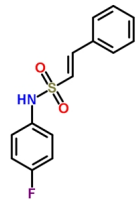
FPSS, ST50051351, interrupts genes control mechanism in food-borne Listeria



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 σB is conserved across diverse Gram-positive bacterial genera. In Listeria monocytogenes, σB 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 σB 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 μM) downregulated the majority of genes previously identified as members of the σB regulon in L. monocytogenes 10403S, thus generating a transcriptional profile comparable to that of a 10403S ΔsigB strain. Specifically, of the 208 genes downregulated by FPSS, 75% had been identified previously as positively regulated by σB. 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 σB activity in both L. monocytogenes and Bacillus subtilis indicates its utility as a specific inhibitor of σB across multiple Gram-positive genera.

IMPORTANCE The σB 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 σB 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 σB 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.