Genome-Wide Analysis of Cadmium Resistance Genes Harbored by Cadmium-Resistant *Listeria monocytogenes* Strains from Sweden

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Introduction: *Listeria monocytogenes* causes listeriosis and often exhibits resistance to cadmium. While multiple cadmium resistance genes have been identified, our understanding of the full landscape of cadmium resistance determinants is far from complete.

Purpose: This study aims to investigate cadmium resistance genes via genome-wide screening of cadmium-resistant *L. monocytogenes* from human listeriosis in Sweden.

Methods: Thirty-two cadmium-resistant isolates were subjected to the whole genome sequencing. Plasmid-borne contigs were identified in silico and cadmium resistance genes were found by BLAST2 with known cadmium resistance genes and pan-genome analysis. These genes were compared and the deduced proteins were aligned with the prototype proteins, bootstrapped, and visualized. To determine the location of the genes, the DNA sequences including flanking regions were compared with each other and, for chromosomal cadmium resistance genes, with the complete genome of strain F2365.

Results: We identified three known cadmium resistance operons (*cadA1C1*, *cadA2C2*, and *cadA4C4*) and two that were novel (*cadD8A8* and *cadA9C9*). *cadA1C1* was found most frequently and was plasmid borne, except for one CC101 strain that harbored a *cadA1C1*-harboring chromosomal island. Chromosomal islands with cadmium resistance genes also included the previously characterized LGI2 (*cadA4C4* and arsenic resistance genes) and a novel island harboring *cadA9C9* and an arsenic resistance gene. All *cadA9C9*-

positive strains lacked plasmids and other cadmium resistance operons. Our analysis also identified *cadA10*, which was chromosomally harbored by all strains in our panel and the cadmium-susceptible strain F2365, suggesting that it mediates innate baseline resistance of *L. monocytogenes* to cadmium.

Significance: Our findings highlight the complex distribution of cadmium resistance genes within *L. monocytogenes*, which will help us understand the genes that facilitate ecological adaptations, potentially leading to persistence in the environment and increased risk of *L. monocytogenes*-contaminated foods and foodborne infections.