ONCOTRAP: Assessing drug response and metastatic potential of patients' renal carcinoma on a chip

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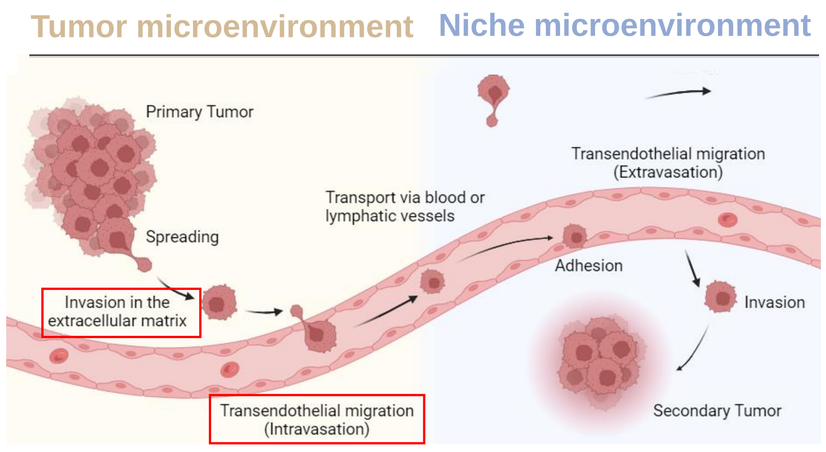
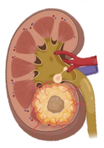
INTRODUCTION



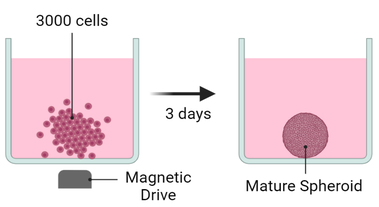
- clear cell Renal Cell Carcinoma (ccRCC) → most prevalent
- RCC **metastasis** (mRCC) can develop in Lung, Liver and **Bone** → highly heterogeneous + poor treatment response rate
- Our goal → develop a microfluidic chip that evaluate :
  - the **invasiveness** of renal cancer cells in a 3D context
  - their **intravasation** potential.



Inserted into a chip named ONCOTRAP, **tumoroids** formed from the primary tumor of patient can provide a robust preclinical test to study metastatic process.

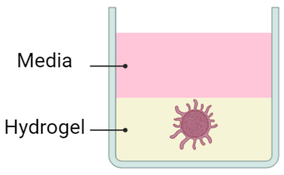
METHODS

SPHEROID MODEL



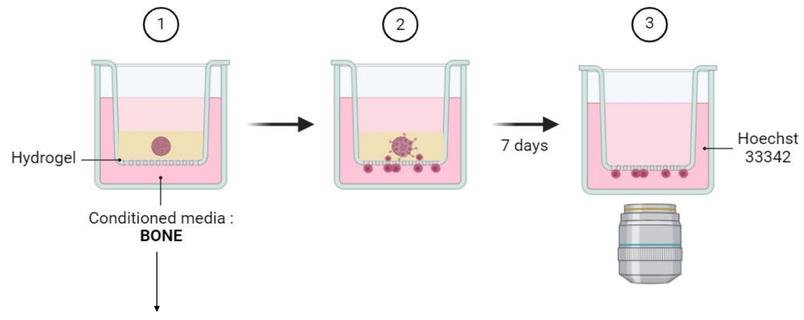
Cell line	Tumor Type	Doubling Time
RCC10	ccRCC	29h
786-O	ccRCC	24h
RCC7	ccRCC	24h
ACHN	papillary	32h

INVASION ASSAY



- Invasion **length** : spheroid border → farthest cell
- Invasion **area**
- Number of invasive **cells**

ATTRACTIVITY ASSAY



human Periosteum Derived Stem Cell (**hPDSC**) are differentiated in **osteoblasts** with a specific medium containing **BMP2**

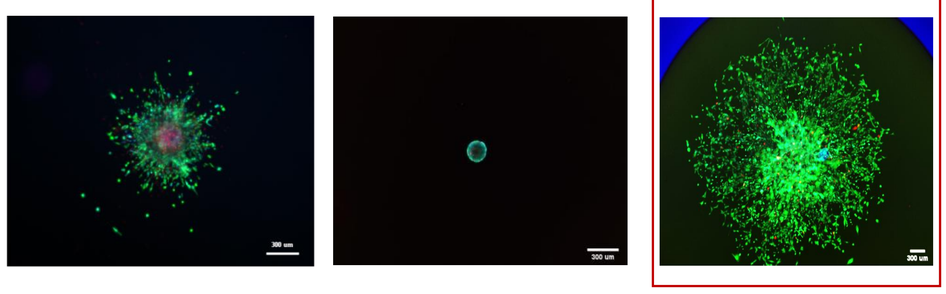
CONCLUSION

- Proof of concept of this device → Spheroids (cell lines)
- Final Aim → Introducing <u>patient-derived</u> **tumoroids**
- **Final Use**
  - Evaluate **invasiveness** of renal cancer cells and the **metastatic capacities** of a patient's tumor
  - Evaluate **drug response**
  - Creating **personalized medicine**

