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Abstract

Tackling Multi-Drug Resistance in *Pseudomonas aeruginosa* Thanks to a New Promising Anti-Virulence Strategy †

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The antibiotic resistance constitutes a critical public health issue. Among incriminated multi-drug resistant microorganisms, *Pseudomonas aeruginosa* has been pointed out by the WHO as a priority threat. Its ability to develop biofilms reinforces its pathogenicity and intrinsic drug resistance. Its virulence is orchestrated by the quorum sensing (QS) that refers to a sophisticated communication network. Three interconnected QS molecular pathways rely on the release and perception of autoinducers. Taking into account the widespread occurrence of *N*-acyl-homoserine lactone-mediated communication *las* and *rhl* circuits in Gram-negative bacteria, the third species-specific *pqs* system appears as a pool of promising therapeutic targets for the development of inhibitors. The main autoinducer of this network is the 2-heptyl-3-hydroxy-4(1*H*)-quinolone named *Pseudomonas* quinolone signal that activates the PqsR transcriptional regulator [1].

In the last decades, the interest of a quorum silencing pharmacological approach has emerged. Indeed, the selective pressure put on sensitive bacteria by conventional antimicrobial molecules causing their death promotes resistant strain survival. Non-bactericidal anti-virulence agents could increase pathogen sensibility to the host immune system response in monotherapy. In combination therapy, they could restore the efficiency of current antibiotics by inhibiting the formation of the hermetic barrier provided by biofilms [1]. A benzamide-benzimidazole compound appears as one of the most promising PqsR inhibitor in preclinical stage [2]. With this in mind, our team has recently developed a novel family of biaryl quinolone-based hybrids as anti-virulence agents through a transdisciplinary research methodology. The synthesis pathway, but also the physicochemical and biological evaluations of these derivatives are described in the poster. A hit anti-virulence agent exhibiting promising anti-biofilm and anti-pyocyanin properties (34% inhibition at 25 μM and 35% inhibition at 100 μM, respectively) without affecting the bacterial growth has been highlighted.

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References

1. Duplantier, M.; Lohou, E.; Sonnet, P. Quorum Sensing Inhibitors to Quench *P. aeruginosa* Pathogenicity. *Pharmaceuticals* **2021**, *14*, 1262. https://doi.org/10.3390/ph14121262.
2. Starkey, M.; Lepine, F.; Maura, D.; Bandyopadhaya, A.; Lesic, B.; He, J.; Kitao, T.; Righi, V.; Milot, S.; Tzika, A.; et al. Identification of Anti-Virulence Compounds That Disrupt Quorum-Sensing Regulated Acute and Persistent Pathogenicity. *PLoS Pathog.* **2014**, *10*, e1004321. https://doi.org/10.1371/journal.ppat.1004321.