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

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Introduction and project outline

Clear cell Renal Cell Carcinoma (ccRCC) is one of the most prevalent kidney cancers, which is often asymptomatic and thus discovered at a metastatic state (mRCC). mRCC are highly heterogeneous tumors composed of subclonal populations that lead to poor treatment response rate. Several recent works explored the potential of ccRCC tumoroids culture derived from patients. Following the observation that ccRCC tumoroids can create their own niche by secreting extracellular matrix components, we developed the first scaffold-free tumoroid model of ccRCC tumors. This model enables to evaluate invasiveness of renal cancer cells in a 3D context toward a metastatic niche. Inserted into a chip named ONCOTRAP, these tumoroids provide also a robust preclinical test to study metastatic process.

Results

Tumoroids from mice or human tumors were generated with high success rate ($\geq 90\%$) using a magnetic suspension method and standard culture media. Immunofluorescence and transcriptomic analysis revealed their self-organization and the reproducibility of the method, highlighting that the majority of gene expression patterns was preserved in tumoroids compared to their matching tumor tissue¹ (Figure 1A). We showed the invasive capacities of tumoroids by inserting them in the right 3D matrix, based of collagen type I (Figure 1B). Using a microfluidic chip, we aim to study the attractiveness of ccRCC invasive cells towards a metastatic niche (Figure 1C and 1D) and, as a proof of concept, we developed a bone metastatic niche.

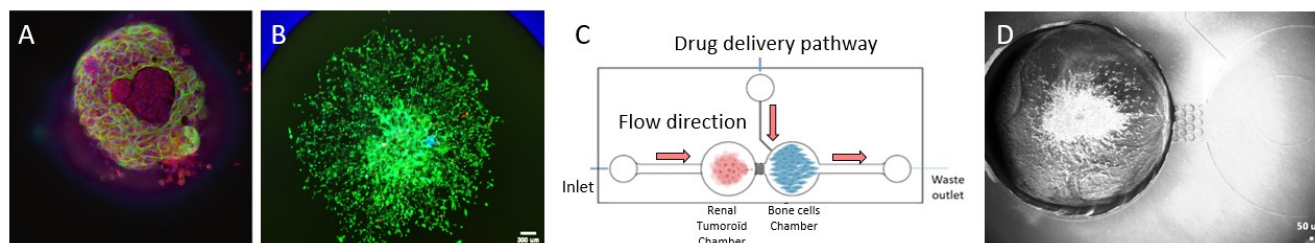


Figure 1 : A. Mature ccRCC tumoroid, labeled with PanCollagen and CD44. B. Invasive ccRCC spheroid, labeled with a Live & Dead staining. C. Oncotrap chip design. D. Invasive ccRCC inside the Oncotrap chip.

Conclusion

Using this device, our goal is now to evaluate the metastatic cell potential in primary tumor samples. Furthermore, it could be adapted to screen for potential metastatic inhibitors.

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