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In This Issue

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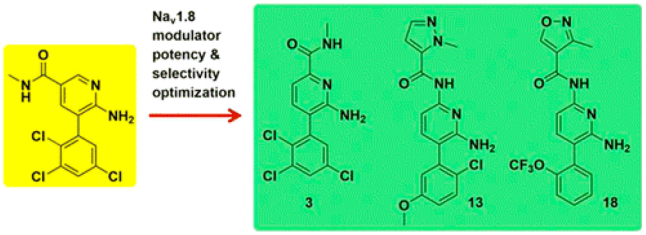
EXPANDING THE USE OF NA_V BLOCKERS

Voltage-gated sodium channels (Na_v) are a family of transmembrane ion channels that play an important role in regulating the firing threshold in neurons. In the clinic, Na_v blockers have been used to treat conditions such as chronic pain and epilepsy. Despite some success with these compounds, use of Na_v blockers is limited due to their nonselective nature resulting in inhibition of sodium channels in the heart and central nervous system.

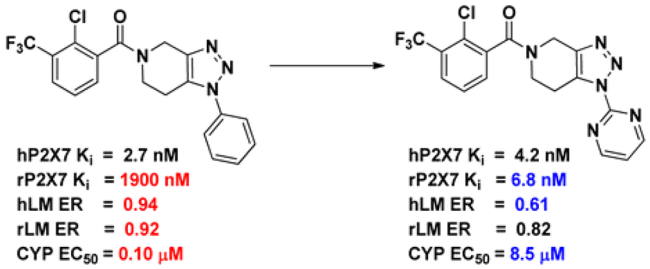
In this issue, Bagal et al. (DOI: 10.1021/acsmedchemlett.5b00059) develop and optimize a series of compounds that selectively inhibit the activity of a single Na_v subtype, $Na_v1.8$, expressed primarily in peripheral neurons. They identify a lead candidate compound that exhibits good oral bioavailability and efficacy in preclinical trials of neuropathic and inflammatory pain.



TARGETING IL-1β PRODUCTION IN THE BRAIN

Cytokines such as IL-1β have recently been found to be associated with drug-resistant depression. Consequently, targeting of IL-1β has been proposed as a novel therapeutic intervention for the treatment of depression.

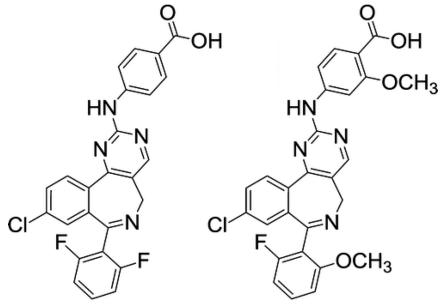
Here, Savall et al. (DOI: 10.1021/acsmedchemlett.5b00089) develop a series of novel compounds that antagonize a receptor, P2X7R, known to activate production of IL-1β. The authors describe synthesis and optimization of these compounds, which demonstrate strong affinity for the receptor, good oral bioavailability, and the ability to penetrate to the desired target site for treatment of depression, the brain.



DESIGNING SELECTIVE INHIBITORS OF AURORA KINASE A

Aurora kinases A and B are enzymes that have been found to be overexpressed in various types of cancer. These kinases are essential for a cell's normal progression through mitosis, and their loss of function can lead to cell death. As such, Aurora kinases are attractive targets for the development of cancer therapies, and Aurora kinase inhibitors have already successfully advanced to clinical trials.

From the perspective of a medicinal chemist, Sells et al. (DOI: 10.1021/ml500409n) describe the design, synthesis, and bioevaluation of two selective Aurora kinase A inhibitors currently in human clinical trials.



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