Introduction

FGF-signaling pathway seems to have an important role in the progression of metastatic prostate cancer, and FGFR inhibitors have provided interesting preliminary results in preclinical studies. However, many of the currently used preclinical tumor models lack typical microenvironment and characteristics of human disease. The aim of this study was to establish patient-derived prostate cancer models (PDX) and study FGFR inhibitors as potential investigational drugs.

Materials and methods

Clinical prostate tumor specimens were collected from robotic-assisted laparoscopic radical prostatectomy operations in Turku University Hospital, Turku, Finland (Figure 1). Patient-derived tissues of Gleason grade 7-9 were cut into 1-2 mm³ pieces and cultured in vitro for 6 days with androgen supplementation. FGFR inhibitors Dovitinib and AZD4547 were administered into the tissue culture medium (Figure 2). Viability and differentiation of cultured tissues were examined immunohistochemically by the expression of Ki-67, androgen receptor (AR) and PSA. PDX in vivo models were developed by implanting tissue pieces either subcutaneously or subrenally, or by digesting and then inoculating intratibially into the bone marrow cavity of Balb/c nude mice. Mice were supplemented with testosterone pellets.

Results

In vitro

Non-cultured Dovitinib AZD4547

FGFR inhibitors demonstrated anti-proliferative effects on patient-derived models in vitro. Challenging PDX prostate cancer in vivo models were successfully established utilizing various tumor microenvironments. These models provide a personalized medicine tool that could be used to test the individual prostate cancer patients’ responses to therapy in the future.

Conflict of interest

Johanna Tuomela and Jussi Halleen are employees of Pharmatest Services Ltd. Authors claim no conflict of interest.

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