



Patient-derived xenograft collection from bladder cancer

A UNIQUE COLLECTION OF 31 PDX FROM MIBC, NMIBC AND UTUC

Model

- Urosphere has developed a biobank of 31 Patient-derived xenografts (PDX)
 - 26 from muscle invasive bladder cancers (MIBC) [1-3];
 - 1 from non-muscle invasive bladder cancer (NMIBC);
 - 4 from upper tract urothelial carcinomas (UTUC)
- These models have been highly characterized: more than 300 cancer genes have been analysed.

Interest

- Test efficacy of new drugs in immunocompromised mice;
 - > Targeted drug therapy (ex: FGFR3, EGFR);
 - > Chemotherapy
- Identify drug combinations;
- Analyse Pharmacokinetics / pharmacodynamics responses;
- Mimic a clinical trial with surrogate models;
 - > Analyse biomarkers in responder and non-responder populations.

Model Description

- Fresh tumours are harvested from donor mice;
- Fragments 20 mm³ are implanted subcutaneously into anesthetized mice;
- Tumours are measured 2 or 3 times a week;
- Mice with tumours reaching 60 to 270 mm³ are included in treatment period;
- Treatment is administered as per protocol.

Parameters evaluated

- Body weight variations;
- Tumour growth inhibition (TGI);
- Tumour growth delay index (TGD_i);
- Mean Relative Tumour Volume (mRTV);
- Response to treatment based on RECIST criteria.

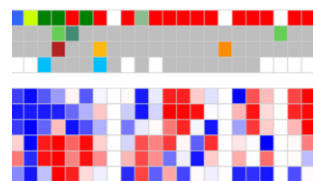
Scientific publications

- [1] Béraud *et al.*, Toulouse OncoWeek 2020, Toulouse, France
 [2] Béraud *et al.*, AACR, Denver, 2019, USA
 [3] Lang *et al.*, AACR, Atlanta, 2019, USA

This biobank is representative of the 6 consensus molecular classes of bladder cancer as described in the literature [2]

Legend Classification

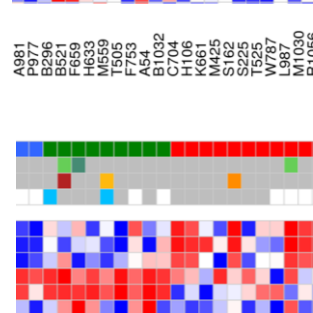
- Ba/Sq
- LumNS
- LumP
- LumU
- NE-like
- Stroma-rich



classification_tumor
mutation_FGFR3
mutation_PPARG
mutation_PIK3CA

Legend Mutation

- FGFR3* R248C
- FGFR3* S249C
- PPARG* I484I
- PPARG* L339F
- PPARG* T475M
- PIK3CA* E545K
- no mutated
- NA

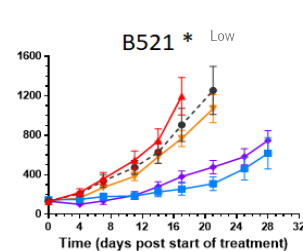
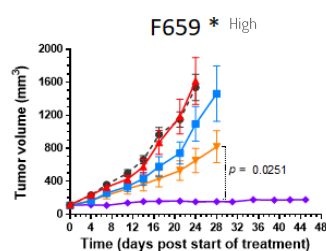


classification_PDX
mutation_FGFR3
mutation_PPARG
mutation_PIK3CA

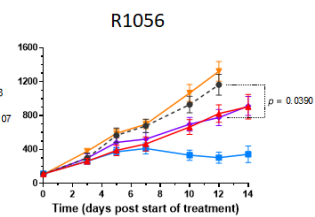
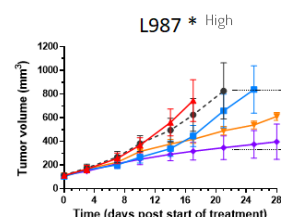
KRT5
KRT6A
KRT14
FOXA1
GATA3
FGFR3

Example of combination therapy with Erlotinib and Erdafitinib highly effective in FGFR3-mutated tumours

Luminal papillary models



Basal/Squamous models



[*] FGFR3 mutated PDX with either high or low protein expression levels are indicated

* FGFR3- mutated

- Vehicle 10 ml/kg
- Gemcitabine 60 mg/kg + Cisplatin 4 mg/kg
- Erlotinib 30 mg/kg
- Erdafitinib 10 mg/kg
- Erlotinib 30 mg/kg + Erdafitinib 10 mg/kg