

Antibiotics and Antibiotic Resistance

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Differential expression profile of *Pseudomonas aeruginosa* in sub-inhibitory concentrations of beta lactam, aminoglycoside and Polymyxin antibiotics

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P. aeruginosa is a unique organism able to grow in the harshest environments and is characterized by both a large genome as well as unique mechanisms that allow for enhanced genomic and metabolic plasticity making this organism a robust nosocomial pathogen equipped with a myriad of virulence factors as well as antibiotic resistance adaptations. Low-level exposure to antibiotics, both in hospital settings as well as from livestock and wastewater pollution showed that resistance selection and phenotypic alterations could already occur at sub-inhibitory concentrations. Using a multiplex labeling strategy followed by mass spectrometry, we showed a differential response of *P. aeruginosa* when challenged with sub-inhibitory concentrations of imipenem, colistin, cefepime and tobramycin by both laboratory strains as well as clinical isolates recovered from Ventilator-Associated Pneumonia (VAP) patients. Low-level exposure to imipenem induced expression of AlgR and AlgC proteins that are known to be involved in biofilm formation as well as in regulating virulence and were observed to be most elevated in the laboratory strains. Moreover, Hcp1 and ClpV1, both main components of H1-type-6 secretion system were increased following imipenem exposure in all isolates used. Tobramycin on the other hand induced marked up-regulation of proteins involved in branched amino acid metabolism, electron transport chain proteins and superoxide dismutase indicating that tobramycin induces oxidative stress, a mechanism previously observed with *E. coli*. Cefepime and colistin only showed a marginal effect on protein expression at sub-inhibitory concentrations. The demonstration of a differential response of *P. aeruginosa* towards different antibiotic classes at sub-inhibitory concentrations gives us further insights in the potential resistance mechanisms and cellular physiology of this highly pathogenic bacterium and will be the focus of the talk.

Biography

Samir Kumar-Singh is a certified Medical Doctor with a Doctorate in Pathology and a Master degree in Laboratory Animals. He is a full-time Research Professor of Molecular Pathology at the Faculty of Medicine, University of Antwerp, Belgium and is affiliated to the Vaccine and Infectious Disease Institute, Belgium. He has published a well-cited body of work on molecular pathology of cancer and neurodegeneration involving patient studies and mouse modeling. He serves on several Review and Editorial Boards and international consortia. Since 2012, his group is engaged in studying the pathomechanism of hospital acquired pneumonia especially Ventilator-Associated Pneumonia (VAP) and has developed several authentic rat and mouse VAP as well as acute and chronic pneumonia models to study disease pathogenesis and for biomarker discovery as well as high-throughput *in vitro* screens for new antimicrobial targets.

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