Extracellular matrix interactions of importance for brain tumor formation and neural development

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Research area:
Cancer/oncology

Brief description
In our projects we incorporate experience of neural stem cells with glioma biology, leveraging the close relationship between these two fields. We also investigate the neuro-inflammatory responses to brain tumors.

Aim
The overall goal of our research is an improved treatment of malignant brain tumors, in particular glioblastoma and medulloblastoma.

Background
The focus of this project is the "brain tumor niche" that allows tumor cells to detach from the original site, remodel the extracellular matrix (ECM) and migrate to seed new tumors that ultimately leads to death of the patient. Based on our increased understanding of the biochemical and molecular determinants of brain tumor invasion, new drug targets in the glioma microenvironment could be identified.

Heparan sulfate (HS) proteoglycans are main components of the ECM where they interact with a large number of physiologically important macromolecules, thereby influencing biological processes. HS modulate growth factor activities, and we have shown a vital role for HS in formation of the neural lineage (Forsberg et al., 2012). The major enzymatic activity degrading HS is heparanse.

Project plan
In this project we address HS proteoglycan biosynthesis and degradation in clinical brain tumor samples, human glioma and medulloblastoma cell culture as well as mouse and human models of glioma and medulloblastoma. We use inhibitors of HS degradation, and gene targeting approaches to modify HS levels with the aim to find new therapeutic targets for brain tumors.

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