Contribution ID: **69** Type: **Poster only**

Poster #69: Characterization of a new NAD+-processing domain involved in antiphage defense and shared across the tree of life

Monday, 5 October 2026 21:17 (1 minute)

Just as eukaryotic cells activate multiple immune pathways to counter viral infection, bacteria employ diverse strategies to resist bacteriophage attack. For a long time, restriction-modification and CRISPR-Cas systems were the main antiphage systems described in bacteria. As these are absent from Eukaryotes, bacterial and eukaryotic immunities have historically remained two distinct fields of investigation. Yet this view has been challenged by the discovery of more than 250 types of bacterial defense systems, some of which share striking homology with known eukaryotic immune proteins or domains, such as cGAS receptor or TIR domains. Most of these conserved immune players were identified in bacterial immunity thanks to our knowledge of eukaryotic immunity. However, the considerable expansion of known antiphage systems raises the possibility that discoveries made in bacterial immunity may help uncover new immune actors in the eukaryotic world.
In this context, we report a novel protein domain found in diverse bacterial proteins with a predicted immune function. We show that this protein domain mediates anti-phage immunity in E. coli against different phage families. Activation of this domain upon phage infection triggers NAD+ depletion, thereby leading to abortive infection. Strikingly, this domain is found in diverse NLR-like proteins in multiple eukaryotic species, including humans. Remarkably, we show that the corresponding domain from the human TEP1 protein also exhibits NADase activity in vitro.
Together these findings identify a new NAD+-processing domain involved in antiphage defense and suggest a potentially conserved immune role for this domain in Eukaryotes, which we are currently investigating.

Reference #1

Reference #2

Reference #3

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Session Classification: Poster-Session