



Ferripyoverdine Receptors: A Probable Entrance Route for the good, the bad and the ugly

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Abstract

Pseudomonas aeruginosa produces pyoverdine in order to chelate iron, the ferri-pyoverdine complexes formed are internalized by ferripyoverdine transporters (fpvA) present on its outer membrane, three fpvA's are known (fpvAI, fpvAII, and fpvAIII), the fpvAI was cloned in 1993 by Poole et al. and the other two fpvA's were cloned by De Chial et al. 2003. Following the speculation that some pyoverdine negative *Pseudomonas aeruginosa* isolates present in the lungs of cystic fibrosis patients (De Vos et al. 2001) and that an fpvA mutant were growth stimulated by iron, an alternative receptor, termed fpvB was identified by Ghysels et al. 2004. A fragment of this gene was determined by Polymerase Chain Reaction, (PCR). For the first time, using PCR procedures, the complete fpvA and fpvB gene sequences were determined and the sequences from this determination have been deposited in the GenBank database (Bodilis et al. 2009) and some variants of these receptor genes are presented.

Introduction and Discussion

The ferripyoverdine receptors is permeable for a number of compounds which may or maynot be beneficial for *Pseudomonas aeruginosa*, the ferri-pyoverdine receptor route in addition to serving as entrance for antibiotics, also serve as entrance for pyoverdine bound to iron. If this receptor route is considered as a "door", and putting in mind that *P. aeruginosa* maybe (or could be) as smart as a human being. As a human being, for instance, living in a house, supposedly with a door , this door may serve as an entrance for family and friends with good intentions, and through this same door, a thief or a burglar tries to or successfully makes an entrance, what would you do as an individual? Change the Lock and key just to prevent unwanted entrance.

The fpvA of *P. aeruginosa* has been clearly demonstrated to be involved in its siderophore (pyoverdine) biosynthesis (Shen et al. 2002) , and siderophore biosynthesis represents an attractive antibiotic target (Quadri, 2000), the fpvA type II may

be considered to be a door through which ferripyoverdine complexes, bacteriocins, antibiotics, and other lethal agents passes, is the fpvA type II trying to change its lock and key? If this is true, it would justify a correlation between amino acid sequence diversity of immunogenic bacterial proteins and evasion of host immune defense mechanisms (Tummler and Cornelis, 2005).

FpvA has been proposed to drive diversity at the pyoverdine locus (Smith et al.2005) and it has also been hypothesized that ferripyoverdine receptors are targeted by antibiotics and bacteriophages and serve as entry points (Wayne and Neilands, 1975; Guerinet, 1994; Andrews et al., 2003; Smith et al., 2005). *P. aeruginosa* alone will go to great lengths to evade the adverse effects of antibiotics and bacteriophages (Budzikiewicz, 2001). One way that this may be accomplished, as presented in this work (Osayande, J.O., 2010: see experimental procedures), may involve the ferripyoverdine receptors (as shown by the separate clustering of some of the test strains on the homology tree), the *Pseudomonas aeruginosa* strains So122, Pr332 and Lo059 were already speculated to belong to another group of the fpvAII receptor gene (Bodilis et al. 2009), and from my PCR analysis, a completely different primer set , different from the already existing primer sets used for ferripyoverdine receptor gene amplification (De Chial et al.2003, Ghysels et al.2004) were designed, and the FpvA sequences following amplification were aligned using the DNA Manager Software to construct homology trees and as already stated above, the strains are kind of deviating to form their own separate cluster, separate from their References strains (Strain Mi162 in particular), till now, there exists fpvAIIa and fpvAIIb, could these strains be said to belong to fpvA II c? It will be difficult to conclude based on the fact that the ferri-pyoverdine receptor genes in *Pseudomonas aeruginosa* is about 2500 bp in size, the fpvA variants identified from this study were not this large, a possible knowledge of the pyoverdine region, including the complete fpvA gene sequences (Poole et al., 1993; McMorran et al., 1996; Lamont and Martin, 2003) in the difficult-to-type *P. aeruginosa* strains (Please see previous paper: Osayande , J.O. 2010) , would be important to evolutionary studies to determine what portion of this region is favored by evolution. Such

knowledge could provide rational starting points for the design of novel antimicrobial agents, especially in connection with their iron requirement (Miller et al., 1993; Clarke et al., 2001). Our future studies or other collaborative studies will plan to address this issue.

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Illustrations

Illustration 1

History of strains used

Strain	City	Country	Year	Source	<i>fpvA</i>
Mi162	Ann arbor (Michigan)	USA	1997	Burn wound	NA (Not analyzed by PCR)
Br678	Brussels	Belgium	1998	Burn wound	NA
US376	San Antonio	USA	1988	Wound	NA
Pr332	Prague	Czech	1996	Urine	NA
Lo059	London	UK	1996	Wound	NA
Is579	Istanbul	Turkey	1997	Burn	NA
EVA3067	Athens	Greece	1994	Urine	NA
So122	Sofia	Bulgaria	1997	Wound	NA

Illustration 2

Figures 7a and 7b:

Gel images of *fpvA* (500 bp) and *fpvB* (2.5 kb) gene amplification in *P. aeruginosa* strain *Mi162*. Bands correspond to *fpvA* (Lane 1; a, and *fpvB* (Lane 1 b) gene amplification in test strain (*Mi162*) and positive controls (*PAO1* for *fpvB* (Lanes 2, Figure 7b) and ATCC 27853 for *fpvA*) (Lane 2, a).

