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In This Issue

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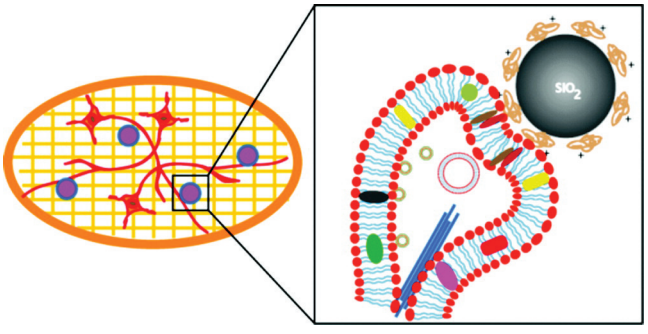
A MULTIPLE SCLEROSIS BREATH TEST

Multiple sclerosis (MS) is the most common neurological disorder afflicting young adults. Typical diagnosis of MS is expensive, since it relies on magnetic resonance imaging of the brain and spinal cord or the use of invasive techniques with painful side-effects. In the current issue, Ionescu et al. (DOI: 10.1021/cn2000603) report the development of a rapid and portable way to diagnose MS in patients.

The authors designed a polycyclic aromatic hydrocarbions array on top of a single-walled carbon nanotube for sensing volatile organic compounds in patients' breath. A clinical study was performed on 51 volunteers and showed significant accuracy in detecting patients suffering from MS. Importantly, the accuracy of this noninvasive test was not affected by factors such as smoking and gender. Hence, this new technology opens the door for developing a much needed noninvasive and inexpensive diagnostic toolkit for detecting MS.

OBSERVING ULTRASTRUCTURAL DETAILS OF SYNAPSES

Synapses are the junctions between axons and dendrites. The synaptic cleft allows the movement of neurotransmitter among neurons and between neurons and muscle cells. Previous studies of synapse formation largely comprised optical microscopic methods. In this issue, Gopalakrishnan et al. (DOI: 10.1021/cn200094j) use cryo-electron microscopy (cryo-EM) to visualize ultrastructural details of artificially produced synapses.

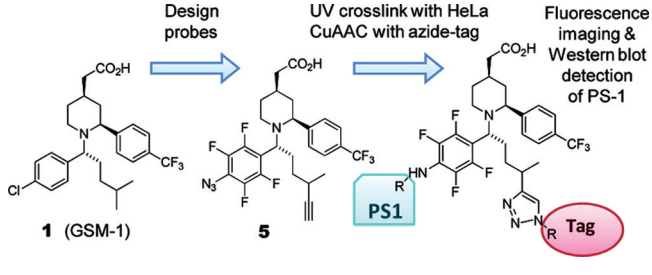


The authors describe a novel way by which primary hippocampal neurons are grown on EM grids in culture with poly-D-lysine or lipid bilayers. Following incubation with 500 nm silica beads, the ultrastructures of axon–bead contacts were studied using cryo-EM. Intriguingly, ultrastructures resembling presynapses were observed that contained 3–100 nm vesicles. Additionally, the authors observed microtubular structures associated with the synaptic junction. The combination of a new approach for growing artificial neurons and cryo-EM offers a much needed label-free approach for detailed observation of artificial synapses.

CLARIFYING MECHANISM OF γ-SECRETASE MODULATORS

Aβ peptides are believed to play a role in the neuropathogenesis of Alzheimer's disease (AD). γ-Secretase is a protease that cleaves amyloid precursor protein (APP) to generate neurotoxic peptides of differing lengths, such as Aβ40 and Aβ42, making this enzyme a good drug target. However, γ-secretase also cleaves other key proteins involved in neuronal development, which complicates targeting this enzyme. As a result, γ-secretase modulators (GSMs) have been a major focus for therapeutic development. In this issue, Crump et al. (DOI: 10.1021/cn200098p) design new clickable photoaffinity GSM probes that significantly improves our current understanding of γ-secretase modulation.

A major determinant of AD progression is the relative Aβ40/Aβ42 ratio. Given the role of γ-secretase in the formation of both peptides makes GSM development highly desirable. Using clickable photoaffinity GSM probes, the authors determined presenilin-1 (PS1), the catalytic subunit of γ-secretase, to be the target of acid GSMs. Moreover, the binding of GSMs leads to a change in γ-secretase conformation in the active site which explains the modulation effect in Aβ production.



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