Abstract

PSTPIP2 is an adaptor protein of the F-BAR family, which is an important regulator controlling the effector mechanisms of innate immune cells. The regulatory functions of this protein were discovered thanks to the CMO mouse strain, which lost the expression of this protein. As a result of PSTPIP2 deficiency, mice of the CMO strain develop an autoinflammatory disease affecting bone tissue and skin. The main mechanism that drives its pathology is the loss of regulation of the neutrophil granulocyte activity. These cells then produce excessive amounts of the pro-inflammatory cytokine IL-1β and reactive oxygen species. However, the exact molecular mechanism of action of the PSTPIP2 protein is unknown. When the PSTPIP2 protein is activated, it is phosphorylated and interacts with other proteins, which mediate its regulatory function. Interaction partners described so far in neutrophil granulocytes include phosphatases of the PEST family, the lipid phosphatase SHIP1 and the non-receptor tyrosine kinase CSK. In this thesis, we identified kinases from the SRC family as kinases that phosphorylate PSTPIP2. Furthermore, we found that the main phosphorylation sites of PSTPIP2 are tyrosines at positions 323 and 329. Finally, we proved that SHIP1 can bind to the phosphotyrosine motif around the tyrosine at position 329 and to a lesser extent also to the phosphotyrosine motif around the tyrosine at position 323. This work contributes to the understanding of regulation of the neutrophil granulocyte activity mediated by PSTPIP2.

Key words

Chronic multifocal osteomyelitis, SRC family kinases, Neutrophil granulocytes, PSTPIP2, SHIP1 phosphatase