1-2020

Manipulation of Genome Integrity Signaling Axes Contributing to Prostate Cancer Aggressiveness

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Introduction: Prostate cancer (PC) is one of the leading causes of death in men, and despite current treatment options patients can develop aggressive disease that spreads to other parts of the body. Little research has focused to date on the effect of centrosome biology in the pathogenesis of PC.

Methods: Two metastatic PC cell lines, DU145 and 22Rv1, as well as highly aggressive derivatives generated in Dr. Rodriguez-Bravo lab (docetaxel-resistant; (DR) variants) were compared through various experiments to determine differences in centrosome proteins expression and functionality. All cells (DU145 /DR and 22Rv1 /DR) underwent electroporations with siRNAs to knockout one of the centrosomal target genes (STIL) and were compared to siRNA controls (not targeting any human gene). Subsequently, western blots, RT-PCRs, colony formation assays, and immunofluorescence microscopy were used to analyze the differences between controls and STIL knockdowns and between different cell lines.

Results: Analysis of the experiments performed suggest that there is a greater effect of the STIL knockdown than the siRNA control in decreasing cell proliferation in PC cells. There was also insufficient evidence to determine if there was a difference between the parental and DR cells.

Discussion: There was statistically significant evidence that knockout of STIL decreased cell proliferation of metastatic PC cells DU154 and 22Rv1. This suggests a potential role between centrosome regulating mechanisms and the aggressiveness of

PC cells. Future research could aim to determine the extent of the effect of the knockdown and potentially be exploited in the future of treatments for late-stage PC.