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**Programme**

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## [P282] DEVELOPMENT OF MULTIDRUG RESISTANCE IN STAPHYLOCOCCI DRIVEN BY EFFLUX

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**Aim:** To study the efflux driven response of two major staphylococcal pathogens, *S. aureus* and *S. epidermidis* to the challenge by non-antibiotic drugs.

**Methods:** We adapted three reference strains to ethidium bromide (EtBr), a broad substrate of bacterial efflux pumps. The parental strains, *S. aureus* ATCC25923, *S. epidermidis* ATCC12228 and *S. epidermidis* RP62A were cultured in varying concentrations of EtBr, to obtain their EtBr-adapted derivatives; ATCC25923_EtBr; ATCC12228_EtBr and RP62A_EtBr. Susceptibility of parental and adapted strains to 10 antibiotics and 6 biocides was evaluated by microdilution MIC determination with or without efflux inhibitors. Efflux activity was established by fluorometric assays and the relative expression of the genes coding for the main efflux pumps (EPs) of each species quantified by RT-PCR.

**Results:** For each strain tested, exposure to EtBr resulted in the development of a multidrug resistance (MDR) phenotype, which included resistance to fluoroquinolones and decreased susceptibility to biocides, including cetrimide, benzalkonium chloride and tetraphenylphosphonium bromide. Efflux inhibitors such as verapamil reduced these resistance levels. The EtBr-adapted cultures showed increased efflux activity, which was accompanied by over-expression of distinct EP genes, in a temporal pattern.

**Conclusion:** These results show that both *S. aureus* and *S. epidermidis* have the potential to develop efflux driven MDR phenotypes when exposed to a non-antibiotic substrate of multidrug EPs, which can be mediated by distinct efflux pumps, depending on the drug and the bacterial genetic background.

*These results were partially presented at Costa et al BMC Microbiology, 2015,15:232; JAC, 2018, 73:320.*