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ESTABLISHING A CELL-BASED HIGH-THROUGHPUT SCREEN TO IDENTIFY PATHWAYS TARGETING ZNF217 LEVELS IN OVARIAN CANCER CELLS

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Ovarian cancer continues to be the fifth leading cause of cancer-associated deaths among women in the United States. Due to the lack of early reliable diagnostic markers, the majority of patients have metastatic disease at diagnosis. The 5-year survival rate in women with metastatic ovarian cancer is extremely low (<30%), highlighting the urgent need to identify new therapeutic targets. Previous studies have revealed that Zinc Finger Protein 217 (ZNF217) is overexpressed in metastatic breast, ovarian, and lung cancer cells. They also revealed that ectopic ZNF217 expression in ovarian cancer cells enhanced the metastatic ability of these cells. Further, siRNA mediated ZNF217 depletion in metastatic ovarian cancer cells resulted in cancer cell death and tumor regression in mice. Despite ZNF217's role in metastatic progression, cancer cell survival, and its potential as an anti-cancer therapeutic target, targeting ZNF217 in a clinically translatable manner has not been achieved yet. To overcome these limitations, I will establish a cell-based high-throughput screen to identify small molecules that cause ZNF217 depletion in ovarian cancer cells. Specifically, I will use lentivirus-mediated gene delivery to stably express Red Fluorescent Protein (RFP)-tagged ZNF217 in the ovarian cancer cell line SKOV3. The expression and cellular localization of RFP-tagged ZNF217 will be verified using Western blotting and fluorescent microscopy respectively. Since the RFP signal intensity will correspond to cellular ZNF217 levels, I will determine the utility of these cells in a high-throughput platform by validating the changes in RFP signals to measure changes in cellular ZNF217 levels. Once the utility of the SKOV3-ZNF217-RFP cells is established and the optimal conditions for the assay is identified, I will collaborate with the high-throughput screening facility at the University of Maryland Baltimore to screen compound libraries and identify novel small molecules capable of depleting ZNF217 in ovarian cancer cells.

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