ACS Medicinal Chemistry Letters

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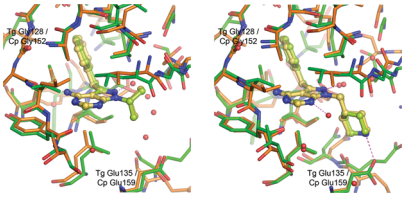
Kinase Inhibitors as Antiparasitic Agents

Cryptosporidium parvum is an obligate intercellular parasite which causes a diarrheal disease known as cryptosporidiosis. *Toxoplasma gondii*, which infects a sizable proportion of the globe, is a protozoan that is a causal agent of toxoplasmosis. New therapeutic agents that target infections caused by both are needed. Small molecules that target calcium-regulated processes are attractive for this purpose because both organisms contain highly specialized calcium-regulated signaling enzymes, which control cellular functions such as secretion, gliding motility, and host cell invasion.

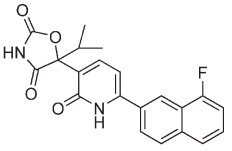
Toward the goal of developing effective antiparasitics, Murphy et al. (DOI: 10.1021/ml100096t) describe a series of small molecule inhibitors that target a unique kinase, calcium-dependent protein kinase 1 in *T. gondii* and *C. parvum*. These inhibitors are highly selective for the parasitic calcium-dependent protein kinase 1 enzymes over mammalian kinases, are not toxic to human cell lines, and can block entry into host cells.



An EP3 Receptor Antagonist

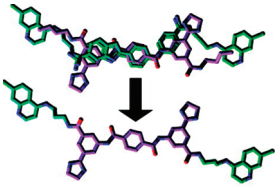
Prostaglandin E2 mediates numerous physiological processes through four receptors denoted as EP1, EP2, EP3, and EP4. Previous studies have implicated EP3 in activities such as neurotransmitter release, the inhibition of gastric acid secretion, and sodium and water reabsorption in the kidney.

Jin et al. (DOI: 10.1021/ml100077x) now describe a lead 3-oxazolidinedione-6-aryl-pyridinone, which serves as a selective EP3 antagonist. This compound is orally bioavailable and potent in vivo. The authors further optimized the lead compound to yield a series of compounds, which might serve as excellent tools for studying the EP3 receptor.



Fighting *Botulinum* Neurotoxins

Botulinum neurotoxin is the most potent biological toxin on the planet. According to estimates, this neurotoxin is lethal to humans at a dose (LD_{50}) of only 1 ng kg^{-1} of body mass. Currently, there are no drugs that counteract the paralysis associated with *Botulinum* neurotoxin. Now, Nuss et al. (DOI: 10.1021/ml100056v) describe a new approach for the design and synthesis of increasingly potent nonpeptidic small molecules that might serve as starting points for the development of therapeutics that neutralize neurotoxin-induced paralysis.



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