The Small Colony Variant of Listeria monocytogenes Is More Tolerant to Antibiotics and Has Altered Survival in RAW 264.7 Murine Macrophages

The Small Colony Variant of Listeria monocytogenes is a slow-growing phenotype that results from specific defects in the electron transport chain. They form pinpoint colonies on agar plates and have a variety of phenotypic characteristics, such as altered carbon metabolism, decreased toxin and lytic enzyme production, aminoglycoside resistance, and increased intracellular persistence. They are clinically relevant in Staphylococcus aureus and Pseudomonas aeruginosa, serving as a reservoir for recurrent or prolonged infections. Here, we found that a SCV mutant in the foodborne pathogen Listeria monocytogenes (strain SCV E18), similar to the high persister mutant phenotype, survived significantly better than the wild type when exposed over a 48-h period to concentrations above Minimal Inhibitory Concentration for most tested antibiotics. SCV E18 survived more poorly than the wildtype in unactivated RAW264.7 macrophage cells, presumably because of its reduced listeriolysin O expression, however, it survived better in reactive oxygen species producing, phorbol 12-myristate 13-acetate-activated macrophages. Although SCV E18 was sensitive to oxygen as it entered the stationary phase, it was significantly more tolerant to H\textsubscript{2}O\textsubscript{2} than the wild type, which may result from a shift in metabolism, however, further investigation is needed to resolve this. SCV E18 is a spontaneous mutant with a point mutation in the hemA gene. A wild type copy of hemA was complemented on plasmid pSOG30222, which restored the wild type phenotype. The results reported here suggest that the SCV of L. monocytogenes could be of clinical importance and highlight a need for adequate clinical screening for this phenotype, as it could affect antibiotic treatment outcomes.

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