Introduction

Bone metastases are frequent and fatal outcome of advanced prostate cancer. Many of the currently used preclinical models lack typical characteristics of the heterogenic human disease. We improved existing methodology by using fresh patient-derived tissues and serially transplantable LuCaP-136 xenografts in bone metastasis models.

LuCaP-136 model

We used serially passaged spheroid cultures of LuCaP-136 xenografts. These spheroids have close molecular and cellular resemblance to the original xenograft and their in vitro culture enables genetic engineering such as luciferase transfection (Figure 1). These spheroids formed highly osteosclerotic intratibial tumors in mice (Figure 2). The tumors responded to castration by strong inhibition of growth, followed by a relapse indicating emergence of castration resistance (Figure 3).

Patient-derived xenografts

Clinical prostate tumor specimens were collected from robotic-assisted laparoscopic radical prostatectomy operations in Turku University Hospital (Turku, Finland). Patient-derived xenografts (PDX) of Gleason grade 7-9 tumors were cut into small pieces and implanted subcutaneously into Te-pellets-bearing nude mice (Figure 4). In another experiment, tumor pieces were digested and inoculated intratibially into the bone marrow cavity of nude mice (Figure 5). Tumor-take was 50-100% in both models, and it was dependent of the aggressiveness of the original tumor. The passaging was performed via intratibial inoculation to preserve the typical microenvironment-related characteristics. So far, intratibial PDXs were grown for 4 passages. They formed osteosclerotic tumors in bone and some metastasized to lungs (Figure 6).

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References


Conclusion

The described models provide new tools for prostate cancer research and personalized medicine.