Small-Molecule Inhibition of Siderophore Biosynthesis in *Mycobacterium tuberculosis* and *Yersinia pestis*

Ryu, Jae-Sang

College of Pharmacy, Ewha Womans University

Mycobacterium tuberculosis and *Yersinia pestis*, the causative agent of tuberculosis and the etiologic agent of plague, respectively. Both pathogens have iron acquisition systems based on siderophores, secreted iron-chelating compounds with extremely high Fe^{3+} affinity. Several lines of evidence suggest that siderophores play a critical role in bacterial iron acquisition inside the human host, where the free iron concentration is well below that required for the bacterial growth and virulence. Thus, siderophore biosynthesis is an attractive target for the development of new antibiotics to treat tuberculosis and plague. We report the design, synthesis, and biological evaluation of a mechanism-based inhibitor of domain salicylation enzymes required for siderophore biosynthesis in *M. tuberculosis* and *Y. pestis*. This novel antibiotic small molecule inhibits siderophore biosynthesis and growth of *M. tuberculosis* and *Y. pestis* under iron-limiting conditions.