Targeting bacterial chronic infections through the development of new cyclopeptides active against persisters

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Résumé :

Persisters are phenotypic variants in an isogenic bacterial population that are able to survive lethal doses of antibiotic treatment by entering a physiologically dormant state that protects essential cellular processes from antibiotic action [1, 2]. Metabolic reactivation of these antibiotic-tolerant cells can lead to the infection relapse and persisters have been reported to directly contribute to the recalcitrance of chronic infections and the development of antibiotic resistance. The development of effective antibacterial therapy against persisters is vital, as the majority of available antibiotics are ineffective in stopping relapses [3, 4].

Olgram is developing molecules rationally designed to directly tackle persistent bacteria implicated in chronic infections, in particular respiratory tract infections in cystic fibrosis patients. We are now modifying the lead candidate from a family of anti-infective cyclic heptapseudopeptides active against multidrug-resistant (MDR) Gram-positive and -negative bacterial pathogens [5]. In order to find the best molecule to treat patients, the lead optimization is based on an original *in-house* screening platform, so far the only one able to screen against persistent bacteria. We will present here: i) the development strategy for this anti-persister screening platform and ii) the ongoing lead optimization to generate a new therapeutic solution against chronic infections.

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