Structural analogues of 3- [(2,6-difluorobenzoyl)amino]-5-(4-ethoxyphenyl)thiophene-2-carboxylic acid as lead compounds for preventing or treating urinary tract infections

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Publication(s)

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External Link(s)

• From the lab of Dr. Patrick Seed

Value Proposition

Uropathogenic Escherichia coli (UPEC) is the leading cause of community-acquired urinary tract infections (UTIs). Over 100 million UTIs occur annually throughout the world, including more than 7 million cases in U.S. adolescents and adults. UTIs in younger children are associated with greater risk of morbidity and mortality than in older children and adults. Antimicrobial resistance among UPEC is on the rise, driving efforts to discover vulnerable targets in the molecular pathogenesis of infection. There are currently no therapeutics that specifically inhibit the formation of any bacterial capsule, and this is a novel strategy for preventing or decreasing the prevalence of chronic or re-occurring urinary tract infections. New insights into the roles of K1 capsules in UPEC virulence during UTI make capsules an attractive target for therapeutic intervention. Antimicrobial resistance among UPEC is on the rise, and the discovery of novel small molecules that can act as probes or lead compounds for the investigation and treatment of UTI will add to the arsenal of compounds available for single or combination therapies.

Technology

Duke inventors have reported new lead compounds to inhibit, prevent, or treat UTIs. The probe compound, 3-[(2,6-difluorobenzoyl)amino]-5-(4-ethoxyphenyl)thiophene-2-carboxylic acid, was identified as a small molecule inhibitor of K1 capsule formation with an IC_{50} value of 4.5 ± 2.4 μM and a >10-fold selectivity index (SI) in BC5637 bladder cells. The probe has been broadly profiled for off-target liabilities and assessed for aqueous solubility, parallel artificial membrane permeability, and hepatocyte microsome and plasma stability. It is suitable for use as a lead compound for inhibition of K1 capsule formation. Please see related technology T-003747.

Advantages

- Has established a conceptually new class of molecules to combat UPEC infection
- Has *in vitro* and *in vivo* data along with pharm/tox data