Abstract

P130Cas (Crk-associated substrate, CAS) is a multiadaptor protein important in integrin signalling where it positively regulates cell motility, invasion, proliferation and survival. CAS lacks enzymatic activity, but its binding to other signalling proteins could lead to the change of phosphorylation status of its substrate domain, which is the main mode, through which CAS takes part in regulating cell behavior. Local tensions in focal adhesions lead to an extension of CAS substrate domain, leaving phosphorylation sites more accessible for kinases, which subsequently leads to an increased CAS substrate domain phosphorylation. The CAS anchorage in focal adhesions is mediated by its SH3 domain, probably through the interactions with FAK, and also by C-terminal domain, where interaction partners are not known. The aim of my project is to find out, which proteins mediate the CAS anchorage to the focal adhesions. The elucidation of CAS anchorage to focal adhesions will contribute to the understanding of mechanosensory function of CAS.

Experimental data suggest that tyrosine phosphorylation of the CAS SH3 domain plays an important role in the regulation of its binding properties. Another goal of my diploma project was to analyze the significance of tyrosine phosphorylation within SH3 domain and other adaptor domains bioinfomatically.