Profiling Metabolic and Signaling Phenotype of Bladder Cancer Cell Lines and Patient Biopsies

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Abstract:
Bladder cancer (BC) is one of the most common malignancies worldwide [1]. Most patients are diagnosed with non-muscle invasive BC with frequent recurrences leading to invasive tumors, reducing survival expectations [2,3]. 3D cultures constitute a more clinically relevant model for studying cancer as spheroids recapitulate in vivo structure, cell-cell interactions, nutrients and oxygen gradients, absent in monolayers [4]. Metabolic characterization in spheroids could reveal dependence on specific enzymatic activities and nutrients toward novel therapies [5].

This project aims to conduct a comparative analysis of metabolism and cellular features of a BC cell lines panel at different stage/grade, grown as monolayer and spheroids.
Samples were analyzed at different timepoints evaluating cellular features by quantitative imaging using Operetta CLS high-throughput microscope, bioenergetic parameters by Seahorse technology and validated by WB analysis of key metabolic enzymes. Moreover, the obtained 3D models and patient biopsies will be analyzed with raman spectroscopy, for preclinical purposes.

High grade cell lines showed an increased capacity to form vital spheroids. Moreover, high grade cell lines grown in monolayer presented higher basal and maximal glycolysis compared to low grade cells, while mitochondrial respiration showed no obvious correlation with the pathological grade. Furthermore, no obvious correlation was observed for changes in use of mitochondrial respiration and glycolysis with the pathological grade during the spheroid formation, although during the process of spheroid formation, some cell lines showed a preferential use of respiration for ATP production. The permanence of this metabolic rewiring in fully formed spheroids and its correlation with the pathological grade is under investigation.

References

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