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Spotlights on Recent *JACS* Publications

NEW PROBE DETECTS HYDROGEN SULFIDE IN LIVE ANIMALS

Hydrogen sulfide is getting an image makeover. Long viewed as a pollutant that gives rotten eggs their foul smell, the molecule now is appreciated as an important signal transmitter in biological systems, such as the cardiovascular, nervous, endocrine, immune, and gastrointestinal. However, an obstacle in studying the physiological roles of hydrogen sulfide has been the limited tools available for the sensitive, selective, and real-time detection of this molecule.

Here, Michael Pluth and colleagues describe a fluorescent probe that is highly sensitive to biological hydrogen sulfide (DOI: 10.1021/jacs.5b04196). The probe, called MeRho-Az, selectively detects the molecule at a concentration as low as 86 nM. MeRho-Az's fluorescence increases over 1000-fold in the presence of hydrogen sulfide, making it one of the strongest known detectors of the molecule.

Besides showing that the probe works in cultured cells, the investigators also demonstrate the probe's action in live animals. When it is combined with a 3D light sheet fluorescence microscopy technique, the real-time release of hydrogen sulfide from donor molecules can be tracked in the intestinal track of zebrafish larvae. The authors suggest that MeRho-Az, in combination with sophisticated imaging methods, will facilitate future investigations of hydrogen sulfide's roles in complex biological systems.

Rajendrani Mukhopadhyay, Ph.D.

IMIDAZOLIUM CATIONS HIGHLY STABLE UNDER HARSH ALKALINE CONDITIONS

Basic conditions in alkaline fuel cells accelerate the electrochemical reactions at the electrodes, and this rate enhancement can allow the use of catalysts that are less expensive than those required for proton fuel cells. However, the lifetime of alkaline fuel cells is limited by carbonate salts that form in a reaction between carbon dioxide and hydroxide in the liquid electrolyte. To inhibit formation of this salt—which reduces fuel cell device performance—researchers use polymeric anion exchange membranes as a solid electrolyte. In these membranes, organic cations, typically ammonium groups, dangle from a polymer backbone. Though these membranes are highly conductive, many ammonium cations are not stable under fuel cell operating conditions.

Now, Geoffrey Coates and his colleagues Kristina Hugar and Henry Kostalik have synthesized a variety of substituted imidazoliums to replace the ammonium cations, tested the molecules' stability under alkaline conditions, and identified some with the highest reported stabilities to date (DOI: 10.1021/jacs.5b02879). Two of the new compounds are stable for 30 days at 80 °C in 5 M potassium hydroxide, conditions more caustic than the operating conditions for an alkaline fuel cell. The researchers write that these new compounds might also be useful for organic catalysis, solar cell electrolytes, and phase transfer catalysis.

Melissae Fellet, Ph.D.

MEDICAL IMAGING AGENT DOES DOUBLE DUTY

Magnetic resonance imaging (MRI) can help doctors find hidden tumors under the skin, but the images are not always clear enough. MRI relies on the signal from water to reveal anatomical detail, and while contrast agents can selectively enhance the signal from a particular area of interest, such as a tumor, the image may remain ambiguous. An alternate approach that offers increased sensitivity is fluorescence imaging, which often relies on dyes that emit in the near-infrared spectrum.

To combine the best of the MRI and optical worlds, Thomas Meade and co-workers have developed a single chemical that acts as both a magnetic resonance (MR) and near-infrared (NIR) contrast agent (DOI: 10.1021/jacs.5b04509). The MR-NIR twin contrast agent consists of chelating groups that bind to gadolinium, which acts as an MRI contrast agent, and a fluorescent dye, IR-783.

The researchers first test the MR-NIR contrast agent on cells, which readily absorb the agent. When they then inject the agent into mice with a breast cancer tumor xenograft they see the tumor light up on fluorescent images. However, MRI does not show a contrast-enhanced tumor image in this case. In future experiments, the researchers hope to increase the solubility of the MR-NIR contrast agent so larger doses may be given to improve sensitivity in MRI.

Erika Gebel Berg, Ph.D.

COMPREHENSIVE ACTIVITY-BASED ASSAY OF NEURONAL PROTEOME

The complete collection of proteins expressed by a cell or organism under specific conditions is called the proteome. When researchers want to inhibit a selected protein in a cell—for diagnostic or therapeutic applications, for example—understanding the inhibitor's efficacy within the complex milieu of the proteome is much more informative than looking at the protein and inhibitor in isolation.

Here, Mario van der Stelt and co-workers use activity-based protein profiling (ABPP) as a powerful tool to demonstrate the selectivity of an inhibitor of diacylglycerol lipase (DAGL), a protein responsible for the biosynthesis of a neuronal signaling lipid (DOI: 10.1021/jacs.5b04883). Even within the complex proteome, the researchers identify a highly potent inhibitor selective for DAGL over other proteins involved in the same and related metabolic pathways.

The authors cover multiple angles of cellular and biochemical activity and selectivity using both specific and general activity-based probes. Ultimately, the inhibitor is shown to be effective in hippocampal tissue slices known to express the DAGL protein. Because DAGL biosynthesizes a signaling lipid implicated in obesity, related metabolic disorders, and neuroinflammation, this inhibitor—the most selective identified to date—could play a role in the development of drugs to treat these diseases, the authors conclude.

Sonja Krane, Ph.D.

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