ACS Chemical Neuroscience

In This Issue

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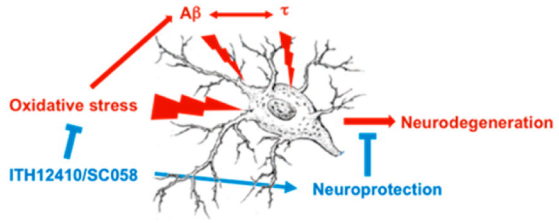
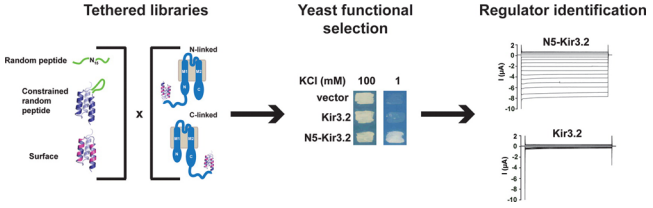
NEW COMPOUND FOR POTENTIALLY TREATING ALZHEIMER'S DISEASE



ITH12410/SC058 is the lead compound of a series of dibenzothiadiazepine derivatives synthesized toward the development of new potential drugs for the treatment of Alzheimer's disease. In the current issue, Romero et al. (DOI: 10.1021/cn500131t) have further studied the neuroprotective properties of the best compound ITH12410/SC058.

With ITH12410/SC058, the authors observed a remarkable antioxidant profile, together with a reduction of the neuronal death elicited by amyloid beta peptide or a model of tau hyperphosphorylation, that is, okadaic acid exposure. These data suggest that this new dibenzothiadiazepine can be considered as a new candidate for preclinical studies for the treatment of Alzheimer's disease.

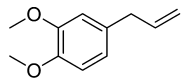
NOVEL APPROACH TO IDENTIFY ION CHANNEL MODULATORS



Ion channels conduct bioelectrical signals central to heart, nerve, and brain function. Many ion channels lack agents that can be used to manipulate their function. Although protein display technologies provide powerful ways to generate soluble protein modulators, their application to membrane proteins, such as ion channels, remains challenging. In this issue, Bagriantsev et al. (DOI: 10.1021/cn5000698) report a new way to identify ion channels modulators.

The authors demonstrate the use of a tethering strategy to display randomized protein libraries coupled with a functional selection as a method to target ion channels and identify a new Kir3.2 (GIRK2) potassium channel modulator that affects channel function by facilitating plasma membrane expression. These results highlight the power of unbiased selection and molecular evolution methods for developing new ion channel modulators and the potential for affecting channel function via trafficking.

METHYLEUGENOL—AN AGONIST OF $GABA_A$ RECEPTORS



1,2-dimethoxy-4-prop-2-en-1-ylbenzene
(Methyleugenol, ME)

Methyleugenol (ME), a natural flavoring constituent isolated from many plant essential oils, is widely used as a supplemental agent in food and as a fragrance in cosmetics and soaps. Despite ME being linked to several appealing biological effects such as neuroprotection, antidepressive, anticonvulsant, and so forth, the underlying mechanism of action is unknown. In the current Issue, Ding et al. (DOI: 10.1021/cn500022e) report that ME acts as a novel ligand of $GABA_A$ receptors ($GABA_ARs$).

At the lower concentrations, ME significantly sensitized the GABA-induced currents in cultured hippocampal neurons; at relatively higher concentrations, ME directly activated the endogenous and recombinant $GABA_ARs$ in a concentration-dependent manner. As a result, ME produced a strong inhibitory effect on the synaptically driven neuronal excitation in hippocampal neurons. These findings are consistent with previously identified pharmacological effects of this compound on central inhibition such as antinociceptive, anesthetic, neuroprotection, antidepressive, and anticonvulsant activities, which added the $GABA_AR$ activation to the list of molecular targets of ME that probably accounts for its biological activities.

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