Abstract

High-grade astrocytic tumours are aggressive primary brain malignancies, from which the most malignant and the most common is glioblastoma multiforme with median survival 15 months. Fibroblast activation protein (FAP) is a serine protease possessing both endo- and exopeptidase activity. Its restricted and increased expression in pathological conditions makes it a promising target for the development of new diagnostic or therapeutic approaches. Previous results of our laboratory and of other authors confirm expression of FAP in high-grade astrocytic tumours, where FAP is expressed by perivascular population of stromal mesenchymal cells.

The aim of this diploma thesis was to analyse the role of FAP positive primary stromal mesenchymal cultures in neovascularisation and extracellular matrix (ECM) deposition in glioblastoma microenvironment.

The results of this thesis describe proangiogenic effect of FAP positive stromal mesenchymal cells derived from human glioblastoma tissue. Using conditioned media, it was proven, that this effect is realized by factors secreted by these cells, even though results of *in vivo* assay on chorioallantoid membrane, where direct cell-to-cell contact of all involved cell types (tumor associated FAP positive mesenchymal cells, endothelial cells, glioma cells) is assumed, suggest, that their mutual direct communication may have important role as well. Proangiogenic effect was verified on human umbilical vein endothelial cells (HUVEC) and also on GBM associated primary endothelial cultures (pECK) derived by our team.

Moreover, positive correlation between collagen type 1, 4, fibronectin and FAP, was shown, what suggests that FAP positive stromal mesenchymal cells may be involved in processes of ECM modification in glioblastoma multiforme. Better understanding the importance of FAP positive stromal mesenchymal cells for angiogenesis and ECM modification in astrocytic tumours may help to identify new therapeutic approaches in their management.

Key words: Glioblastoma, fibroblast activation protein, FAP positive stromal mesenchymal cells, angiogenesis, extracellular matrix