ACS Chemical Neuroscience

In This Issue

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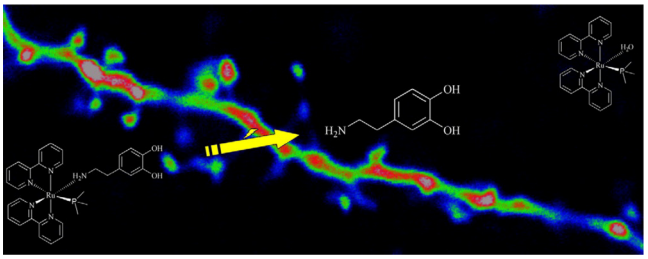
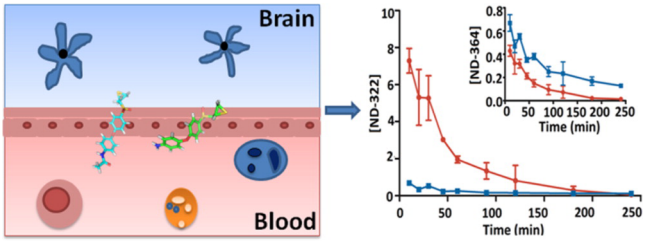
MANIPULATION AND SENSING OF A SINGLE DENDRITIC SPINE



Despite substantial research, dopamine-dependent modulation of neuronal circuits, neurons and synapses are still poorly understood. High-resolution methodologies to study dopaminergic inputs could fill the gap. Toward this goal, Araya et al. (DOI: 10.1021/cn4000692) report the development of a new way to noninvasively map functional dopamine receptors in brain tissue.

The authors developed a caged dopamine (RuBi-Dopa) which can be precisely controlled by two-photon uncaging. They combined this tool with traditional Ca^{2+} indicators to perform the interrogation of dopaminergic transmission in single dendritic spines at high spatial resolution.

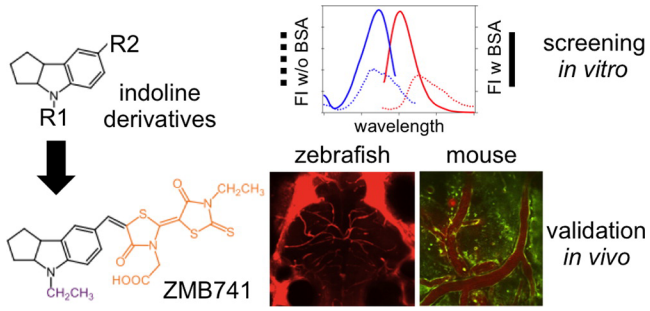
IDENTIFYING A PRODRUG'S MOST ACTIVE METABOLITE



Matrix metalloproteinases (MMPs) play an important role in structural development and maintenance of the nervous system. They are, however, also known to play a deleterious role (specifically MMP-9) in several neurological problems including stroke, Alzheimer's disease, and multiple sclerosis. Inhibition of MMP-9 is therefore an important therapeutic strategy. In the current issue, Song et al. (DOI: 10.1021/cn400077d) study the brain and plasma levels of prodrug ND-478 and its hydrolyzed, active MMP-9 inhibitor forms, ND-322 and ND-364, to pinpoint the most effective therapeutic agent.

Using an appropriate analytical method, the authors showed that compound ND-478 does not cross the blood-brain barrier. However, ND-322 and its more potent *N*-acetylated form, ND-364, distribute to the brain. The observation that ND-364 reaches required therapeutic levels in the brain indicates this compound has promise to treat MMP-related neurological disorders.

VISUALIZING BLOOD-BRAIN BARRIER DISRUPTION



The blood-brain barrier (BBB) is breached in conditions such as cerebral ischemia. Imaging tools are needed to visualize this disruption in vivo. Now, Nishimura et al. (DOI: 10.1021/cn400010t) describe the development of a fluorescent indoline compound to visualize this phenomenon in zebrafish and mouse models.

The authors developed nine structurally related indoline derivatives. One, ZMB741, proved to be a superior fluorescent tool as compared to Evans blue and indocyanine green, due to high affinity for serum albumin. Because of the ease of use in zebrafish and living mouse models, this compound provides a new way to identify genes related to BBB disruption and for identifying new therapeutic compounds.

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