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3703

Development of Oncopig Urothelial Carcinoma Cell Lines

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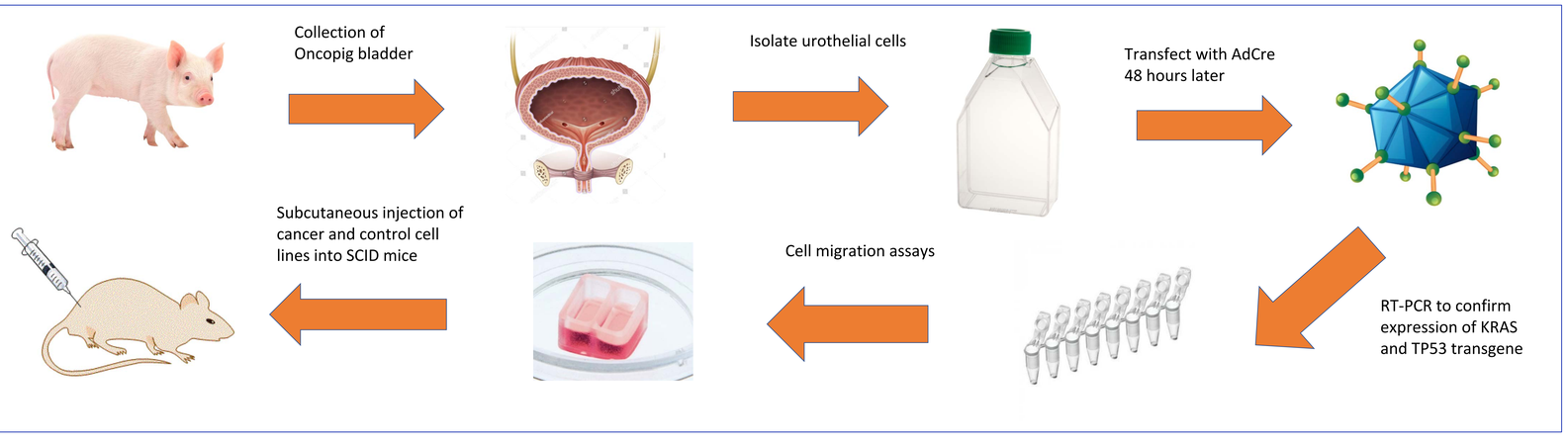
Background

- Urothelial carcinoma, or bladder cancer, is the fourth most common type of cancer among men.
- 90% of people affected by bladder cancer are older than 55, and if the cancer has metastasized the 5-year survival rate is 35%.
- The Oncopig Cancer Model (OCM) is a novel transgenic swine model that recapitulates human HCC through development of site and cell specific tumors after Cre recombinase induced expression of heterozygous *KRAS*^{G12D} and *TP53*^{R167H} transgenes.

Objective

- To establish a standard protocol for the isolation and growth of OCM urothelial carcinoma cell lines.
- To develop an *in vitro* urothelial carcinoma model from OCM tissue.

Materials & Methods



Results

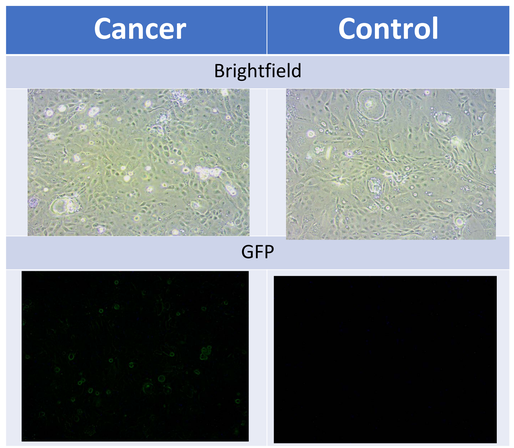


Figure 1: *Brightfield and GFP fluorescence of cells indicating AdCre uptake and expression in urothelial cells.*

