Reaction-based Fluorescent Probes for Detection of Zinc
Technology #16227

Applications

The technology comprises a new class of reaction-based fluorescent sensors that selectively detect zinc ions in live cells. The invention can be applied to a variety of fluorophore scaffolds including fluorescein, coumarin, resorufin, and benzoresorufin. These probes could be used for applications such as live cell imaging, flow cytometry, and the detection of zinc in biological fluids.

Problem Addressed

Zinc is an essential nutrient. Chelatable or “mobile” forms of zinc can act as signaling agents, the actions of which have been directly implicated in numerous physiological and pathological processes, such as neurotransmission, neurogenesis, cancer, diabetes, and acute inflammation. Understanding the role of mobile zinc in biology requires tools that can be used to visualize and track the changes of mobile zinc levels in diverse cellular and subcellular environments. Unfortunately, most commercially available small-molecule probes for mobile zinc have a narrow dynamic range, adventitious localization, and/or a pH-sensitivity, which limits their utility.

Technology

A zinc-reactive protecting group is added to the sensor scaffold, thereby creating a non-fluorescent sensor precursor. Upon binding of zinc, the ester is hydrolyzed via a zinc-mediated process, resulting in a restoration of fluorescence. This modification increases the dynamic range, reduces the pH-sensitivity of the metal-free state, and improves the efficiency with which the probes can be targeted to intracellular locales by reducing endo/lysosomal entrapment. These probes also offer improved solubility and can be applied to cells at lower probe concentrations than are typical. Furthermore, unlike most reaction-based probes, the zinc-induced fluorescence can be partially reversed in the presence of a chelator.

Advantages

- A significantly improved dynamic range and pH profile
- Resistance to water and esterase-mediated hydrolysis both in vitro and in vivo
- The ability to target subcellular organelles such as mitochondria

Categories For This Invention:

Life Sciences
Diagnostics
Other (Diagnostics)
Markers
Medical Devices
Research Tools
Other (Research Tools)

**Intellectual Property:**
Reaction-based fluorescent probes for detecting zinc
Issued US Patent
9,700,637

**Inventors:**
Stephen Lippard
Robert Radford
Wen Chyan

**Publications:**
 Reaction-based Fluorescent Sensor for Investigating Mobile Zn2+ in Mitochondria of Healthy Versus Cancerous Prostate Cells
Proceedings of the National Academy of Sciences
2014
 Peptide Targeting of Fluorescein-based Sensors to Discrete Intracellular Locales
Chemical Science
2014
 New Sensor Tracks Zinc in Cells
MIT News
December 9, 2013

**External Links:**
Lippard Research Group
http://lippardlab.mit.edu/

**Image Gallery:**

255 Main Street, room NE 18-501
Cambridge, MA 02142-1601
Phone: 617-253-6966 Fax: 617-258-6790
http://tlo.mit.edu
Contact the Technology Manager: tlo-inquiries@mit.edu