Acinetobacter baumannii | capsule degrading depolymerase | Antibiotic resistance | Acinetobacter baumannii phage

Building a collection of phage-derived capsular depolymerases to tackle relevant *A. baumannii* capsular types

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A. baumannii is the major cause of nosocomial and drug-resistant infections, its capsule representing a major virulence factor. This pathogen evolved to display a high variety of capsular types for evading host defenses and protecting themselves from predators. Some bacteriophages also evolved to produce capsular depolymerases, enzymes that specifically bind and degrade the bacterial capsules, allowing these phages to overcome this barrier and proceed with the infection.

In this study, 94 carbapenem-resistant *A. baumannii* clinical isolates (Northern region of Portugal, 2005-2012), were screened for their resistance genes by PCR. Genes *Oxa-23, Imp-like* and *Oxa-24* were present in 76%, 20% and 16% of the isolates, respectively. Based on their resistance gene profile, the genomes of 23 strains were sequenced. Using *in silico* typing with Kaptive, we found 4 prevalent capsular types, namely, KL2 (39%), KL7 (30%), KL9 (4%) and KL120 (26%).

Aiming at implementing an effective depolymerase-based anti-virulence strategy to control *A. baumannii* infections, we isolated novel capsular depolymerases from lytic and prophages, ending with an in-house collection of enzymes targeting 10 capsular types (KL1, KL2, KL9, KL19, KL30, KL32, KL38, KL44, KL45, KL67). Experiments using a human serum model proved that all capsular depolymerases can effectively sensitize *A. baumannii* to the host complement killing activity, that otherwise were resistant. Therefore, capsular depolymerases have demonstrated to be a very powerful anti-virulence weapon and an emerging solution to treat *A.baumannii*-related infections.

As a result, the collection of capsular depolymerases available was expanded to 17 K-specific depolymerases, advancing the prospects of application of these enzymes to control *A. baumannii* infections.