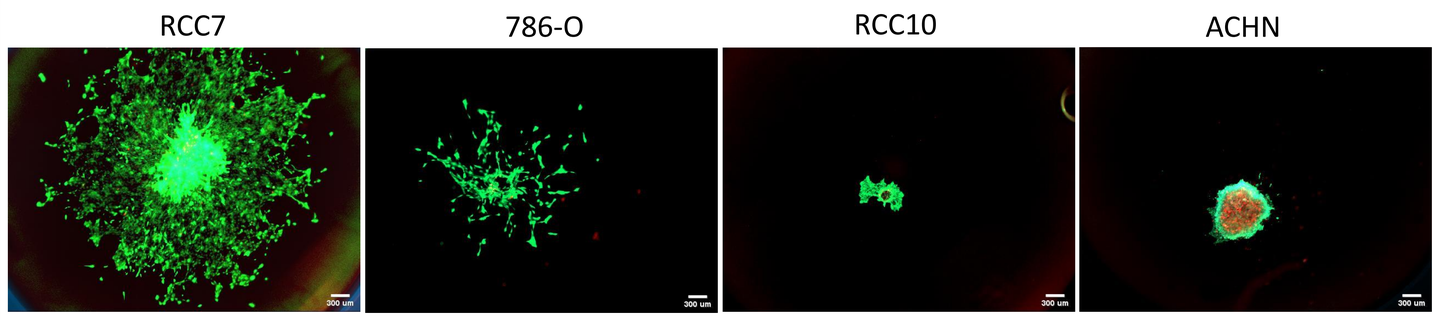
RESULTS

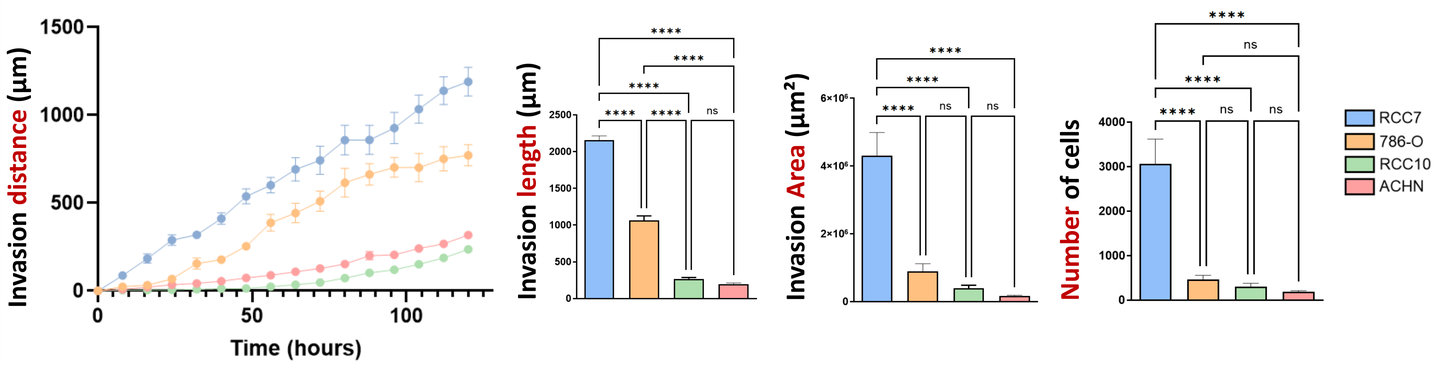
HYDROGEL CHOICE

Spheroid included in a **3D** environment = study the **invasive capacities** of cells
→ Hydrogel choice for ccRCC tumor = **COLLAGEN I**



