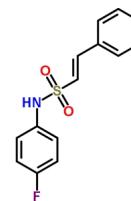


FPSS, ST50051351, interrupts genes control mechanism in food-borne Listeria



bacterium

IDNUMBER ST50051351 , ST100787

Formula: C14H12FNO2S

MW: 277.32

Name: 4-fluoro-phenyl-styrene-sulfonamide

SMILES: c1c(cccc1)/C=CS(=O)(Nc1ccc(cc1)F)=O

MDL: MFCD02333805

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Reference:

Palmer E. M., et. al. (2011) The *Listeria monocytogenes* σ -B Regulon and Its Virulence-Associated Functions Are Inhibited by a Small Molecule. *mBio* vol. 2 no. 6 e00241-11. doi: 10.1128/mBio.00241-11

ABSTRACT

The stress-responsive alternative sigma factor σ B is conserved across diverse Gram-positive bacterial genera. In *Listeria monocytogenes*, σ B regulates transcription of >150 genes, including genes contributing to virulence and to bacterial survival under host-associated stress conditions, such as those encountered in the human gastrointestinal lumen. An inhibitor of *L. monocytogenes* σ B activity was identified by screening ~57,000 natural and synthesized small molecules using a high-throughput cell-based assay. The compound fluoro-phenyl-styrene-sulfonamide (FPSS) (IC₅₀ = 3.5 μ M) downregulated the majority of genes previously identified as members of the σ B regulon in *L. monocytogenes* 10403S, thus generating a transcriptional profile comparable to that of a 10403S Δ sigB strain. Specifically, of the 208 genes downregulated by FPSS, 75% had been identified previously as positively regulated by σ B. Downregulated genes included key virulence and stress response genes, such as *inlA*, *inlB*, *bsh*, *hfq*, *opuC*, and *bilE*. From a functional perspective, FPSS also inhibited *L. monocytogenes* invasion of human intestinal epithelial cells and bile salt hydrolase activity. The ability of FPSS to inhibit σ B activity in both *L. monocytogenes* and *Bacillus subtilis* indicates its utility as a specific inhibitor of σ B across multiple Gram-positive genera.

IMPORTANCE The σ B transcription factor regulates expression of genes responsible for bacterial survival under changing environmental conditions and for virulence; therefore, this alternative sigma factor is important for transmission of *L. monocytogenes* and other Gram-positive bacteria. Regulation of σ B activity is complex and tightly controlled, reflecting the key role of this factor in bacterial metabolism. We present multiple lines of evidence indicating that fluoro-phenyl-styrene-sulfonamide (FPSS) specifically inhibits activity of σ B across Gram-positive bacterial genera, i.e., in both *Listeria monocytogenes* and *Bacillus subtilis*. Therefore, FPSS is an important new tool that will enable novel approaches for exploring

complex regulatory networks in *L. monocytogenes* and other Gram-positive pathogens and for investigating small-molecule applications for controlling pathogen transmission.