

**המדרשה לתארים מתקדמים ע"ש משפחת סמולרש**

 **THE SMOLARZ FAMILY GRADUATE SCHOOL**

“Studying population dynamics of Listeria monocytogenes phage elements"

THESIS SUBMITTED FOR THE DEGREE "DOCTOR OF PHILOSOPHY"

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**Abstract**
Listeria monocytogenes, a Gram-positive pathogen, poses significant risks to immunocompromised populations, causing severe illnesses with high morbidity and mortality. Within the genome of strain 10403S, two distinct phage-derived elements coexist: the infective prophage Φ10403S and a cryptic bacteriocin-like monocin element. Here, we explore the intricate regulatory interplay between these elements and their broader implications for bacterial adaptability and virulence.

Using fluorescent reporter constructs and flow cytometry, we discovered that the monocin element and Φ10403S undergo a coordinated, hierarchical induction. In response to the host SOS response, MpaR first cleaves the monocin CI-like repressor, initiating monocin lytic gene expression. Subsequently, LmaD—a putative regulatory protein- becomes highly expressed and upregulates the monocin lytic genes. Notably, once LmaD accumulates to sufficient levels, it interacts directly with the Φ10403S CI-like repressor, facilitating its cleavage by MpaR and thereby triggering phage induction. These findings highlight the co-evolution of Φ10403S and monocin in L. monocytogenes, enabling finely tuned decision-making processes (e.g., when to undergo lytic induction) to optimize bacterial survival under stressful conditions.

This work advances our understanding of polylysogeny and inter-phage communication in L. monocytogenes, shedding light on bacterial evolution and pathogenesis. By elucidating how the monocin and Φ10403S orchestrate their mutual regulation, this study underscores the complex adaptive strategies that bacterial pathogens employ to navigate fluctuating environments.