Translation inhibitor antibiotics decrease immunosuppression induced by anti-CRISPR proteins

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Résumé

Pathogenic bacterial infections can be treated by phage therapy, sometimes in combination with antibiotics. However, bacteria have a wide range of defence mechanisms against phage, among which is CRISPR-Cas. CRISPR-Cas system relies on storage of phage genetic material from previous failed infection which is then used to guide sequence-specific cleavage of phage genetic material in subsequent infections. On the other hand, phages have evolved counter-defence mechanisms, such as anti-CRISPR (Acr) proteins. These proteins are expressed in the early stages of the infection and can inhibit one or several steps of the CRISPR-Cas mechanisms to allow the phage to replicate. Since Acr-phage infection success depends on a strong and early expression of Acr proteins, we hypothesized that translation inhibitor antibiotics could disadvantage Acr-positive phages when infecting CRISPR immune bacteria. Consistently with this hypothesis, we show that sub-inhibitory doses of translation inhibitor antibiotics decrease the efficiency of AcrIF1 from phage DMS3vir in its host *Pseudomonas aeruginosa* PA14 carrying a type I-F CRISPR-Cas system. As a result, when infecting CRISPR immune cells by Acr-phage, the presence of antibiotics prevents phage amplification while protecting bacteria from lysis. These results highlight a potential role for translation inhibitors when selecting antibiotics for combined phage-antibiotics therapy.

Mots-Clés: CRISPR, Cas, Anti, CRISPR, translation inhibitors

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