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Exploring paraoxonases/lactonases as a tool to interfere with *Pseudomonas aeruginosa* infection

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Pseudomonas aeruginosa is the major cause of clinically relevant infections in cystic fibrosis (CF) due the antibiotic resistance, which demands for new strategies of microbe proliferation control. CF represents a model biofilm infection. During the course of CF, *P. aeruginosa* starts to produce exo-polysaccharides and forms biofilm characterized by cellular aggregates embedded within the mucus layer present in the airways. Biofilm formation in the CF lung is controlled by bacterial quorum-sensing (QS) mechanisms. QS signaling can be disrupted by lactonases. Three lactonases are present in human: PON1, PON2 and PON3; among these only PON2 is expressed in all tissues and in airways epithelial cells it seem to be involved in the first step of defense against bacterial infection. *P. aeruginosa* uses acyl-homoserine lactone (HSL) quorum sensing molecules, prevalently 3OC12-HSL, to regulate the expression of genes implicated in virulence and biofilm formation. It has been shown that all the human PONs can inactivate 3OC12-HSL. We have started studying thermostable members of the newly identified family of phosphotriesterase-like lactonase (PLL) and PON2 as mean to counteract *P. aeruginosa* infection *in vitro* and *in vivo* animal model (*Drosophila*). Evidences were obtained that thermostable PLLs reduce the production of virulence factors *in vitro*. An engineered version of PON2 has been designed and expressed in *E. coli*, purified, characterisedand used in *in vitro* tests.

Biography

Luigi Mandrich is currently a staff researcher at the Institute of Protein Biochemistry of the National Research Council. He graduated in Biological Sciences at the University of Naples "Federico II", and in 2004 received the PhD in Industrial Biotechnology.During his training he moved to The Netherland and Argentina to exploit new approaches to the use of exogenous enzymes in cheese making. He has carried out research in the field of biochemistry, and enzymes biotechnological applications. He is involved in research projects concerning the technology of recombinant DNA to produce and study human and bacterial proteins involved in detoxification of pesticides and to counteract pathogens infections. He is co-author of more than 40 papers on international peer reviewed journals, and he is Editor of the "Cloning and Transgenesis" journal.

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