

Intricate regulatory circuit of *Pseudomonas aeruginosa* AmpR revealed through whole genome approach

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Bacteria rapidly respond and adapt to changing environmental conditions by altering gene expression. A gram-negative opportunistic bacterium, *Pseudomonas aeruginosa* is a major human pathogen implicated in a number of acute and chronic infections. Of particular concern is the wide prevalence of antibiotic resistant *P. aeruginosa* in hospitals. Expression of virulence factors that contribute to *P. aeruginosa* pathogenicity is tightly regulated. Regulators make up ~8-10% of the *P. aeruginosa* genome. A transcriptional regulator of the LysR family, AmpR plays a major role in conferring resistance to β -lactams by positively regulating ampC encoding a lactamase. Whole genome approaches such as microarrays, deep RNA sequencing, CHIP-Seq and proteomics analyses of the *P. aeruginosa* prototypic strain PAO1 and its isogenic ampR in-frame deletion mutant, PAO Δ ampR, in the absence and presence of β -lactams, revealed that the regulatory repertoire of AmpR is extensive and includes over 500 genes. AmpR regulates diverse phenotypes such as β -lactam and non- β -lactam resistance, many virulence processes and metabolism. AmpR regulated positively and negatively, phenotypes associated with acute and chronic infections, respectively. Furthermore, RNA-Seq and ChIP-Seq studies identified lasR, encoding the quorum-sensing regulator, to be a direct target of AmpR regulation. *In silico* comparative transcriptomics analyses further identified genes that are exclusively regulated by AmpR and core set are involved in bacterial homeostasis. In summary, AmpR is identified as a critical regulator of pathogenesis and metabolism in *P. aeruginosa* and is a potential therapeutic target.

Biography

Kalai Mathee received her BS (Genetics) and MS (Microbial Genetics) degrees from the University of Malaya and did her Ph.D. in Molecular Microbiology at the University of Tennessee, Memphis. She had published more than 60 articles in the fields of molecular microbiology, forensic science and bioinformatics - many of which are recognized as seminal and have been selected for journal highlights. She had mentored over 60 individuals at all levels, and in 2011, she received the Mentor of the year award. In addition, she was bestowed with the highest honor of her career in FIU with the 2011 Faculty of the Year (President's Council Worlds Ahead Faculty Award) in recognition of outstanding achievement as a student-centered professor who makes an impact and exceeds expectations. She also serves as an Editor of Journal of Medical Microbiology and BMC Microbiology.

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