GUIDE
Groningen University Institute for Drug Exploration

Antibiotarget

"Molecular and functional genomic approaches to novel antibacterial target discovery"

PvdQ: an acylase with multiple functions

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Introduction

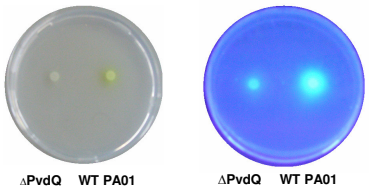
Acylases (*N*-terminal nucleophile hydrolase family) are widely distributed in the genomes of prokaryotic and eukaryotic organisms. Despite being used in industry for more than 50 years in the production of ß-lactam antibiotics, the function of these enzymes remains unclear.[1] We recently crystallized the structure of PvdQ acylase from *Pseudomonas aeruginosa* (Bokhove et al, unpublished results). The ability of this enzyme to degrade long chain *N*-acyl homoserine lactones (quorum sensing (QS)[2] molecules used by gram negative bacteria to regulate virulence in response to cell density) makes it an interesting pharmaceutical drug.

Aim of the project

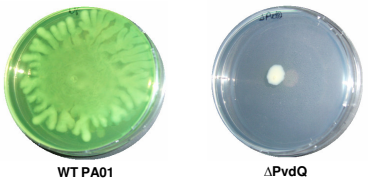
- Unravel the function of PvdQ in *P.aeruginosa* and the relationship between the phenotypes altered by this enzyme.

- Develop enzymatic variants to interfere in the virulence factors production in this pathogen.

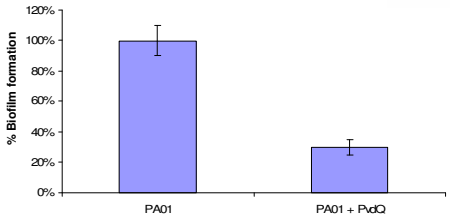
Results

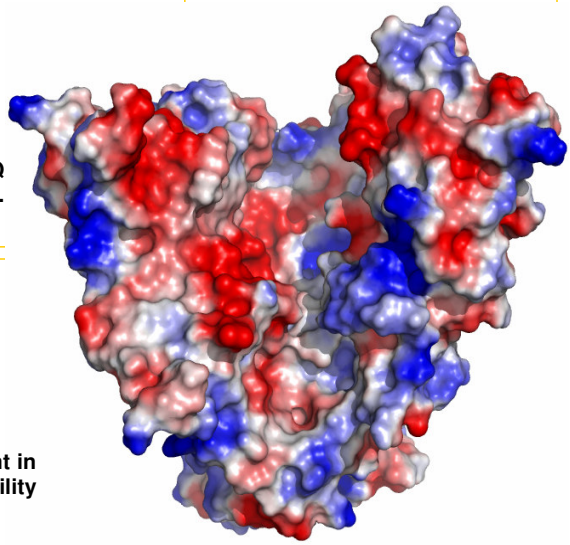


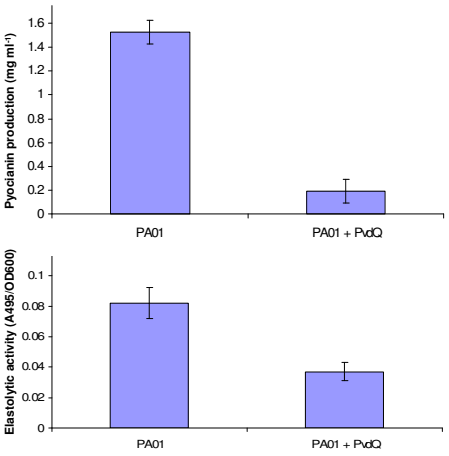
Chromosomal knockout mutants of PvdQ are impaired in pyoverdine production. The knockout shows no fluorescence.



***PvdQ* chromosomal knockout is deficient in iron related phenotypes: swarming motility and biofilm formation.**

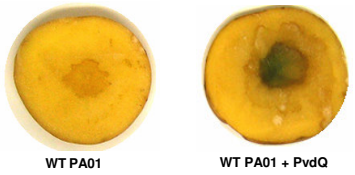






Overexpression or exogenous addition of PvdQ to *P. aeruginosa* cultures reduces the production of pyocyanin, elastase, lectin and several other virulence factors.

Exogenous addition of PvdQ to iron depleted environment (vegetable model system) leads to enhanced tissue maceration through still unproven reasons.



Conclusion and further perspectives

PvdQ acylase may be involved in two different pathways in *P. aeruginosa*:

- **The degradation of QS molecules for regulation of gene expression.**
- **The maturation/transport of pyoverdine to sequester iron from the environment.[3]**

The development of improved/selective variants of this enzyme is a promising strategy to develop novel antibacterial compounds against Gram-negative pathogens.

References

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2 Sio CF, Otten LG, Cool RH, Diggle SP, Braun PG, Bos R, Daykin M, Camara M, Williams P, Quax WJ. (2002). Infect Immun. ***74,*** 1673-1682.

3 Visca P, Imperi F, Lamont IL. (2007) Trends Microbiol. ***15 (1)***, 22-30.

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