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Structure and function of C-terminal catalytic region of Pasteurella multocida toxin

Kengo Kitadokoro^{*1}, Shigeki Kamitani², Aya Fukui², Hiromi Toshima², Masami Miyake² and Yasuhiko Horiguchi²

Address: ¹Kyoto Institute of Technology, Matsugasakigosyokaidou-cho, Sakyo-ku, Kyoto, Kyoto 606-8585, Japan and ²Research Institute for Microbial Diseases, Osaka University, Yamada-oka 3-1, Suita, Osaka 565-0871, Japan

Email: Kengo Kitadokoro* - kengo@kit.ac.jp * Corresponding author

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Pasteurella multocida toxin (PMT) is one of the virulence factors responsible for pathogenesis in some Pasteurellosis. We determined the crystal structure of the C-terminal region of PMT (C-PMT), which carries an intracellularly active moiety. The overall structure of C-PMT displays a Trojan horse structure, composed of three domains arranged in feet, body and head subunits with each linker loops, which were designated C1, C2, and C3 domains from the N- to C-terminus, respectively.

The C1 domain showing marked similarity in steric structure to the N-terminal domain of *Clostridium difficile* toxin B, was found to lead the toxin molecule to the plasma membrane. We found in the C3 domain the Cys-His-Asp catalytic triad that is organized only when the Cys is released from a disulfide bond. The steric alignment of the triad corresponded well to that of papain or other enzymes carrying the Cys-His-Asp triad. Our results indicate that PMT is an enzyme toxin carrying the cysteine protease-like catalytic triad dependent on the redox state, and functions oncytoplasmic face of the plasma membrane of target cells.