

Characterisation of CemR regulons of selected pathogenic *Campylobacteria* species

Helicobacter pylori, *Campylobacter jejuni* and *Arcobacter butzleri*, are gram-negative, microaerophilic human gastrointestinal pathogens of the *Campylobacteria* class. *H. pylori* is the leading cause of peptic ulcer disease, gastric lymphoma, and gastric adenocarcinoma. *C. jejuni* is the leading cause of bacterial gastroenteritis disease, while *A. butzleri* is an emerging enteric pathogen associated with gastroenteritis, diarrhoea and bacteremia, with increasing incidence worldwide. These species face different stress conditions during infection and transmission, including changing oxygen levels, pH, temperature and reactive oxygen species. Thus, they need to adjust their metabolism and respiration to the changing environment of the colonisation sites.

HP1021, Cj1608, and Abu0127 are homologous proteins of *H. pylori*, *C. jejuni*, and *A. butzleri*, respectively. They belong to the orphan, atypical response regulators of signal transduction systems; however, their regulatory function has not been well established except for HP1021, which was previously partially characterized and defined as a redox switch.

This research used a comprehensive set of omic techniques (RNA-seq, ChIP-seq, and LC-MS/MS) and phenotypic analyses to determine HP1021, Cj1608, and Abu0127 regulons.

The study indicated that each investigated regulator controls the transcription of more than 30% of genes in each species. The regulatory proteins control genes of many clusters of orthologue groups (COGs) under microaerobic conditions and upon oxidative stress, indicating a pleiotropic character of the regulators. The regulators control the transcription of genes involved in similar processes in all species and species-specific processes.

We have shown that the most impacted COGs in all three species are associated with metabolic and energy conservation processes, particularly the tricarboxylic acid cycle and the electron transport chain. Using phenotypic analyses, we confirmed that energy conversion processes in HP1021/Cj1608/Abu0127 deletion mutants are disturbed. Moreover, our combined data indicated that genes controlled by Cj1608 and Abu0127 responded to oxygen levels to optimize the energy conversion processes. Thus, we named these response regulators C*ampylobacteria* energy and metabolism regulators – CemR.

In conclusion, this research highlights the crucial role of CemR in the *Campylobacteria* species, showing a tremendous impact on cell physiology.