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Abstract (oral session)

Pyomelanin-producing Pseudomonas aeruginosa emerge during host adaptation due to large genomic deletions

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Objectives Pyomelanin-producing P. aeruginosa (pPA) mutants are repeatedly isolated from chronically-infected patients. Pyomelanin production is due to the deletion of the gene hmgA, implicated in the catabolism of aromatic amino-acids (AAA). However, several features of clinical pPA mutants in antibiotic resistance, fitness, metabolism and virulence are not fully explained by the hmgA deletion. Here, we determined the genomic changes that occurred in the pPA mutants and assessed their phenotypic properties. Methods We studied 1 PAO1-derived and 4 clinical pPA mutants, along with their isogenic parental strain. Clinical pPA mutants were isolated from patients with endocarditis, cystic fibrosis, chronic sinusitis and endotracheal colonisation. The genomes of the 5 pairs were completely sequenced and compared. The pPA mutants were compared with their WT parents with respect to susceptibility to antibiotics, pyocins, extreme pH conditions and osmotic shock. We further compared growth, fitness, assimilation of AAA and terpens, production of virulence factors (pyocyanin, elastase, hemolysin, rhamnolipids) and the O-serotype (reflecting lipopolysaccharide [LPS] integrity). Results Genome sequence comparison revealed that large deletions ranging from 64 to 226 kbp that consistently encompassed the hmgA gene had occurred in the chromosome of the pPA mutants. Although all clinical pPAs showed a growth defect in rich medium, one of them could overgrow its WT parent in co-culture. The pPA mutants were more susceptible to aminoglycosides, to osmotic shock, to extreme pH conditions and showed a growth defect when AAA or terpens were the sole carbon source. The production of two virulence factors (among the four tested) was decreased in the clinical pPAs. In contrast to their WT parents, the pPA mutants were nonserotypable (indicating a substantial change of the LPS composition) and were resistant to the pyocins AP41, S1, R1 and/or R2. Conclusion The genome reduction that occurred in the pPA mutants led to a restriction of their metabolic capabilities, a lower resistance to harsh conditions and a reduced virulence. Chronic infections/colonizations of different anatomical sites surprisingly seem to favor the emergence of pPA mutants with similar features. Hence, despite their lower fitness, pPA mutants may gain an edge over other P. aeruginosa populations potentially due to their marked resistance to pyocins and may be the result of an adaptation to chronic infections.