ACS Chemical Neuroscience

In This Issue

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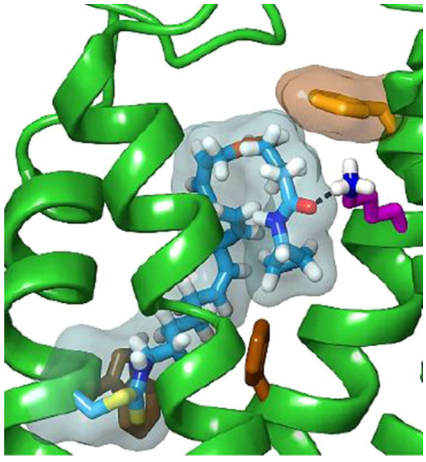
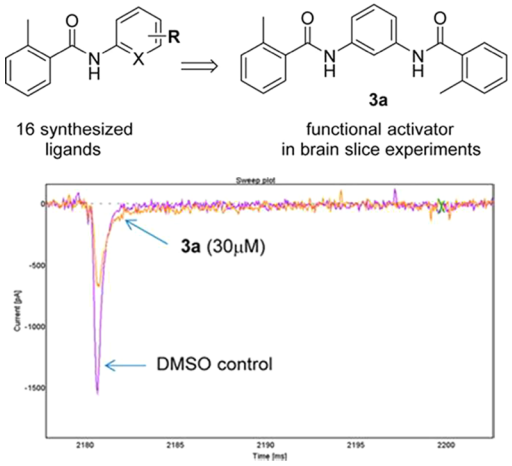
SELECTIVE PROBE FOR A CANNABINOID RECEPTOR



The cannabinoid receptor type 1 (CB1R) is the predominant G protein-coupled receptor in the mammalian central nervous system and plays important neurobiological roles in several processes critical to health, including control of neurotransmitter release, the generation of new neurons, and neuronal repair. Now, Janero et al. (DOI: 10.1021/acschemneuro.5b00090) report an initial molecular interaction and activity profile of AM3677, the first reported covalent partial agonist selective for cannabinoid receptor type 1 (CB1R).

As such, typical agonists able to potentiate CB1R activity have already been commercialized for various indications, although their adverse-event profiles tend to restrict their wider exploitation as drugs. Consequently, novel ways of modulating and directing CB1R activity through targeted small-molecule ligands such as the compound presented in this study inform the quest for improved CB1R-targeted therapeutics. AM3677 serves as a useful chemical probe for interrogating CB1R structure−function correlates.

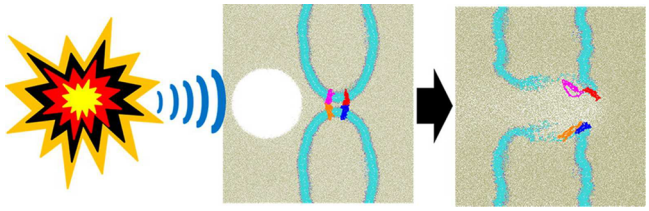
TARGETING SODIUM CHANNELS



Voltage-gated sodium channels (Na_v) are crucial components of the central nervous system, and knowledge on the functional importance of these channels is imperative especially given their therapeutic potential. In the current issue, Crestey et al. (DOI: 10.1021/acschemneuro.5b00147) report a series of compounds that modulate the $Na_v1.1$ channel.

The authors used a 2-methylbenzamide scaffold as a template to synthesize and evaluate 16 analogues on $Na_v1.1$ activity. Compound *N*,*N*′-(1,3-phenylene)bis(2-methylbenzamide) was shown to increase this channel's activity and paves the way for the development of new drugs targeting this channel linked to epilepsy and other CNS disorders.

BLOOD-BRAIN BARRIER DISRUPTION BY CAVITATION EFFECT



Shock waves cause the formation of bubbles in the blood vessels and capillaries. Driven by the hypothesis that traumatic brain injury may be caused by damage to blood-brain barrier (BBB), Goliaei et al. (DOI: 10.1021/acschemneuro.5b00116) performed molecular dynamics computer simulations to investigate how collapse of a nanobubble can damage this barrier.

The authors simulated systems that contained a model of tight junction from the BBB. In this model, they represent the tight junction by two pairs of interacting proteins, claudin-15. The simulation studies showed that even a low-intensity shock wave can induce the collapse of a nanobubble which results in tight junction damage. This study is the first simulation that considers a model of a BBB tight junction and also the first that considers the connection between bubble implosion (cavitation effect) and tight junction damage.

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