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Poster #14: Molecular mechanisms of the synergistic interactions of Druantia III and ARMADA II in the antiphage defense of enterohaemorrhagic Escherichia coli strain EDL933

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The EHEC O157:H7 outbreak strain EDL933 exhibits strong resistance against a broad range of phages and harbors three co-localized defense systems on O-island 172 (O172): Zorya II, Druantia III, and a ARMADA II system. To investigate the contribution and interplay of these systems, single and combined deletion mutants of these three Systems were generated in EDL933 and analyzed by EOP assays against the BASEL phage collection. Druantia III and ARMADA II provided broad-spectrum protection against most phage families, whereas Zorya II showed specific protection against Autographivirales. Notably, Druantia III and ARMADA II displayed strong synergistic interactions, resulting in enhanced phage resistance beyond the additive effects of the individual systems. To elucidate the molecular mechanism of ARMADA II, all four components were recombinantly produced and purified. Interaction studies revealed stable complex formation between two protein pairs, and cryo-EM enabled the structural characterization of a complex comprising a methyltransferase and a Snf2-type NTPase/helicase. Complementation with interaction-deficient variants demonstrated that complex formation is essential for antiviral activity. Moreover, a cofactor-bound structure revealed a unique conformational toggling mechanism of the NTPase/helicase relative to the methyltransferase, suggesting coordinated regulation of ARMADA II activity. Furthermore, global phage-host proteome and ArmC interactome analyses are underway to elucidate possible interactions among Druantia III and ARMADA II as well as host interactions of these systems. Together, our findings establish Druantia III and ARMADA II as key contributors to EHEC phage resistance and provide structural insights into the molecular mechanism of ARMADA II-mediated antiviral defense.

Reference #1

Reference #2

Reference #3

Author: LI, Huihui (Freie Universität Berlin,Institute of Biology-Microbiology)

Co-authors: HIMPICH, Stephanie (Freie Universität Berlin, Laboratory of Structural Biochemistry); Dr LOI, Vu Van (Freie Universität Berlin, Institute of Biology-Microbiology); Dr GRASS, Lena (Freie Universität Berlin, Laboratory of Structural Biochemistry); ILIOPOULOS, Alexandros (Freie Universität Berlin, Laboratory of Structural Biochemistry); BORELLI, Costanza (Freie Universität Berlin, Institute of Biology-Microbiology); Dr KLAUCK, Eberhard (Freie Universität Berlin, Institute of Biology-Microbiology); Dr HILAL, Tarek (Freie Universität Berlin, Research Center of Electron Microscopy and Core Facility BioSupraMol); Dr LOLL, Bernhard (Freie Universität Berlin, Laboratory of Structural Biochemistry); Prof. WAHL, Markus C. (Freie Universität Berlin, Laboratory of Structural Biochemistry); Prof. ANTELMANN, Haike (Freie Universität Berlin, Institute of Biology-Microbiology)

Presenter: LI, Huihui (Freie Universität Berlin,Institute of Biology-Microbiology)

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