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Cross regulation of intracellular metabolism and virulence in Listeria monocytogenes

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ntracellular bacterial pathogens are metabolically adapted to grow within mammalian cells. While these adaptations are fundamental to the ability to cause disease, we know little about the relationship between the pathogen's metabolism and virulence. My lab focuses on studying the bacterial pathogen Listeria monocytogenes. We investigate the intracellular metabolism of this bacterium during infection and how it senses host derived metabolites as localization signals. We recently discovered that L. monocytogenes responds to low availability of BCAAs within mammalian cells by triggering virulence gene expression. This response is dependent on the nutrient global regulator CodY, which directly activates the major virulence regulator, PRfA.

Furthermore, we reported that L-glutamine, an abundant nitrogen source in host serum and cells, also serves as an environmental indicator and inducer of virulence gene expression. Rapid intercellular uptake of L-glutamine is the signal as listerial intracellular concentration of L-glutamine had to cross a certain threshold to activate virulence gene expression, acting as an on/off switch. The mechanisms behinds these metabolic signals were identified, revealing how intracellular pathogens gouge for host derived metabolic cues and use them to cross-regulate metabolism and virulence.

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