

Accepted Manuscript

Activity modulation of the oligopeptidase B from *Serratia proteamaculans* by site-directed mutagenesis of amino acid residues surrounding catalytic triad histidine

Anna G. Mikhailova, Tatiana V. Rakitina, Vladimir I. Timofeev, David M. Karlinsky, Dmitry A. Korzhenevskiy, Yulia K. Agapova, Anna V. Vlaskina, Marina V. Ovchinnikova, Valentina A. Gorlenko, Lev D. Rumsh

PII: S0300-9084(16)30323-6

DOI: [10.1016/j.biochi.2017.05.013](https://doi.org/10.1016/j.biochi.2017.05.013)

Reference: BIOCHI 5208

To appear in: *Biochimie*

Received Date: 7 November 2016

Revised Date: 15 May 2017

Accepted Date: 17 May 2017

Please cite this article as: A.G. Mikhailova, T.V. Rakitina, V.I. Timofeev, D.M. Karlinsky, D.A. Korzhenevskiy, Y.K. Agapova, A.V. Vlaskina, M.V. Ovchinnikova, V.A. Gorlenko, L.D. Rumsh, Activity modulation of the oligopeptidase B from *Serratia proteamaculans* by site-directed mutagenesis of amino acid residues surrounding catalytic triad histidine, *Biochimie* (2017), doi: 10.1016/j.biochi.2017.05.013.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.



Abstract

Oligopeptidase B (OpdB; EC 3.4.21.83) is a trypsin-like peptidase belonging to the family of serine prolyl oligopeptidases; two domain structure of the enzyme includes C-terminal peptidase catalytic domain and N-terminal seven-bladed β -propeller domain. Importance of the interface between these domains and particularly of the 5 salt bridges for enzyme activity was established for protozoan OpdBs. However these salt bridges were not conserved in γ -proteobacterial OpdBs including the peptidase from *Serratia proteamaculans* (PSP). In this work, using comparative modeling and protozoan OpdBs crystal structures we created 3D-models of PSP in open and closed forms to elucidate the mechanism underlying inactivation of the truncated form of PSP1-655 obtained earlier. Analysis of the models showed that in closed form of PSP charged amino acid residues of histidine loop, surrounding the catalytic triad His652, participate in formation of interdomain contact interface between catalytic and β -propeller domain, while in open form of PSP disconnection of catalytic triad and distortion of these contacts were observed. Complete destruction of this interface by site-directed mutagenesis caused inactivation of PSP while elimination of the individual contacts caused differential effect on the enzyme activity and substrate specificity. Thus we identified structural factors regulating activity of PSP and supposedly of other γ -proteobacterial OpdBs and discovered the possibility of directed modulation of their enzymatic features.

Keywords: Oligopeptidase B; *Serratia proteamaculans*; interdomain interface; comparative modeling; site-specific mutagenesis; modulation of enzymatic activity

Download English Version:

<https://daneshyari.com/en/article/5508958>

Download Persian Version:

<https://daneshyari.com/article/5508958>

[Daneshyari.com](https://daneshyari.com)