Role of small RNA-based regulatory systems in cystic fibrosis airways infection by Pseudomonas aeruginosa: a new frontier in the identification of molecular targets for novel antibacterials

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Background. The comprehension of molecular mechanisms underlying CF airways infection by Pseudomonas aeruginosa is instrumental to the design of clinical protocols to prevent and contrast it. Emerging candidates as molecular regulators of infection and virulence in P. aeruginosa are small RNAs (sRNAs), which in other bacterial pathogens have been shown to play key roles in modulating cellular processes linked to pathogenesis (1).

Hypothesis and objectives. From this perspective, the main aim of this project was the evaluation of the impact on P. aeruginosa virulence and infection of three new sRNAs recently identified in our lab and named ErsA, ReaL and PesA (2, 3).

Methods. This main goal was mainly achieved monitoring the secretion of the pro-inflammatory interleukin IL-8 and cell viability following infection of a CF bronchial epithelial cell line with P. aeruginosa wt and sRNA knock-out mutant strains.

Results. Remarkably, the sRNA mutants showed to be less pro-inflammatory than the wt inducing a lower production of IL-8. In addition, the sRNA mutants induced lower cell death of infected bronchial epithelial cells. To evaluate in vivo the behaviour of the sRNA mutants, challenges of them in murine models of airways infection are in progress. Finally, the diffusion of ErsA, ReaL and PesA among P. aeruginosa isolates was evaluated. The conclusion of this approach was that these three sRNAs are widespread among P. aeruginosa clinical isolates from CF patients and environmental strains.

Spin-off for research and clinical purposes. The achievements of this project have the potential to foster the development of innovative antimicrobial strategies. In fact, illuminating the functional roles of sRNAs in host/pathogen interaction can provide the fundamental knowledge for the development of next-generation antibiotics using sRNAs and the virulence functions that they regulate as novel targets. In the case of the use of sRNAs as novel targets, the information resulting from mechanistic studies on the interactions with target genes will be invaluable for identifying drug molecules that can bind and inhibit sRNA functions. In addition, due to their specificity, these drugs would preserve CF patient healthy commensal flora.

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