Glioma refers to a highly heterogeneous group of neoplasms that account together for the majority of primary tumors arising within the brain parenchyma. Unfortunately, even with the best medical care, glioma is invariably incurable and life-limiting, although the prognosis and natural history can vary widely between the different disease subtypes. Moreover, the lack of targeted therapies and the fact that once the disease recurs it is largely resistant to treatment, limits the ability of physicians to offer life-extending treatments to patients.

In the past decade or so we have witnessed major scientific breakthroughs that lead to a significant progress in our understanding of the biological mechanisms governing and driving the evolution of glioma, including paradigm-shifting insights gained from dissection of the glioma intra-tumor ecosystem at the unprecedented resolution provided by single-cell genomic technologies. However, despite these important leaps forward, numerous challenges still have to be overcome to bring cure for the patients suffering from this horrible disease.

In the scope of my PhD research, we chose to focus on characterizing the common longitudinal molecular trajectories in the two main adult glioma subtypes - IDH-WT and IDH-mutant glioma - by profiling using single-cell RNA sequencing pre- and post-treatment samples resected from patients throughout their disease course. First, we analyzed IDH-mutant glioma samples from patients that were treated with a mutant-IDH inhibitor, which has shown significant benefit in IDH-mutant acute myeloid leukemia but failed to show benefit in IDH-mutant glioma, and show that it acts as a differentiation-inducing agent in a subset of patients. Second, we analyzed matched primary and post-recurrence IDH-WT glioma samples resected from patients treated with standard-of-care treatment to unveil the cellular evolution upon recurrence and characterize the biological mechanisms that govern and drive this evolution as it may significantly contribute to emergence of resistance to treatment and disease progression.