ACS Chemical Neuroscience

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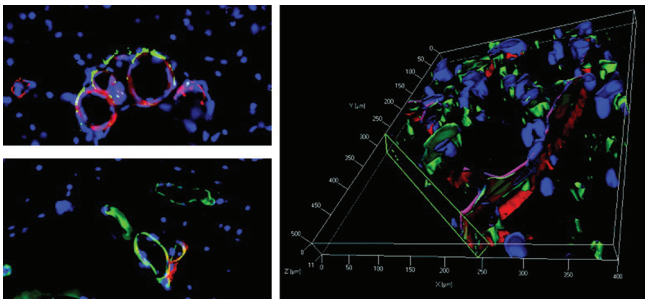
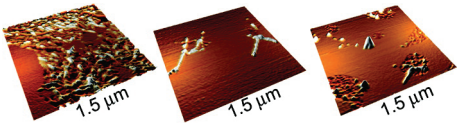
Identifying Phosphodiesterases in the Brain



Cyclic nucleotide phosphodiesterases (PDEs) comprise an enzyme superfamily of great clinical significance. These enzymes are involved in the regulation of key cellular molecules, cAMP and cGMP. Eleven PDE families have been identified thus far. PDE activities seem to be tissue-specific and have been known to exist in brain microvessels where they are implicated in controlling the blood-brain barrier and cerebral blood flow. However, the role of PDEs in these processes has remained unclear. In this issue, He et al. (DOI: 10.1021/cn2000487) shed light on the identities of PDEs in the brain microvessels of rats.

Using microarray technology, the authors studied the gene expression profile in rat brain microvessels with particular emphasis on PDE expression patterns. These studies yielded 16 PDE transcripts. Additional characterization led to the identification of the cAMP-specific PDE4D and cGMP-specific PDE5A as the main forms of PDEs expressed in rat brain microvessels. This study is an important advance toward understanding the role of PDEs in the brain.

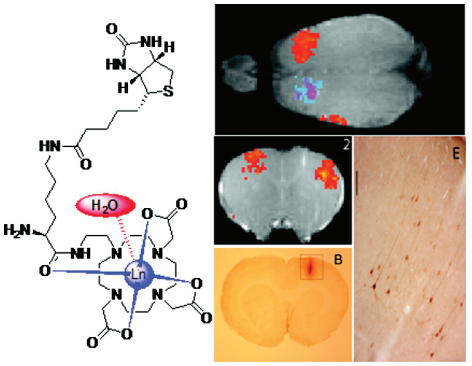
Effect of Apolipoproteins on β-Amyloid Aggregation



The aggregation of β-amyloid (Aβ) peptides which accumulate as plaques in the brain is a well-established pathophysiological observation linked to Alzheimer's disease (AD). These aggregates' disruption of the lipid membrane is a possible mechanism underlying AD. The apolipoprotein ApoE is thought to control Aβ interaction with the lipid membrane. Legleiter et al. (DOI: 10.1021/cn2000475) observe the effect of ApoE on Aβ-aggregation and lipid membrane disruption.

Using atomic force microscopy (AFM), the authors studied the effects of different ApoE isoforms on Aβ-dependent disruption of total brain lipid extract bilayers. The apoE3 allele disrupted lipid bilayers to a greater extent than the apoE4 allele, an observation confirmed by scanning probe acceleration microscopy studies. These observations could help spark the development of novel therapeutics that reduce the deleterious effects of Aβ peptide.

New Tool for Studying Brain Networks



Understanding the way brain networks function is critical to curing some of the most debilitating brain diseases. External stimuli such as drug addiction, brain disease, and stroke are known to influence these networks. Methods to understand the link between connectivity changes in the brain to cognitive function is of paramount importance. In this issue, Mishra et al. (DOI: 10.1021/cn200022m) provide a new platform for studying neural networks.

To date, magnetic resonance imaging (MRI) has been the best approach to scrutinize the dynamics of neural networks. The well-established neuronal tracer biocytin was functionalized using a gadolinium caged macrocylic moiety, making it a magnetic resonance reporter for observing brain network dynamics in live animals using MRI. Additionally, a biotin moiety allowed for subsequent avidin-based isolation, allowing for post-mortem histological characterization. Therefore, this new probe has given researchers the ability to study neural networks in live animals and subsequent post-mortem microscopic analysis.

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