ACS Chemical Neuroscience

In This Issue

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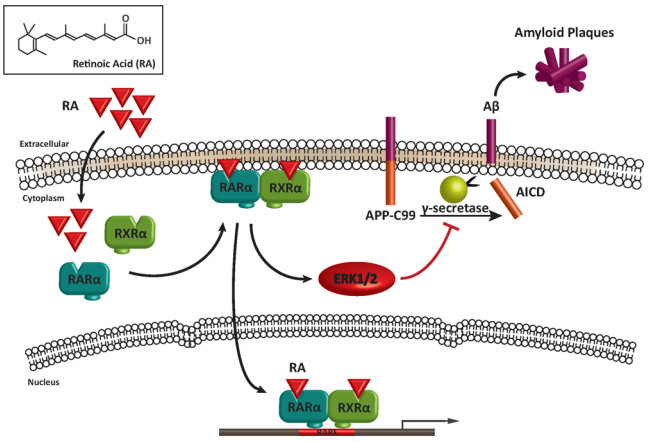
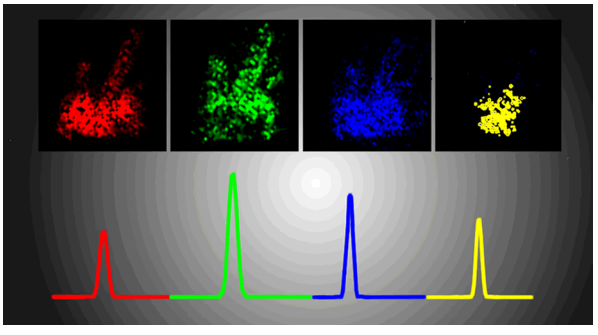
RETINOIC ACID SIGNALING, A NEW TARGET FOR ALZHEIMER'S DISEASE THERAPY



Cytotoxic amyloid-β (Aβ) peptide deposition on the brain is widely implicated in Alzheimer's disease (AD). Aβ is generated by the cleavage of amyloid precursor protein by enzymes such as γ-secretase. In the current issue, Kapoor et al. (DOI: 10.1021/cn400039s) establish that retinoic acid (RA) plays a neuroprotective role by inhibiting γ-secretase.

Opposing effects of JNK- and ERK-dependent MAP kinase modulate the activity of γ-secretase. The authors show that ERK activation is essential for the RA elicited downregulation of γ -secretase activity. Additionally, retinoic acid receptor α (RARα) and retinoid X receptor α (RXRα) are important for RA signaling-induced inhibition of γ-secretase activity and modulate the γ-secretase-mediated production of Aβ.

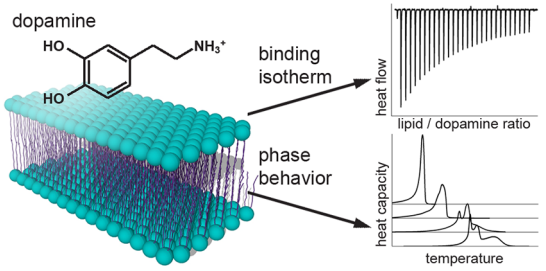
IMAGING METABOLITES AND NEUROTRANSMITTERS IN TISSUES



Abnormal expression of metabolites and neurotransmitters has been linked to several diseases. Techniques combining chromatography and mass spectrometry using homogenized extracts have provided valuable insights into expression levels of these molecules. However, previous work has not yielded sufficient information regarding the spatial distribution of metabolites and neurotransmitters in the central nervous system. Now, Ye et al. (DOI: 10.1021/cn400065k) present an application of high resolution mass spectrometry for imaging of the metabolites and neurotransmitters in tissues.

A state-of-the-art high mass spectral resolution and high accuracy mass spectrometric imaging (HRMSI)-based platform was used to produce MS images of multiple metabolites such as amino acids, nucleobases, and organic acids, as well as neurotransmitters like acetylcholine from crustacean and rodent model organisms. This powerful new approach will facilitate the discovery and design of therapeutics for diseases associated with abnormally expressed metabolites and neurotransmitters.

DOPAMINE AND LIPID BILAYERS INTERACT



Dopamine (DA) is a neurotransmitter which participates in a number of motor and mental functions. Minor changes in normal regulation of DA activity are implicated in neurological disease. The possible interaction between dopamine and lipid membranes is an unexplored area. In this issue, Jodko-Piorecka and Litwinienko (DOI: 10.1021/cn4000633) describe the mechanism of action of catecholamine neurotransmitters.

The authors determined the binding constants and thermodynamic parameters of the formation of DA/lipid complexes and showed that the protonated nitrogen atom of DA is electrostatically attracted by the lipid headgroup anions. It is possible that the loss of "free" DA to lipid membrane binding could affect synaptic transmission and contribute to neurodegenerative disease. Additionally, binding to neuronal membranes could reduce the effectiveness of L-DOPA therapy in the treatment of Parkinson's disease.

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