ACS Chemical Neuroscience

In This Issue

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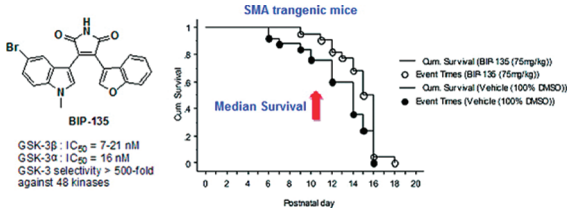
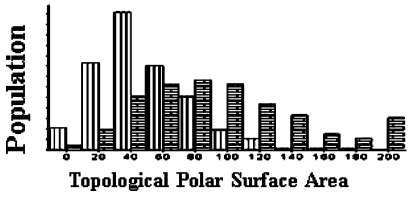
TREATING SPINAL MUSCULAR ATROPHY



Currently, small muscular atrophy (SMA) is an untreatable disease that leads to infant fatality. SMA is caused by a mutation or deletion of the *survival motor neuron 1* (*SMN1*) gene resulting in lack of the corresponding SMN protein. Inhibition of glycogen synthase kinase-3 (GSK-3) has been shown to increase SMN levels and, as a result, has emerged as a possible drug target for treating SMA. Chen et al. (DOI: 10.1021/cn200085z) report a GSK-3 inhibitor that offers increased SMA protection in mice.

The authors tested a potent GSK-3 inhibitor, BIP-35, in a transgenic Δ7 SMA KO mouse model, which features several phenotypes of human SMA disease. BIP-3 was found to prolong survival in this mouse model. Moreover, this compound elevated SMN in fibroblasts and was neuroprotective in a cortical neuronal model of oxidative stress. This study is the first evaluation of a GSK-3 inhibitor in an animal model of SMA.

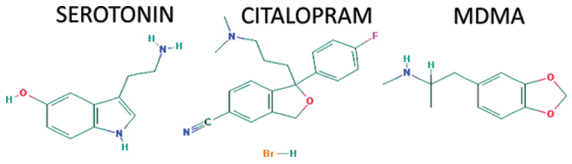
OPTIMIZING CNS DRUG DISCOVERY



Not only do diseases of the central nervous system (CNS) exact an enormous emotional toll, they also create a huge economic burden running into trillions of dollars. As a result, the discovery and development of effective therapies against CNS diseases such as Alzheimer's, Parkinson's, brain cancer, and stroke are highly sought. To catalog desirable features of CNS and non-CNS drugs, Ghose et al. (DOI: 10.1021/cn200100h) describe a chemoinformatic medicinal chemistry approach for effective CNS drug discovery.

The authors systematically analyzed the physicochemical and structural features of ~1000 CNS and non-CNS drugs. Based on this analysis, they provided desirable properties for lead compound selection and optimization which included ways to separate CNS from non-CNS drugs. They also described guidelines for designing superior CNS drugs based on physicochemical properties that should form the template for future CNS drug development.

REDUCING METHAMPHETAMINE TOXICITY



Ecstacy or 3,4-methylenedioxymethamphetamine (MDMA) is a popular drug of abuse which disrupts serotonin signaling. It has been demonstrated that rats exposed to MDMA experience long-term deficits in learning and memory. Additionally, in pregnant women, MDMA can cross the placenta posing significant risk to fetal development. In this issue, Schaefer et al. (DOI: 10.1021/cn2000553) look to reduce MDMA-induced toxicity using a selective serotonin reuptake inhibitor, citalopram (CIT).

Using pretreated rats, the authors tested the effects of varying doses of CIT on MDMA-induced serotonin depletion in the brain. Two doses of 5 mg/kg of CIT per day resulted in attenuation of MDMA effects on serotonin levels without losing effectiveness during brain development. This observation opens the door for better understanding the long-term side-effects of using MDMA and could lead to treatment of affected infants.

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