A VersaTile-driven, AI-augmented platform for the development of customized phage lysin-based antibiotics.

Bjorn Criel[1], Dennis Grimon[1], Maria Fonseca[1], Yves Briers[1,2]

[1]Obulytix, Valentin Vaerwyckweg 1, 9000 Gent, Belgium

[2]Laboratory of Applied Biotechnology, Department of Biotechnology, Ghent University, Gent, Belgium

The current antimicrobial resistance crisis urges for transformative innovation in antibiotic development. Obulytix is a recently launched spinoff focusing on the discovery and development of a groundbreaking class of enzyme-based antibiotics to combat the most severe antibiotic-resistant bacteria. The cornerstones of the approach are phage lysins, peptidoglycan-degrading enzymes produced by bacteriophages. Exposure to these enzymes results in rapid osmotic lysis and bacterial death. The enzymatic nature of these antibiotics classifies them as an innovative and new class of antibiotics, fulfilling all WHO innovation criteria for antibiotics (new target, new mode-of-action, new modality, no cross-resistance). Phage lysins are featured by a rapid and strong bactericidal effect (including against persisters), a low probability to provoke resistance development and microbiome-friendliness. What distinguishes them the most is their modularity, creating an unprecedented opportunity to create tailor-made modular phage lysin variants with optimized performance against any specific pathogen under any condition. We have developed a platform for the creation of a practically infinite number of modular phage lysin variants (VersaTile method) combined with screening methods and artificial intelligence to run and steer a hit-to-lead development process of phage lysins, reminiscent of the traditional funnel-based approach for drug discovery based on small molecules. We will show the results of different screening campaigns that resulted in lysins with strong activity under harsh conditions.