**Multi-cellular spheroid as a new *in vitro* system to study tumor endothelial cell heterogeneity**

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Lung cancer is the leading cause of cancer death worldwide causing more than 1.6 million deaths every year. Clinically, it is classified as small and non-small cell lung cancer, the latter representing >85% of the total cases. Non-small cell lung cancer is a highly vascularized tumor and currently several anti-angiogenic agents, in combination with chemotherapy, are approved in advanced stages. Unfortunately, despite the remarkable clinical benefits of these combinational approaches on response rate and progression free survival, the overall survival benefits were modest due to acquired drug resistance.

Recent evidence from single cell RNA-sequencing allowed us to uncovered an impressive endothelial cell heterogeneity in various models of non-small cell lung cancers. We postulate that tumor endothelial cells (the cells lining the inner side of tumor blood vessels), by interacting with other cell types from the tumor microenvironment, are important players that may influence therapeutic response and patient outcome. In this project we aimed at modeling and studying tumor endothelial cell heterogeneity using an *in vitro* model of 3D multi-cellular spheroid, and assess therapeutic response to clinically-approved anti-cancer treatments.

As such, we believe our results will help to pave the way to a better understanding of how tumor endothelial cell heterogeneity may influence response to anti-cancer treatments.