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Poster #93: The role of phage Thanatos ADP-ribosyl-transferases Alt1 and Alt2 in disarming and preparing the host

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ADP-ribosyl-transferases (ARTs) are versatile enzymes found across prokaryotes, eukaryotes, and viruses. Genomic analyses have shown that ARTs are also widespread among bacteriophages. However, their functions in phage infection remain poorly understood. These enzymes modify host proteins through ADP-ribosylation or RNAylation, particularly targeting proteins involved in transcription and translation, thereby contributing to host cell reprogramming. Here, we investigate two ARTs, Alt1 and Alt2, encoded by the *Shewanella* phage Thanatos. Both enzymes are injected directly by the phages and actively modify host proteins immediately after infection. We show that the Thanatos ARTs are highly promiscuous: They modify more than 500 host and phage proteins within the first minutes after phage infection, before their activity is terminated by automodification. Primary targets appear to be the host transcription and translation machinery. In addition, potential components of bacterial anti-phage defense systems are targeted by the ARTs. Notably, Alt1 and Alt2 partially restore the infectivity of *E. coli* phages T5 and T7 when they are co-expressed with a dGTPase, a known anti-phage defense factor. Together, our findings support a role for Alt1 and Alt2 as early infection effectors that can not only counteract host defense mechanisms but also prepare the host cell for phage replication.

Reference #1

Reference #2

Reference #3

Author: KEMMLER, Alina (Institute for Microbiology and Molecular Biology, Justus-Liebig-University Giessen, Germany)

Co-authors: TYPAS, Athanasios (European Molecular Biology Laboratory, Molecular Systems Biology Unit, Heidelberg, Germany); GOHLUS, Daniel (Institute for Microbiology and Molecular Biology, Justus-Liebig-University Giessen, Germany); BECHER, Isabelle (European Molecular Biology Laboratory, Molecular Systems Biology Unit, Heidelberg, Germany); THORMANN, Kai (Institute for Microbiology and Molecular Biology, Justus-Liebig-University Giessen, Germany); SAVITSKI, Mikhail (European Molecular Biology Laboratory, Molecular Systems Biology Unit, Heidelberg, Germany); SCHMID, Nicole (Institute for Microbiology and Molecular Biology, Justus-Liebig-University Giessen, Germany); BARTOLEC, Tara (European Molecular Biology Laboratory, Molecular Systems Biology Unit, Heidelberg, Germany)

Presenter: KEMMLER, Alina (Institute for Microbiology and Molecular Biology, Justus-Liebig-University Giessen, Germany)

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