A New Immune Competent, Androgen Receptor Positive Mouse Model of Prostate Cancer Bone Metastasis.

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Background: Prostate cancer (PCa) metastasis research has been hamstrung by lack of animal models that closely resemble the disease present in most patients – that metastasizes to bone, is dependent on the androgen receptor, and grows in an immune competent host. Here, we adapt the androgen dependent Myc-CaP cell line for use as a PCa bone tumor model.

Methods: The Myc-CaP cell line was obtained from ATCC and cultured as recommended in DMEM with 10% FCS. It was labeled by lentiviral transduction with either; tdTomato (CloneTech Lenti-LVX-IRES) and selected by FACS, or labeled with firefly luciferase (Genecopoeia hLUC-Lv105) and selected with puromycin, as indicated. 5 x 10^5 or 5 x 10^4 cells were injected in the left ventricle or tibia respectively of syngeneic FVB/NJ mice. Tumors were detected by necropsy and H&E histology, bioluminescence imaging or fluorescence imaging. Bone formation was examined by µCT. PCa origin of tumors was confirmed by IHC for androgen receptor (Millipore antibody #06-680) and EPCAM (Abcam antibody #71916).

Results: After injection of parental (unlabeled) cells into the left ventricle, these cells formed large mediastinal tumors but also formed bone metastases in the majority of animals; easily visible on H&E sections and confirmed by IHC for the androgen receptor (AR) and epithelial cell adhesion molecule (EPCAM). We labeled Myc-CaP cells with tdTomato and again visualized mediastinal tumors by fluorescent imaging in 10/14 animals and confirmed the presence of cancer cells in bone by flow cytometry. To adapt the model to a bone predominant metastasis pattern, we labeled the cells with luciferase and injected in the tibia and observed gross tumor formation only in tibia. These tumors were osteoblastic on µCT analysis.

Conclusions: Overall, Myc-CaP cells injected in the left ventricle or tibia of syngeneic mice recapitulates key aspects of human metastatic PCa.

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