Bladder cancer organoids

A TUMORAL AVATAR AS A ROBUST PRECLINICAL MODEL

Model

- Organoids were generated from specimens obtained from patients that underwent either transurethral resection of bladder tumors (TUR-B) or cystectomy (Patient-derived organoids, PDO) or from Patient-derived xenograft tumors (PDX-derived organoids, PDXO)
- Urosphere has developed a biobank of 10 organoid models
- These models have been highly characterized by molecular, histological and pharmacological analyses.

Interest

- Organoids from bladder cancer keep the characteristics of patient's tumour and the biobank represents patient's heterogeneity;
- They could be used alone or in co-culture (with immune cells for example);
- They allow a rapid *in vitro* screening of chemotherapeutic or immunotherapeutic subtances;
- For PDXO, *in vivo* studies with their PDX counterpart could be realized;
- This collection could be used to realize an organoid clinical trial;
- Development of organoid-resistant models (example of Padcev®-resistant model).

Model description

- Urothelial progenitors are isolated from tumour samples and seeded in Matrigel® with proprietary adapted culture medium;
- Organoid culture is treated with test and reference substances for 5 days.

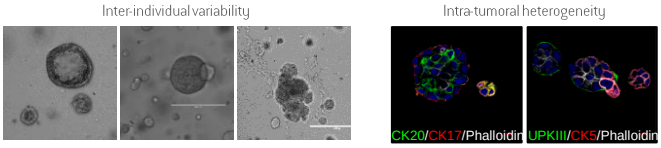
Parameters evaluated

- Morphology: number of organoids per condition, area (µm²), length (µm), volume (µm³);
- Cell viability measured with CellTiter-Glo® 3D (luminescence);
- Apoptosis measured with Caspase-Glo® 3/7 assay (luminescence);
- Cytokine release with Luminex assay.

Scientific publications

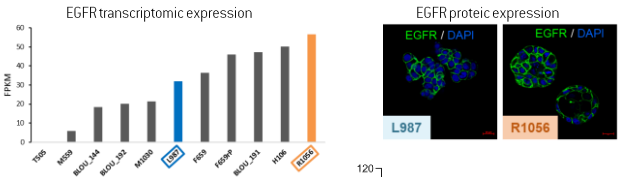
- Decaup *et al.*, AACR, San Diego, 2024

Organoid models reflect inter-individual variability and tumors' heterogeneity

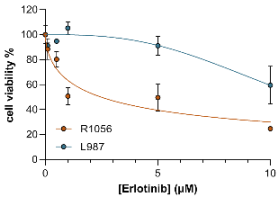


Targeted EGFR by 2 therapeutic approaches

Organoid model selection according to EGFR expression

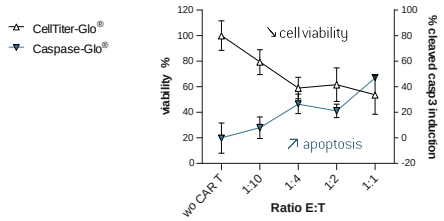


Direct targeting with erlotinib (EGFR inhibitor)

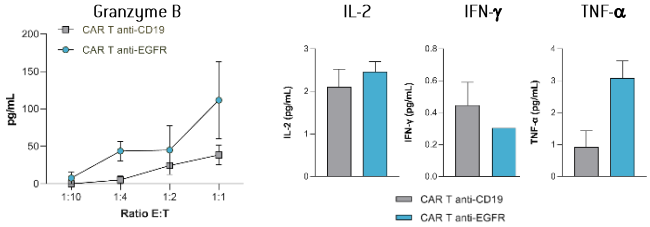


Immunotherapeutic approach using anti-EGFR CAR-T cells

Viability and apoptosis analysis after 48h of co-culture



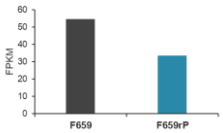
Pro-inflammatory cytokines and granzyme B release after 72h of co-culture



Padcev®-resistant organoid model

Persitance of Nectin-4 in both naive (F659) and their resistant counterpart (F659rP) models

Nectin-4 transcriptomic levels



Differential responses to Padcev® between F659 and F659rP models

Pharmacological analysis

F659rP
F659