Poster

Structural insights into Polymorphic toxin – Immunity pair system of *Bacillus subtilis*.

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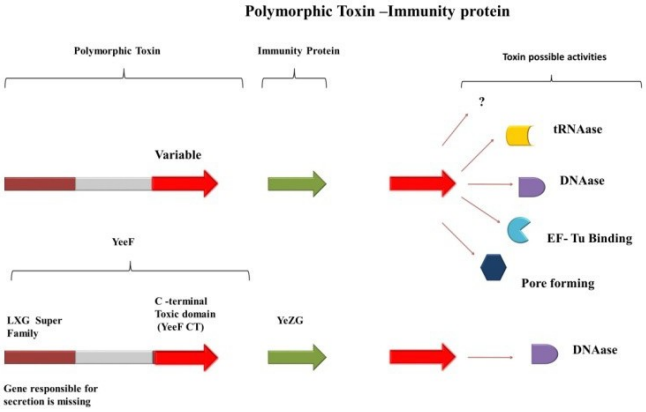
Polymorphic toxins are weapons of bacterial warfare which are being used to restrict competitors, aid kin selection and shape bacterial communities. Polymorphic toxin systems (PTS) are well studied in gram negative bacteria however there are limited studies from gram positive bacteria. In *Bacillus subtilis*, several members of toxin- immunity protein pairs including YeeF-YezG, YobL-Y, obK YxiD-YxxD, have been reported. There are few studies describing structural/mechanistic details of these toxin-immunity pairs. This toxin requires typeVII secretion system. We have shown that the C-terminal domain of YeeF (YeeF-CT) harbours the toxin having DNase activity. The expression of YeeF-CT causes growth defect and leads to morphological changes in *Escherichia coli.* While co- expression of toxin-immunity pair restores normal bacterial growth. Here we report crystal structure of $YeeF^{-CT}$ bound to its cognate antitoxin YezG at 2.1 Å resolution. Crystal structure reveals that toxin (YeeF-CT) undergoes major conformational changes upon binding its cognate immunity protein (YezG). Comparative structural analysis reveals that six β-sheets of the toxin, required for the nuclease activity, are ripped apart into two sub-domains upon binding immunity protein. This mechanism is unlike other Type II toxin-antitoxin systems, where intrinsically disordered region of the antitoxin binds at the active site of toxin hence sterically occluding binding of its substrate. We are currently working on the structure-guided detailed characterization of this toxin-immunity protein pair.



1. Kaundal, S., Deep, A., Kaur, G., & Thakur, K. G. (2020). Molecular and biochemical characterization of YeeF/YezG, a polymorphic toxin-immunity protein pair from Bacillus subtilis. *Frontiers in Microbiology*, *11*, 95.
2. Wang, Y., Zhou, Y., Shi, C., Liu, J., Lv, G., Huang, H., ... & Zhang, Z. M. (2022). A toxin-deformation dependent inhibition mechanism in the T7SS toxin-antitoxin system of Gram-positive bacteria. *Nature Communications*, *13*(1), 6434.