Quest for a Drug to Treat Cryptosporidiosis

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Chemistry Seminar on Drug Discovery

Monday
April 1 at 4
pm in 303
Schrenk

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Abstract: Cryptosporidiosis is a neglected diarrheal disease that is caused by infection of the intestines by the parasite Cryptosporidium. This disease disproportionately afflicts young and malnourished children in low-middle income countries resulting 132,000 deaths annually, greatly exceeding that of all other recognized neglected tropical diseases. The only FDA-approved therapeutic, nitazoxanide, is only marginally effective in malnourished children (34% improvement versus placebo) and is ineffective in immunocompromised adults. To address this significant unmet medical need, we have conducted screening of known anti-Plasmodium compounds and other advanced clinical candidates for leads for the development of novel anti-Cryptosporidium therapeutics. We identified three series of compounds with unique modes of action for medicinal chemistry optimization. The series likely inhibit CpPDE(s), CpPI4K(s), and an unknown target. The most potent compounds identified to date have EC₅₀ values ranging from 50-200 nM in HCT-8 cells infected with C. parvum. Compounds from each class have oral in vivo efficacy in an immunocompromised mouse model of Cryptosporidium infection, some at doses as low as 5 mg/kg. Ongoing efforts to identify a safe and potent therapeutic will be discussed.

About the speaker: Meyers is an experienced medicinal chemist and drug discovery scientist. Upon completion of his PhD in Chemistry at the University of Illinois-Urbana Champaign, he spent a decade at Pharmacia and Pfizer working on new drug discovery for a variety of diseases resulting in two novel compounds entering human clinical trials. Since joining Saint Louis University in 2010, his research focus shifted to the design and synthesis of novel drug candidates for rare and infectious diseases, focusing on parasitic, fungal, bacterial and viral diseases with few, if any, treatment options. This work is highly collaborative where the Meyers lab uses organic synthesis to develop structure-activity relationships on lead molecules in partnership with leading disease experts towards the goal of identifying drug candidates for clinical trials. These efforts are supported by grants from the National Institutes of Health and the SLU Research Institute. His work has resulted in 61 peer-reviewed publications, 34 patent applications and 7 issued US patents. In 2021, he was elected as a Senior Member of the National Academy of Inventors.