

Probiotic *Enterococcus faecalis* Symbioflor® down regulates virulence genes of EHEC in vitro and decrease pathogenicity in a *Caenorhabditis elegans* model.

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Abstract

Enterohemorrhagic *E. coli* O157:H7 (EHEC) shorten the lifespan of *Caenorhabditis elegans* compared to avirulent bacteria. Co-feeding EHEC with *Enterococcus faecalis* Symbioflor® significantly increased the worms' lifespan. The transcriptome of EHEC grown in vitro with or without Symbioflor® was analyzed using RNA-seq. The analysis revealed downregulation of several virulence-associated genes in the presence of Symbioflor®, including virulence key genes (e.g., LEE, flagellum, quorum-sensing). The downregulation of the LEE genes was corroborated by lux-transposon mutants. Upregulated genes included acid response genes, due to a decrease in pH exerted by Symbioflor®. Further genes indicate cellular stress in EHEC (e.g. prophage/mobile elements involved in excision, cell lysis, and cell division inhibition). Thus, the observed protection of *C. elegans* during an EHEC infection by the probiotic Symbioflor® is suggested to be caused by triggering concomitant transcriptomic changes. To verify the biological relevance of this modulation, exemplary genes found to be influenced by Symbioflor® were knocked out (*fliD*, *espB*, Z3136, Z3917, and L7052). The lifespan of nematodes changed when using knock-outs as food source and the effect could be complemented in trans. In summary, Symbioflor® appears to be a protective probiotic in the nematode model.

KEYWORDS:

Caenorhabditis elegans; EHEC; *Enterococcus faecalis* Symbioflor®; Transcriptome; Virulence; lux transposons