

Leveraging the PDeX (Patient Derived eXplant) model to determine the basis for response to AR-directed therapeutics in prostate cancer

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Prostate cancer (PCa) is the most common non-cutaneous cancer and the third leading cause of cancer-related death in American men. Androgen receptor (AR) is a hormone-activated transcription factor that plays an important role in both the development and progression of PCa. Androgen deprivation therapy is a common first-line therapy for disseminated disease. However, virtually all tumors become resistant to such therapy and the tumor recurs and is termed castration resistant prostate cancer (CRPC). There is no durable cure for CRPC; thus, there is a vital need for the development of novel, more effective drugs. One major hurdle in this aspect is the lack of adequate preclinical models. Current models do not effectively recapitulate the heterogeneity and the microenvironment of human PCa tumors, significantly hindering the ability to accurately predict therapeutic response. Our collaborative group has utilized and characterized a method to culture patient tumors *ex vivo*, termed Patient Derived eXplant (PDeX). This approach maintains the integrity of the native tumor microenvironment (TME), tumor tissue morphology, and endogenous molecular signaling. Importantly, our PDeX model can be manipulated both chemically (drugs/compounds) and genetically (shRNA) in order to determine specific reactions and mechanisms of response on individual tumor growth. Furthermore, with this model we can quantitatively assess drug efficacy on numerous parameters (i.e. AR levels, Ki67 staining, apoptosis screening, and desmoplastic indices). Data to be discussed will assess the variances in response to AR-directed therapeutics and underlying mechanisms of action, while also utilizing TME characteristics as a means to predict response to therapy. In addition, we can potentially identify clinically relevant subpopulations of patients and molecularly profile their cultured tissue to uncover new pathways for therapeutic intervention. Thus, the PDeX model allows for a comprehensive evaluation of individual tumors in their native microenvironment to ultimately develop more effective therapies. This study will have transformative clinical impact discerning novel metrics for the inclusion of precision medicine for advanced PCa.

Conflicts of Interest: None

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