ACS Chemical Neuroscience

In This Issue

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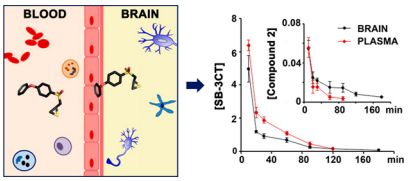
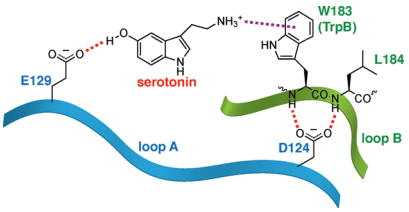
FOLLOWING BRAIN PENETRATION OF A GELATINASE INHIBITOR



One of the great challenges in the development of neurological disease treatments is the relative impenetrability of the blood-brain barrier (BBB). In the current issue, Gooyit et al. (DOI: 10.1021/cn300062w) show that SB-3CT, a potent and selective inhibitor of matrix metalloproteinases (MMP)-2 and -9 (also known as gelatinases), that shows efficacy in animal models of neurological diseases, crosses the BBB.

The authors developed a sensitive analytical method to measure levels of SB-3CT and related active metabolites in plasma and the brain. The methodology was based on the use of ultraperformance liquid chromatography using electrospray ionization for quantification of compounds in both plasma and brain homogenate. The studies showed these compounds are rapidly absorbed and distributed in the brain, do not accumulate in the brain, and are not neurotoxic.

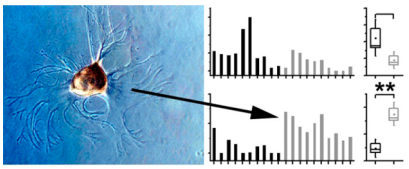
KEY RESIDUES IN SEROTONIN RECEPTOR ACTIVATION



The serotonin type 3 receptor (5-HT_3) is prevalent in central and peripheral nervous systems and is implicated in several psychiatric and neurological disorders. The receptor is a pentameric neurotransmitter-gated ion channel which binds serotonin leading to an excitatory response in neurons. Miles et al. (DOI: 10.1021/cn3000586) elucidate new functional interactions between amino acid residues at the binding pocket of the 5-HT3A receptor.

The authors utilized site-directed and unnatural amino acid mutagenesis to establish strong interplay between W183, E129, and D124 residues and their roles in receptor function. Moreover, significant functional differences between serotonin and competitive partial agonist *m*-cholorophenyl bioguanide (mCPBG) at these three residues were observed showing that mCPBG elicits receptor activation very differently.

METABOLIC COMPOSITION OF CULTURED NEURONS



The metabolome comprises all small molecules found in a given biological sample. Careful assessment of the metabolome can shed light on the biological state of a cell or tissue. In the current issue, Nemes et al. (DOI: 10.1021/cn300100u) measure changes in the metabolic profiles in individual neurons caused by variations in culturing conditions.

By using single-cell capillary electrophoresis coupled to electrospray ionization mass spectrometry, the authors compared the amounts of 35 different biomolecules in freshly isolated and cultured B1 and B2 buccal neurons from *Aplysia californica*. The studies revealed differences in metabolic profiles which were subsequently validated with statistical analysis. The methodology utilized in this study provides a great way for comparing metabolomes of cells.

Published: October 17, 2012

dx.doi.org/10.1021/cn3001685 | *ACS Chem. Neurosci.* 2012, 3, 729–729