

Patient-derived, Murine Model of Prostate Cancer

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BACKGROUND

Bone metastases are detected in 80-100% of men who die of prostate cancer and such metastasis leads to painfully debilitating fractures, spinal compression and rapid decline. In addition, metastases to bone tissue often become resistant to standard therapies including androgen deprivation, radiation and chemotherapy. The scarcity of primary human prostate cancer bone metastasis tissues has crippled direct analysis and options to better understand the disease. In addition, spontaneous bone metastasis of prostate cancer in murine models, even to implanted human bone, is an exceedingly rare event. The development of a patient-derived xenograft (PDX) model of bone metastatic prostate cancer presents new options for improving therapeutic options.

TECHNOLOGY DESCRIPTION

Injection of patient-derived prostate cancer bone metastasis specimens into femurs of immunodeficient (Rag2^{-/-};IL2Rγ^{-/-}) mice engendered serially transplantable tumors, which have been used to dissect the complex interactions between prostate cancer and the bone. In addition, the model enables new approaches to understand mechanisms of therapy-resistance that inevitably arise for bone metastatic prostate cancer.

APPLICATIONS

The PCSD1 xenograft model is helping unravel the complex mechanisms of interaction of prostate cancer with the bone microenvironment and patient variation in response to therapies. Enigmas that may now be addressed include:

- ▶ Treatments for patients with significantly lowered PSA levels after treatment with abiraterone, who still showed positive bone scans, and
- ▶ Treatments for patients treated with Cabozantinib (c-Met TKI, XL184), who showed dramatic reductions in positive bone scans but, paradoxically, no decrease in their PSA levels.

ADVANTAGES

In broad terms, the PCSD1 model is more representative and predictive of the bone metastatic prostate cancer tumors found in patients.

Specifically:

- ▶ Current prostate cancer cell line (SCID mouse) xenograft models, include:
 - PC3, which produces purely osteolytic lesions in intra-tibial xenografts;
 - LAPC9, which produces purely osteoblastic lesions; and for over a decade, PCSD1 has low passage numbers with cryopreserved cells from the primary tumor and subsequent passages. Transplantation into Rag2^{-/-};IL2Rγ^{-/-} immunodeficient mice (which completely lack B, T and NK cells) provides superior, highly efficient engraftment relative to SCID mice, which are not completely immunodeficient.
 - VCaP, which produces mixed osteoblastic/osteolytic lesions
- While these three collectively comprise the range of bone lesions produced by prostate cancer metastases, none recapitulates the full range of mixed osteoblastic/osteolytic lesions, observed in most patients.
 - ▶ Where the previous models have been passaged *ex vivo* for over a decade, PCSD1 has low passage numbers with cryopreserved cells from the primary tumor and subsequent passages.
 - ▶ Transplantation into Rag2^{-/-};IL2Rγ^{-/-} immunodeficient mice (which completely lack B, T and NK cells) provides superior, highly efficient engraftment relative to SCID mice, which are not completely immunodeficient.

STATE OF DEVELOPMENT

PCSD1 is ready for use in pre-clinical drug testing as well as basic research on castration-resistant prostate cancer and tumor growth in the bone microenvironment/niche. Validation includes:

- ▶ Tumors were characterized as advanced, luminal epithelial prostate cancer (PSA+, AR+, TMPRSS2;ERG-) by RT-PCR and immunohistochemical biomarker analyses.

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OTHER INFORMATION

KEYWORDS

murine, model Patient-derived, cancer, oncology, PC, in vivo, metastasis, metastases, prostate cancer, xenograft, PDX, drug development, PC3, LAPC9, VCaP, osteoblastic, ostoblast, osteolytic, pre-clinical, drug development, drug testing, castration-resist

CATEGORIZED AS

- ▶ **Medical**
 - ▶ [Disease: Cancer](#)
 - ▶ [Research Tools](#)
- ▶ **Research Tools**
 - ▶ [Animal Models](#)

RELATED CASES

2012-105-0

► MicroCT scanning showed that PCSD1 intra-femoral xenografts induced mixed osteoblastic/osteolytic lesions that closely recapitulated bone metastatic prostate cancer lesions in patients.

INTELLECTUAL PROPERTY INFO

Worldwide rights available; Pending patents available under confidentiality.

RELATED MATERIALS

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PATENT STATUS

Patent Pending

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