

OFFICIAL ABSTRACT and CERTIFICATION

Optimization of Murine Organoids in Modeling Prostate Cancer Through Infection With Adenovirus Containing Cre

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Prostate cancer, which causes over 30,000 deaths each year, is one of the most widespread cancers affecting the male population in the United States. These deaths are unevenly distributed among metastatic and non-metastatic forms of the disease; there is a 99% survival rate for early forms of the disease, but the rate drops to 30% when the cancer metastasizes. Many genes have a role in the development of this disease, but three prominent genes regulating cell division in the development of prostate cancer are Pten, P53, and Phlpp2. These genes have secondary impacts on metabolism because they affect the expression of Akt and Myc. The aim of this study was to gain further insight into the role of each gene in prostate cancer progression through the generation of organoids. As mouse-derived organoids have shown promise in modeling other forms of cancer, they were used for this study and analyzed with western blots and immunofluorescence. IF showed that organoid cells formed lobes resembling the shape of the prostate, but no luminal cells were found in the organoid. Additionally, Ki67 detection showed regions of high cell proliferation and tumor formation. Western blots also reinforced the relationship between cell division genes and metabolism genes. The results of this study reinforce the potential of mouse-derived in modeling prostate cancer. Organoid phenotypes matched with previously observed in vivo phenotypes for each genotype, and in vivo signaling pathways were maintained.

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