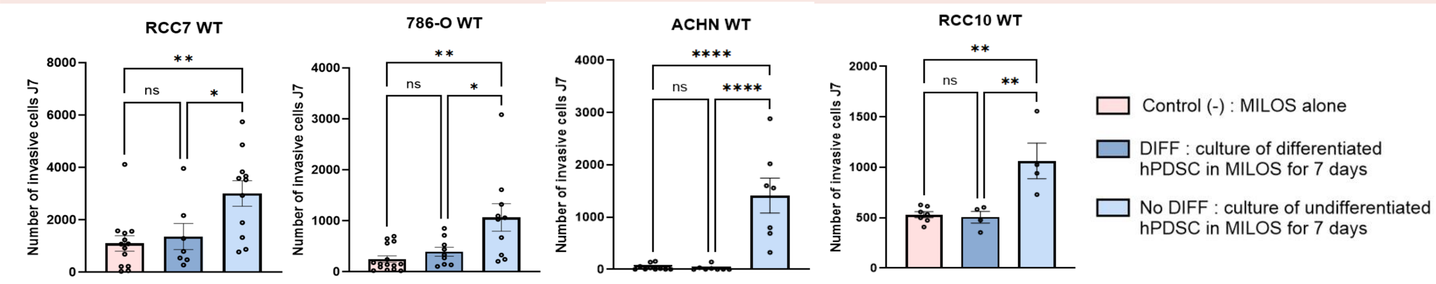
INVASION ASSAY – day 7





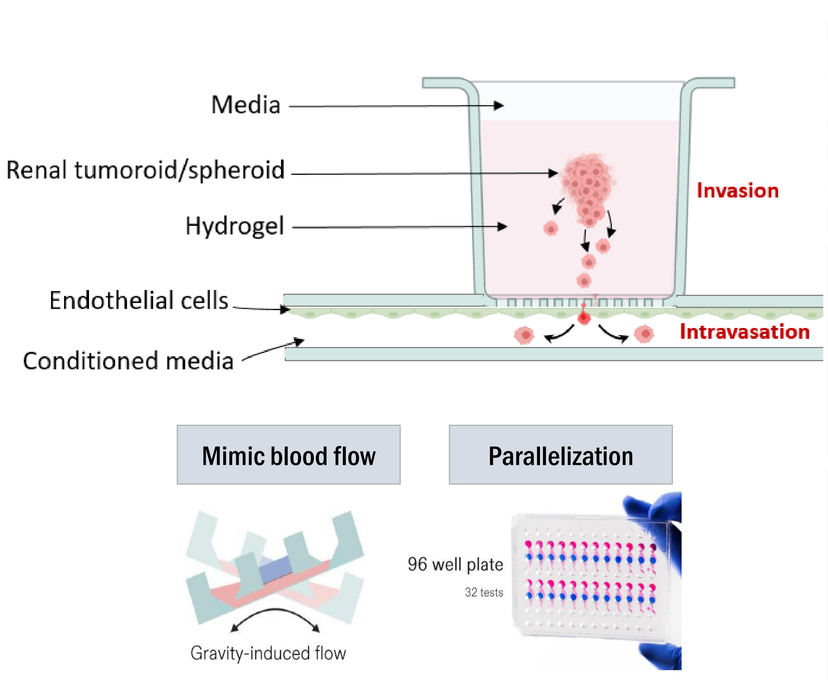
→ Identification of the most aggressive cell line : **RCC7** and **786-O**

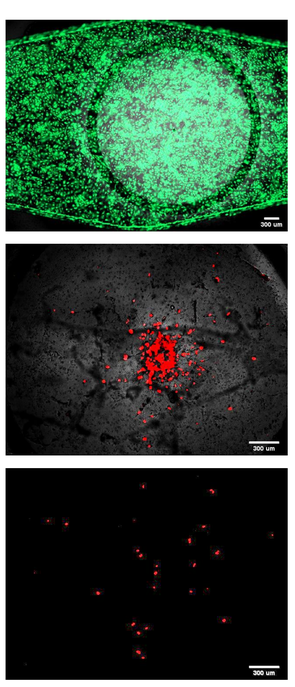
ATTRACTIVITY ASSAY



→ Cancer cells are attracted by the non-differentiated osteoblasts

APPLICATION : AKITA MICROFLUIDIC CHIP





HUVEC cells layer after 7 days of culture inside the microfluidic chip
→ Permeability assay performed with DEXTRAN 40

786-O mcherry <u>spheroid</u> invading inside the top-chamber of the microfluidic chip

Removal of the hydrogel shows **786-O mcherry** <u>cells</u> that have undergone intravasation

• Séraudie et al - A new scaffold-free tumoroid model provides a robust preclinical tool to investigate invasion and drug response in Renal Cell Carcinoma – Cell death & disease (2023)
• Giacosa et al - Cooperative Blockade of CK2 and ATM Kinases Drives Apoptosis in VHL-Deficient Renal Carcinoma Cells through ROS Overproduction - Cancers (2021)