

Patient-Derived Ex Vivo Prostate Cancer Models for the Development and Evaluation of Targeted Therapies

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Background

Preclinical models that reliably recapitulate the complexity of human prostate tumors remain limited. The development of novel prostate cancer therapies however requires preclinical models that preserve key features of the native tumor while remaining experimentally accessible. Current model systems often incompletely recapitulate tissue architecture, cellular heterogeneity, and interactions within the tumor microenvironment. We are developing patient-derived ex vivo tissue cultures as a versatile platform for therapeutic testing and targeted experimental manipulation.

Methods

Primary prostate cancer tissue was used to establish ex vivo tissue slice cultures. Tissue slices were characterized by histology and immunohistochemistry for tissue architecture, prostate epithelial/tumor markers, and immune cell populations, with proliferation and apoptosis assessed over time. As part of a collaborative study, the slice model was used to evaluate the response to the combination of the CDK12/7/9 degrader BSJ-5-63 and the PARP inhibitor Olaparib, complementing in vitro and in vivo studies. In parallel, viral gene-delivery approaches were used to investigate the feasibility of manipulating cells within intact prostate tissue.

Results

Ex vivo prostate cancer tissue slices remained viable and preserved key tumor features over the 14-day culture period evaluated. Immunohistochemical analysis demonstrated retained proliferative capacity by Ki-67 staining, no increase in apoptosis as assessed by cleaved PARP, strong AR expression, and patient-specific levels of immune cell infiltration as assessed by CD45, CD3, and CD20.

Within the collaborative therapeutic study, treatment with the CDK12/7/9 degrader BSJ-5-63 plus the PARP inhibitor Olaparib resulted in strong induction of apoptosis as assessed by cleaved PARP immunohistochemistry, validating effects observed in complementary in vitro and in vivo models. These findings demonstrate the utility of the ex vivo slice model for evaluating therapeutic responses in intact patient-derived tumor tissue.

Initial gene delivery studies using GFP-expressing vectors demonstrated successful transduction and tissue penetration, providing proof-of-concept that the model is amenable to genetic manipulation. Ongoing work is extending this approach toward selective targeting of tumor cells and distinct cellular populations within the tumor microenvironment.

Conclusions

Patient-derived ex vivo prostate cancer tissue cultures preserve key features of the native tumor while remaining amenable to therapeutic testing and experimental manipulation. Their application in a collaborative treatment study demonstrates their value as a complementary preclinical model alongside conventional in vitro and in vivo systems. Ongoing development is expanding the platform toward cell type-specific manipulation, advanced targeted and immunotherapeutic strategies, and future application to metastatic prostate cancer biopsies. Together, these approaches establish a versatile platform for studying prostate cancer biology and supporting preclinical therapeutic development.

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Conflict of Interest Disclosure Statement

The authors have no conflicts of interest to disclose.