Patient-derived xenograft collection from kidney cancer

A UNIQUE COLLECTION OF 30 PDX FROM KIDNEY CANCERS

Model

- Urosphere has developed a biobank of 30 Patient-derived xenografts (PDX) from kidney cancers [1;2];
- This biobank is representative of the diversity of the clinical RCC pathologies (all stages and grades) described in the literature [1];

Interest

- Test efficacy of SoCs in immunocompromised mice;
  > Targeted drug therapy (ex: Sunitinib, Sorafenib, Everolimus);
  Identify drug combinations;
- 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 mm^3 are implanted subcutaneously into anesthetized mice.
- Tumours are measured 2 or 3 times a week;
- Mice with tumours reaching 60 to 270 mm^3 are included in treatment period;
- Treatment is administered as per protocol.

Parameters evaluated

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

Scientific publications

[1] Lang *et al.*, Oncotarget, 2016
[2] Béraud *et al.*, Toulouse OncoWeek 2018, Toulouse, France

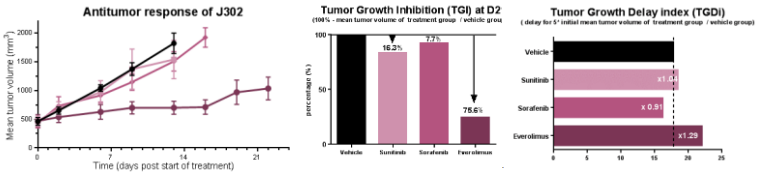
Diversity of the clinical RCC covered by our PDX from kidney cancers

	Original Tumor n (%)	PDX models n (%)
ccRCC	262 (78)	24 (80)
Papillary RCC	26 (7.7)	1 (3.3)
Oncocytoma	21 (6.3)	-
Chromophobe RCC	18 (5.4)	1 (3.3)
Composite	5 (1.5)	2 (6.7)
Medullary RCC	2 (0.6)	1 (3.3)
Unclassified RCC	2 (0.6)	1 (3.3)
TOTAL	336	30

Tumour type repartition of Urosphere's kidney models collection. Each tumoral grade and stage are represented.

TNM stage	Original Tumor	PDX models
pT1	5	-
pT1a	109	1
pT1b	60	6
pT2	23	-
pT3	10	2
pT3a	42	5
pT3b	45	10
pT3c	3	3
pT4	10	3

Example of characterizations of kidney PDX models: pharmacological studies with standard of care (SoC) molecules



Representative preclinical studies with reference drugs (sunitinib 40 mg/kg *per os*, one period wash-out, 3 times/week; sorafenib 30 mg/kg, 5 times/week; Everolimus, 10 mg/kg, 5 times/week).

PDX ID	Sunitinib	Sorafenib	Everolimus
M62	NR	R*	NR
S60	NR	NR	R*
Z81	R*	R**	R**
D55	R**	NR	R**
S393	NR	R*	R*
H33	R*	ND	ND
J302	ND	NR	R*
W1006	ND	NR	R***
K111	NR/PP	ND	ND
F57	NR	ND	ND

NR: non responder; R: responder; PP: predictive of patient's therapeutic response ; ND: not determinated;

Variable drug's efficacy profiles were observed.
For 1 patient that had been treated in the clinic, we have obtained concordance between patient and PDX tumour response (PDX model K111).