Prophage SOS-response Acinetobacter baumannii

The *Acinetobacter baumannii* SOS gene *ddrR* is crucial for prophage maintenance and induction

Rodrigo Monteiro [1,2,3*], Luís D. R. Melo, Rita Domingues [1,2], Hugo Oliveira [1,2], Jan Maarten van Dijl [3], Joana Azeredo [1,2]

1. CEB, Centre of Biological Engineering, Laboratory of Research in Biofilms Rosário Oliveira (LIBRO), University of Minho, Braga, Portugal
2. LABBELS – Associated Laboratory, Braga, Guimarães, Portugal
3. Department of Medical Microbiology - Molecular Bacteriology, UMCG, University Medical Center Groningen, Groningen, Netherlands

Correspondence:
rodrigo.m@ceb.uminho.pt

Acinetobacter baumannii, considered a number one priority pathogen by WHO, is threatening hospitals due to its high ability to acquire antibiotic resistance. We have recently shown that mobile elements, such as prophages, are highly prevalent and encode several fitness/virulence-related genes, suggesting that they may serve as vectors for the spread of virulence. Here, we want to understand how stress factors influence the prophage behavior and disclose the role of the unique SOS response system, *umuDAb* and *ddrR*, in prophage induction. First, the *A. baumannii* ATCC 17978 strain was subjected to different sub-mic concentrations of mitomycin C (MMC), H_2O_2, and ciprofloxacin (cip), followed by incubation, RNA extraction and qRT-PCR analysis. After verifying the prophage behavior under these stress conditions, a *ddrR* knockout mutant was engineered using CRISPR-Cas9 to assess its influence on prophage expression. As expected, all conditions triggered an SOS response in the type strain as well as prophage induction, as both the *ddrR* and *umuDAb* genes, and the *cro* and capsid genes were overexpressed. Different levels of induction were observed between the conditions tested. For example, prophage induction was lower when challenged with cip than with MMC. In terms of growth curves, we observed that the *ddrR* mutant grew at faster than the type strain. Curiously, when challenged with MMC, the type strain showed significantly decreased CFUs in contrast to the *ddrR* mutant strain. Our findings show that each stress condition leads to different levels of prophage responses and that some can increase the fitness/virulence expression without detrimental effects on the host. The SOS gene *ddrR* is important for prophage induction and, consequently, its absence contributes to the bacterial robustness during growth. In conclusion, it is important to understand how prophages are affected by host genes under different stresses to improve antimicrobial efficacy.