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In This Issue

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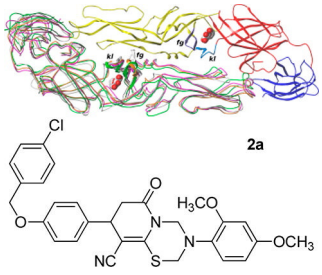
INHIBITORS OF TICK-BORNE FLAVIVIRUS

Flaviviruses are a large genus of enveloped viruses transmitted by mosquitoes or ticks. While mosquito-borne flaviviral infections, such as dengue fever, West Nile fever, and yellow fever, are widely studied and publicized, tick-borne infections, such as tick-borne encephalitis causing up to 10,000 cases per year throughout Europe and Asia, Omsk hemorrhagic fever, and Powassan encephalitis, represent a serious health concern in the Northern hemisphere, leading to serious disabilities or even death. Drug development against Omsk hemorrhagic fever and Powassan encephalitis viruses is necessary to suggest a prophylactic and/or treatment scheme for a large number of people exposed to risk of infection in the tick-inhabited areas.

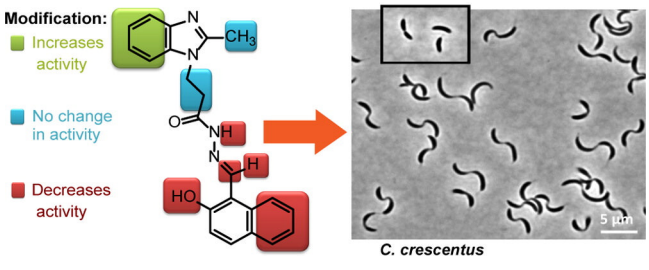
In this issue, Osolodkin et al. (DOI: 10.1021/ml400226s) describe two series of compounds designed to inhibit the reproduction of tick-borne flaviviruses. Virtual screening and homology modeling lead to identification of compounds that exhibited antiviral activity and low toxicity. These compounds are the most potent among the ones reported to date, demonstrating low toxicity and selectivity.



A NEW INHIBITOR OF BACTERIAL CELL DIVISION

A number of factors regulate bacterial cell division making the division machinery an ideal target for antimicrobial therapies. Divin, a recently described small molecule inhibitor of bacterial cell division that acts by perturbing the assembly of proteins at the site of cell septation, may aid the mechanistic studies of this process.

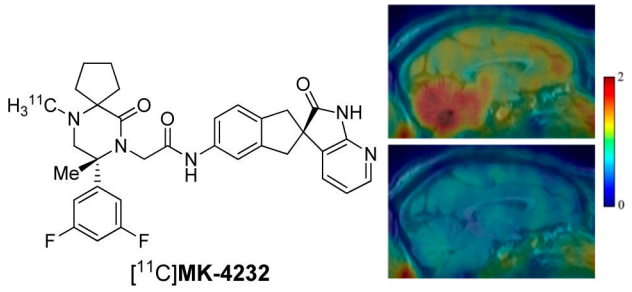
Here, Zhou et al. (DOI: 10.1021/ml400234x) describes the synthesis and structure−activity relationship (SAR) studies of divin and its potent analogues through a sequential 3-component coupling, allowing for utmost diversity. The SAR studies pointed to the structural part of divin that confers activity. Future design of divin photoaffinity probe could lead to identification of its target in bacteria and the development of therapeutic agents.



PET TRACER FOR A KEY RECEPTOR IN MIGRAINE

Migraine is a common neurovascular disorder, characterized by moderate to severe headaches. While the exact mechanism of migraine pathogenesis is not known, the calcitonin gene-related peptide (CGRP) is thought to play a key role in it. Several structurally distinct calcitonin gene-related peptide (CGRP) receptor antagonists have demonstrated clinical efficacy for the acute treatment of migraine. However, the question of whether these novel agents act in the central nervous system or in the periphery has been the subject of much debate.

The present letter by Bell et al. (DOI: 10.1021/ml400199p) describes the design and discovery of a positron emission tomography (PET) tracer for the CGRP receptor that can be used to interrogate key questions concerning the mechanism of action of the receptor antagonists. The work highlights some design principles that are helpful for the identification of PET tracers and also demonstrates approaches to improving central nervous system penetrance.



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