The response of the food-borne pathogen L. monocytogenes to sub-inhibitory levels of \( \beta \)-lactam antibiotics

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*Listeria monocytogenes* is a food-borne pathogen causing listeriosis, with symptoms ranging from mild diarrhoea to life-threatening conditions such as septicaemia, encephalitis and meningitis. The mortality rate of listeriosis is relatively high (>25%) although only 3.8% of all food-related hospitalisations originates from infections with *L. monocytogenes*. Patients infected by *Listeria* are typically treated with a β-lactam antibiotic in combination with an aminoglycoside antibiotic. Despite the use of antibiotics in the treatment of listeriosis, it is remains unclear how sub-inhibitory levels of antibiotics affect global gene expression in *L. monocytogenes*.

In this study, we have used a global transcriptomic approach to analyse how *L. monocytogenes* LO28 responds to the presence of sub-inhibitory concentrations of the β-lactam antibiotic Cefuroxime. Furthermore, we investigated the role of the two-component gene regulatory systems CesRK and LisRK in this response. We observed that *L. monocytogenes* alters the expression of 20% of its annotated genes in response to Cefuroxime; 284 genes being significantly up-regulated and 274 genes being significantly down-regulated. Using Clusters of Orthologous Groups (COGs) we found that cell-cycle control, cell-wall biogenesis, amino acid transport and -metabolism pathways were up-regulated, whereas pathways involved in energy production, translation and carbohydrate transport/metabolism were down-regulated by Cefuroxime. Interestingly, the top ten most up-regulated genes depend on LisR and/or CesR for optimal expression, suggesting that the two-component systems play central regulatory roles in the response of *L. monocytogenes* to β-lactam antibiotics. The role(s) of the ten most up-regulated genes with respect to antibiotic resistance is currently under investigation.