, and underlying mechanisms of ADRB2 in the growth and development of prostate cancer. Our ultimate hope is that the functional characterization of ADRB2 in metastatic prostate cancer will one day lead to an effective therapy for this invariably lethal disease.

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