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In This Issue

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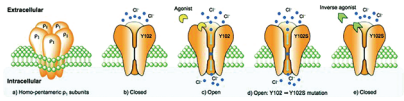
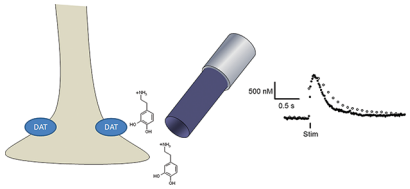
ASSESSING INVERSE AGONISTS OF A GABA RECEPTOR



The $GABA_C$ receptor is one of three receptors activated by the neurotransmitter γ-amino butyric acid (GABA). $GABA_C$ receptors are part of the Cys-loop ligand-gated ion channel superfamily and have been implicated in the onset of myopia, memory enhancement, and fear and anxiety disorders. Therefore, development of modulators to this receptor is of importance. In this issue, Yamamoto et al. (DOI: 10.1021/cn200121r) assess the activities of different antagonists on this receptor.

$GABA_C$ receptors are composed of five ρ_1 subunits which possess a tyrosine residue at position 102 implicated in agonist binding and channel gating. By mutating this residue to a serine, cysteine, or alanine, the authors showed that the channel could be stabilized in a constitutively open or closed conformation. This observation allowed the evaluation of several $GABA_C$ agonists which resulted in the identification of ligands whose potencies differ according to the conformation state (open versus closed) of the receptor.

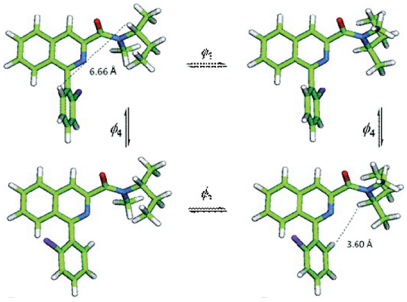
REFINING FAST-SCAN CYCLIC VOLTAMMETRY MEASUREMENTS



Dopamine is a key neurotransmitter in the brain associated with reward-driven learning. Its aberrant functioning has been connected with several neurological system disorders. Accurate quantitative measurement of the release and uptake of dopamine in the brain is therefore of significant interest. Kile et al. (DOI: 10.1021/cn200119u) tweak fast-scan cyclic voltammetry (FSCV) to provide a method for more accurate measurement of dopamine concentration.

Carbon-fiber based microelectrode technology for quantifying dopamine concentration fluctuation has steadily improved over the years. Constant potential amperometry (CPA) provides a means for measuring rapid fluctuations of compound concentration, but lacks the ability to identify the chemical species being studied. On the other hand, FSCV is a method of choice for identifying the electroactive chemical compound, but is compromised in terms of sensitivity. To achieve CPA-level sensitivity using FSCV, the authors used uncoated carbon-fiber electrodes in combination with increased sampling frequency. The improved methodology was applied in vivo for more reliable dopamine measurements.

STRUCTURE OF IMPORTANT TRANSLOCATOR PROTEIN LIGAND



The 18 kDa translocator protein (TSPO) is implicated in a variety of neuropsychiatric disorders. Apart from being a great target for drug discovery, it is also pursued as a target for imaging the brain and inflammatory processes. The classical ligand that binds TSPO is the compound known as PK 11195. In the current issue, Lee et al. (DOI: 10.1021/cn3000108) elucidate the structure of PK 11195 with broader consequences of aiding in the development of better imaging tools and therapeutics targeting TSPO.

The interaction between PK 11195 and TSPO has been largely unclear. In the current study, the solution structure of this small-molecule ligand was determined using a combination of dynamic $^1H/^{13}C$ NMR spectroscopy and quantum chemistry. The experimental and theoretical data pointed to the presence of four interconverting PK 11195 rotamers. Further study of these isomers revealed the most stable form of PK 11195.

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