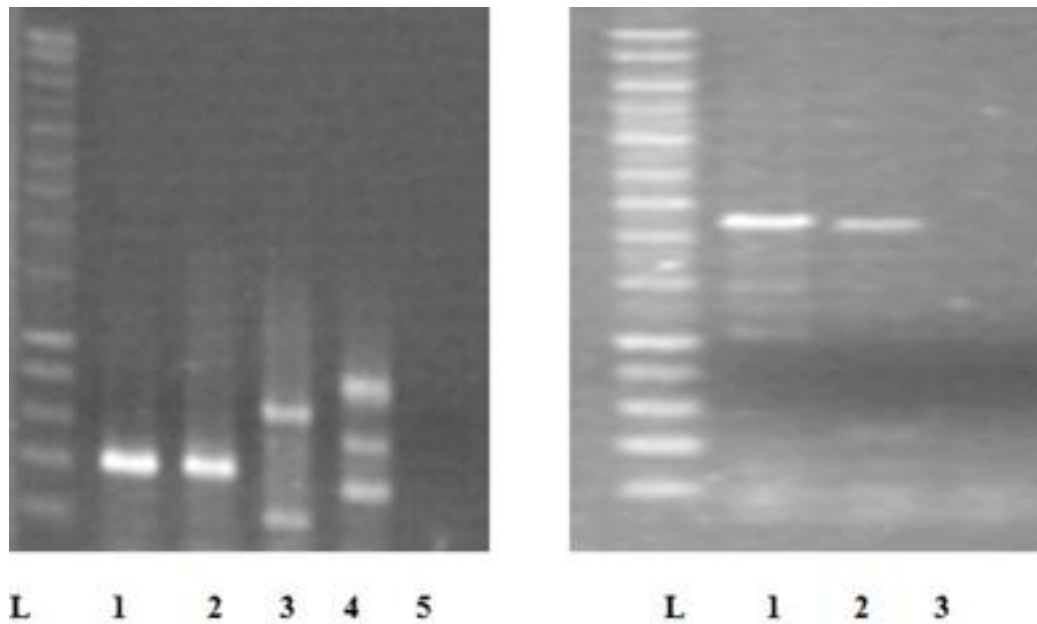


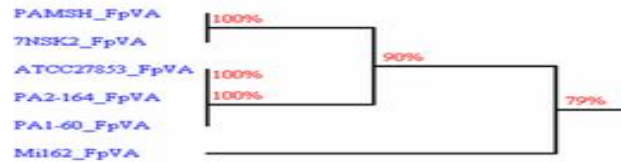
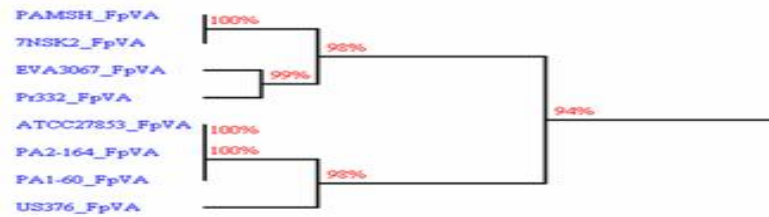
Figure 7a

Figure 7b

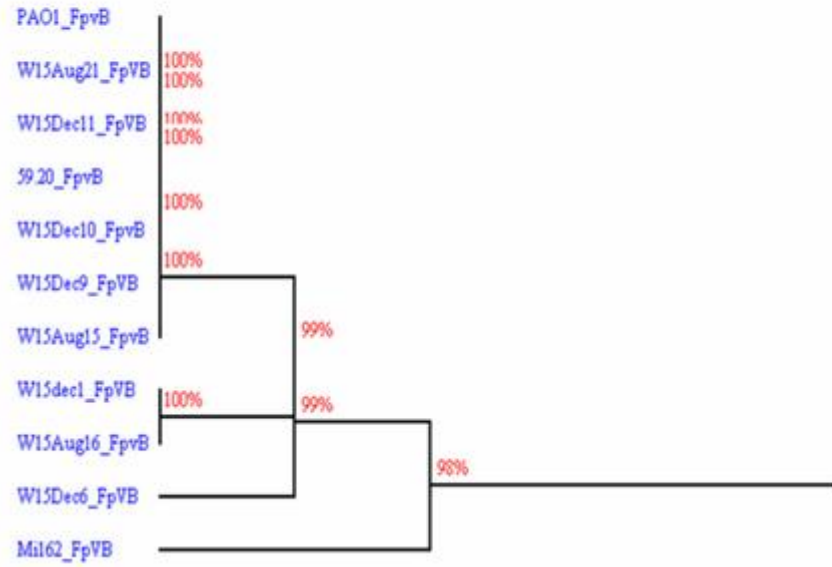
Illustration 3

Fig 3

Homology tree a: show the percent relatedness of the *fpvA* and *fpvB* genes in *P. aeruginosa* strains Mi162, So122, EVA 3067 and other test strains to those of reference strains MSH (Smith *et al.*, 2005), ATCC 27853, 1-60, 2-164 (Spencer *et al.*, 2003), 7NSK2 (De Chial *et al.*, 2003), and PAO1 (Stover *et al.*, 2000). Trees were constructed using the DNA manager software following the alignment of all the nucleotide (*fpvA* and *fpvB*) sequences for the individual *P. aeruginosa* test and reference strains.



fpoB (bp) ~2,500 bp for the primers used



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