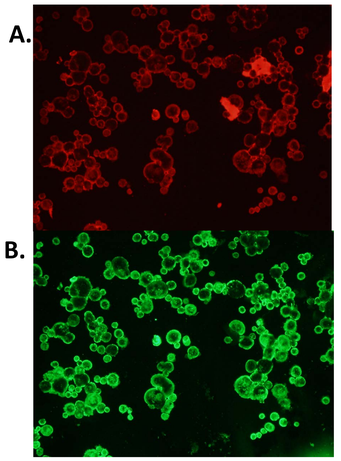


Figure 2: *Image A. shows positive staining for Uroplankin II, a marker for urothelial carcinoma. Image B. shows positive staining for pan-Cytokeratin (PCK-26), a marker for urothelial cells. These pictures indicate successful transformation of urothelial cells into urothelial carcinoma.*

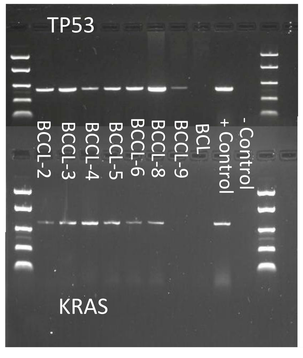


Figure 3: *RT-PCR results indicating bladder cancer cell lines' (BCCLs') and bladder control line's (BCL) expression of TP53*^{R167H} *and KRAS*^{G12D} *transgene. In BCCL lines, TP53 and KRAS are positively expressed. BCL is negative for both KRAS and TP53.*

Results

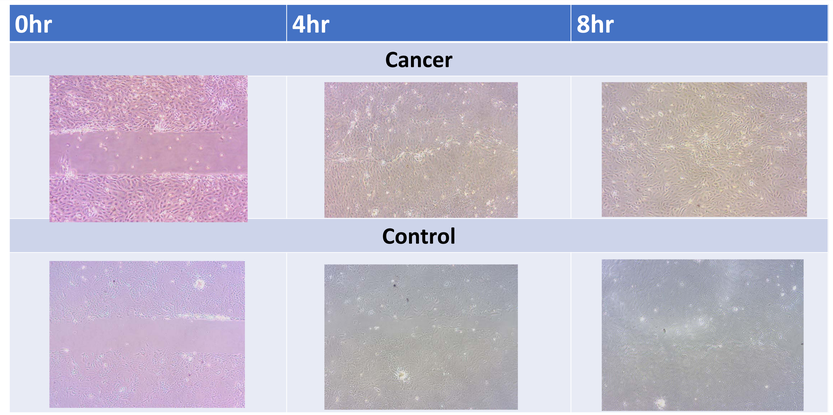


Figure 4: *Cell migration assay results for one bladder cancer cell line (BCCL) and bladder control cell line (BCL). BCCL results show gap close at 4 hours, while BCL shows gap close at 8 hours, indicating phenotypic difference between cancer and control cells. Mean cancer* $t_{1/2}$ *gap=2 hours, mean control* $t_{1/2}$ *gap = 4 hours*

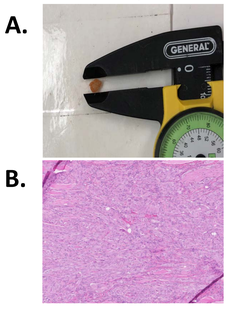


Figure 5: *Image A. shows a gross mass found in mice after subcutaneous injection of BCCL lines. Image B. shows the histology of the mass in Image A., confirming malignancy.*

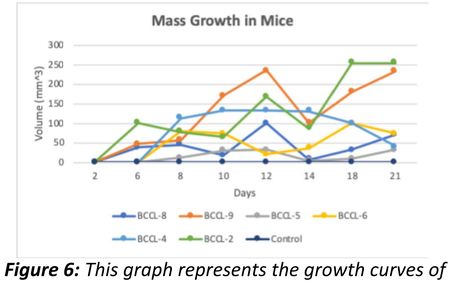


Figure 6: *This graph represents the growth curves of masses found in mice after subcutaneous injection of BCCLs' and BCL. Each mouse was given two SQ injections each containing 5x10^6 cells. Mice were monitored for 21 days post-injection for mass growth. After 21 days, mice are necropsied and masses are harvested for histology. The success rate of BCCLs'* in vivo *is 75%, while BCL's success rate is 0%.*

Conclusions & Future Work

- In the future, the Oncopig Cancer Model may be developed as a validated model for urothelial carcinoma.
- As a model of disease, OCM characterizations can be correlated with human expression of urothelial carcinoma.
- *In vitro* similarities between OCM cells and human cells allow for innovative treatments and drug discovery.