

Regulatory pathways and virulence inhibition in *Listeria monocytogenes*

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Abstract

Listeria monocytogenes is a rod-shaped Gram positive bacterium. It generally exist ubiquitously in nature, where it lives as a saprophyte. Occasionally it however enters the food chain, from where it can be ingested by humans and cause gastro-intestinal distress. In immunocompetent individuals *L. monocytogenes* is generally cleared within a couple of weeks, but in immunocompromised patients it can progress to listeriosis, a potentially life-threatening infection in the central nervous system. If the infected individual is pregnant, the bacteria can cross the placental barrier and infect the fetus, possibly leading to spontaneous abortion.

The infectivity of *L. monocytogenes* requires a certain set of genes, and the majority of them is dependent on the transcriptional regulator PrfA. The expression and activity of PrfA is controlled at several levels, and has traditionally been viewed to be active at 37 °C (virulence conditions) where it bind as a homodimer to a “PrfA-box” and induces the expression of the downstream gene.

One of these genes is ActA, which enables intracellular movement by recruiting an actin polymerizing protein complex. When studying the effects of a blue light receptor we surprisingly found an effect of ActA at non-virulent conditions, where it is required for the bacteria to properly react to light exposure.

To further study the PrfA regulon we tested deletion mutants of several PrfA-regulated virulence genes in chicken embryo infection studies. Based on these studies we could conclude that the chicken embryo model is a viable complement to traditional murine models, especially when investigating non-traditional internalin pathogenicity pathways. We have also studied the effects of small molecule virulence inhibitors that, by acting on PrfA, can inhibit *L. monocytogenes* infectivity in cell cultures with concentrations in the low micro-molar range.

Keywords

Listeria monocytogenes, PrfA, ActA, infection

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