

**Title:** Therapeutic approach against the novel molecular target SerpinB3 for glioblastoma

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**Background:** Despite therapeutic interventions for Glioblastoma (GBM), cancer stem cells (CSCs) drive recurrence but the precise mechanisms underlying CSC resistance, are unclear.

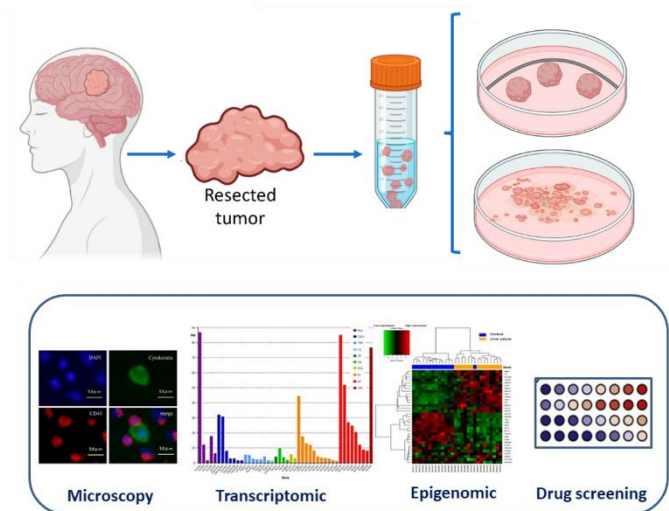
It was recently reported that suppression of SerpinB3 increases cell death, decreases self-renewal and tumor initiation, and enhances the response of CSCs to radiation via lysosomal-mediated cell death.

**Aim of this PhD project** is to investigate the biological role and prognostic significance of SerpinB3 and related genes in GBM and preclinical therapeutic strategies.

This will be pursued through the following tasks:

- 1) A comprehensive molecular characterization in terms of tumorigenic potential and drug-response, with simultaneous profiling of the transcriptome and epigenome, will be performed by using CSC cultures and patients derive GBM organoids.
- 2) Disclosure of the biological role (mechanisms and signalling pathways involved) of SerpinB3 and related genes in the progression of experimental GBM development.
- 3) Validation of new preclinical therapeutic strategies to interfere with potential pro-carcinogenic role of SerpinB3.

**Techniques:** GMB cell isolation and patient derived 3D cultures, disease modelling and drug screening, transcriptomic, epigenomic and proteomic analysis, cytofluorimetric analysis, gene silencing, microscopy analysis, spatial imaging.



**Bibliography:** Lauko A, et al. SerpinB3 drives cancer stem cell survival in glioblastoma. Cell Reports 2022;40(11):111348. doi: 10.1016/j.celrep.2022.111348.