Abstract

High grade astrocytomas are very progressive brain tumors. Glioblastoma multiforme is the most frequent and the most malignant type with very infiltrative phenotype of the tumor cells. Fibroblast activation protein FAP is a predominantly membrane bound prolyl peptidase bearing exo- and endopeptidase hydrolytic activities. FAP is known to play a role in wound healing, cell migration and invasion and its expression is linked to the pathogenesis of several malignancies. mRNA expression of FAP is upregulated in 48% of glioblastomas according to The Cancer Genome Atlas microarray data. The involvement of FAP in the pathogenesis of astrocytic tumors is largely unknown.

The aims of this work are to analyse the expression of FAP in primary cell cultures derived from high grade gliomas and to analyse the influence of FAP on the growth, migration and invasion of glioma cells.

Our ELISA and western blot results showed heterogenous expression of FAP in the studied glioma primary cell cultures and cell lines. Both enzymatic activities characteristic of FAP were detected in the primary glioma cell culture P11 with high expression of FAP. In these cells, FAP was present not only in the typical plasma membrane localization, but also in the cytoplasm as demonstrated by immunofluorescence staining. The P11 cells were tumorigenic in immunodeficient mice and retained FAP expression in vivo. In three primary glioma cell cultures, high expression of FAP was associated with slow growth rate in vitro. No such effect was observed on transfected cells expressing either enzymatically active or enzymatically inactive form of transgenic FAP. Therefore, FAP might be rather a marker of slower proliferation than a molecule directly influencing growth rate. Interestingly, the migration in the transwell assay and invasion of glioma cells from spheroids into the collagen gels was decreased in the transfected cells expressing the enzymatically active form of FAP. These effects were dependent on the enzymatic activity of FAP as we did not observe the decreased migration or invasion in glioma cells expressing the enzymatically inactive form of FAP. Although, FAP is presented in many studies as a proinvasive molecule, our data show transgenically expressed FAP is not sufficient to increases invasion of the glioma cells normally negative for this protein