

Abstract

Dipeptidyl peptidase-IV (DPP-IV) is a multifunctional transmembrane glycoprotein removing X-Pro dipeptide from the amino-terminus of the peptide chain. This evolutionary conserved sequence protects a number of biologically active peptides against the unspecific proteolytic cleavage. DPP-IV belongs into the group of “Dipeptidyl peptidase-IV Activity and/or Structure Homologues” (DASH), which, except the canonical DPP-IV, comprises fibroblast activation protein- α /seprase (FAP), and several other molecules. However several of DASH molecules are the enzymes, they execute at least some of their biological functions by non-proteolytic protein-protein interactions. DASH molecules, their substrates and binding partners are parts of “DASH system” which is affected in several pathological process including a cancer. Specifically DPP-IV and its closest structural relative FAP are among others expected to be involved in the development and progression of malignant glioma.

In this study we showed the expression and colocalization of DPP-IV and FAP in glioma cells *in vitro* and in human high grade gliomas. In addition to the DPP-IV/FAP double positive transformed glial cells, we also identified a subpopulation of FAP positive mesenchymal cells located in the perivascular compartment. Moreover we described the correlative expression of DPP-IV and FAP in the glioblastoma-derived primary cell cultures and the associated expression dynamics of both molecules in astrocytoma cell lines. Uncoupled expression of the endogenous FAP and DPP-IV transgene, placed into the non-physiological genomic context argues for the joint control of DPP-IV and FAP genes expression rather than the indirect reciprocal regulation, involving the changes of their mRNA and/or protein. Our experiments focused on the functional relevance of DPP-IV and FAP to cancer progression demonstrate that the overexpression of both molecules impaired the cell adhesion to proteins of extracellular matrix.

Understanding of the DPP-IV and FAP expression pattern and their functional coordination in the tumour microenvironment may help to clarify their biological role and molecular mechanisms in the malignant gliomas.