Malignant brain tumors are amongst the most lethal solid tumors. The standard treatment consists of surgical resection followed by adjuvant radiochemotherapy. It has been proposed that glioma cells with stem cell features contribute to both, initiation and progression of primary and recurrent glioma. It remains elusive, how their growth is regulated and how the stem-like cells, which constitute only a subfraction of the brain tumor, could contribute to tumor progression and relapse. Here we investigated the responsiveness of stem-like tumor cells to mitogens and growth factor withdrawal. Moreover, we analyzed the expression of receptor tyrosine kinases and peptide growth factors in stem-like brain tumor cells and their non-stem-like counterparts from the same tumor.

We identified stem-like cells in all brain tumor biopsies analyzed so far. These cells exhibited a substantial heterogeneity with respect to morphology, proliferation rate, growth modus and the expression of neural markers and stemness factors. Therefore, we refer to these cells as subtypes of stem-like cells (SCIC-subtypes). Both, bulk tumor cells and SCIC-subtypes coexpressed several receptor tyrosine kinases (RTK), including members of the HER-family (HER: human epidermal growth factor (EGF) receptor), as well as receptors for PDGF (platelet-derived growth factor), FGF (fibroblast growth factor) and SCF (stem cell factor). Except for the SCF receptor c-kit, RTK expression appeared unrelated to the cell type, tumor type, and the WHO grade of the original tumor. SCIC-subtypes were maintained in serum-free medium containing the growth factors EGF and bFGF (basic fibroblast growth factor). Withdrawal of either one or both growth factors only moderately impaired growth in a cell line-specific way, indicating that stem-like glioma cells are largely independent of the exogenous growth factor supply. This is explained by the co-expression of EGF, heparin-bound EGF, bFGF, SCF and both, PDGF A and B in a large subset of the SCIC subtypes. The expression pattern showed some variation between the various SCIC subtypes and amongst SCIC and the corresponding bulk tumor. The responsiveness to EGF and bFGF differed, and PDGF AB mediated a cell line-specific growth reduction. Together our data suggest that the bulk tumor cells and SCIC within malignant gliomas exert autocrine growth control and that the various cell populations within the tumors may cross-talk via paracrine mechanisms.