Molecular and functional aspects of bacteriophage endolysins

Hugo Oliveira, Luís D. R. Melo, Sílvio B. Santos, Franklin L. Nóbrega, Eugénio C. Ferreira, Nuno Cerca, Joana Azeredo and Leon D. Kluskens

Following infection and replication, phages depend on host lysis to release their progeny in the environment. This is accomplished by the regulated expression of lysis proteins at the end of the lytic cycle. One of these proteins is the endolysin, an enzyme that specifically degrades the bacterial peptidoglycan layer, consisting of alternating residues of β-(1,4) linked N-acetylglucosamine and N-acetylmuramic acid, linked by a peptide chain of three to five amino acids.

From the moment their genetic identity became known, endolysins have sparked the interest as alternatives for existing antibiotics, to control bacteria *in vitro* and *in vivo*. Owing to the omics era, which has resulted in the sequencing of over a thousand bacteriophage genomes, numerous endolysins have been identified. Several of them have been heterologously produced (e.g. in *E. coli*) and characterized. Based on their amino acid sequence and their mode of activity they have been classified into several groups. Roughly divided, endolysins display their activity on the sugar polymer (muramidase), the peptide chain (peptidase) or the N-acetylmuramoyl residue-amino acid linkage (amidase). Despite their conserved biological function, phage endolysins are enzymatically and architecturally extremely diverse and vary hugely in length and size. Many of them have a modular (in contrast to globular) structure, containing different cell binding domains and signal sequences. This structural modularity implies that endolysins are malleable and, to a certain extent, can be genetically altered.

This work will give an overview of the different molecular aspects of bacteriophage endolysins, their production and characterization, and how they can serve as alternatives for existing antibiotics when applied on foodborne pathogens.