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Purpose:
Prostate, bladder and kidney cancers represent 1 900 000 new cases and 620 000 deaths per year worldwide and their incidence is increasing by 1-10% each year. These pathologies are refractory to current therapies at advanced and metastatic stages. Patient-derived tumor xenografts (PDX) faithfully reproduce the heterogeneity of patients’ tumors. They became over the last decade essential preclinical tools to improve drug development process and identification of predictive biomarkers. Here, we developed a unique panel of well-characterized PDX models for the three main urological cancers.

Experimental design:
Tumor tissues were obtained from patients undergoing surgery. Patient informed consent and clinical history are available for all patients. Tumor fragments were subcutaneously xenografted into nude mice and serially passaged. To assess the stability of the PDXs, various analyses were performed including growth characteristics, histopathology, microscopic +/- immunohistochemical findings, transcriptomic profile analysis, genetic stability and pharmacological response to standards of care. In addition, specific features for each cancer type were also explored.

Results:
Since 10 years, we have collected 247, 152 and 574 prostate, bladder and kidney tumors respectively at all stages and grades and developed 6, 30 and 30 models respectively, i.e. 2.1, 19.7 and 8.9 % success rate. For all cancer types, tumor growth data and all histological, molecular and genetic analyses confirmed the stability of the models compared to the parental tumor. Molecular profiling revealed that less than 5% of genes were differentially expressed between the primary tumors and PDX tumors at various passages. In contrast to other organs, the take rate for kidney PDXs was correlated to tumor features (stage, grade, sarcomatoid component). Interestingly, for bladder PDXs, several molecular subtypes were defined including basal phenotype as well as FGFR3 mutation subgroups. Responses to current therapies recapitulated the clinical state.

Conclusion:
We developed an extensive panel of prostate, bladder and kidney PDX models. These models will be of great importance for the development of efficient therapies and hopefully for personalized medicine.

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