Role of CRISPR-cas system on antimicrobial resistance in *Campylobacter jejuni*

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Antibiotic resistant *Campylobacter jejuni* is one of major and consistent public health threat worldwide. The role of CRISPR-cas system on development of resistance in *C.jejuni* is uncertain. The involvement of cas9 gene in antimicrobial resistance in 17 clinical isolates was revealed by associating the CRISPR spacer with their resistance phenotype of minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) and mutant prevention concentration (MPC). The transcriptional change of cas 9 was determined by IQ5 Multicolor Real-time PCR after exposure of standard strain *C.jejuni* NCTC 11168 to 12 different antimicrobial agents. The cas 9 gene was knowed out to construction of Δcas9 deletion mutant. The ability of transformation and *in vitro* resistance development of Δcas9 mutant compared with its parent strain was evaluated by Electro-transformation and step-wise selection. The transcripome of Δcas9 mutant and wide strain was analyzed by RNA sequencing. Our results showed that different CRISPR spacer conferred different resistant phenotype of MIC, MBC and MPC in clinical isolates. The exposure to different antimicrobial agents, such as erythromycin, azithromycin and so on, could induce the overexpress of cas9 gene. The Δcas9 mutant exhibited lower MIC, MBC and MPC value, slower growth rate, slower development of resistance to different antibiotics and higher natural transformation than its parent strain. Transcriptomic analysis revealed a significant role of cas9 gene in enhancing antimicrobial resistance. It was observed that cas9 gene regulate several genes to promote the antimicrobial resistance in *C. jejuni*. Given the zoonotic implications of bacterium and potential to acquire antimicrobial resistance against different drugs, the identification of cas gene (cas9) and subsequent outcomes ascertain future investigations to better elucidate resistance mechanism and bacterium evolution accordingly.

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