

PATENT ASSIGNMENT

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Invention Title: Zinc-Chelating Ratiometric Fluorescent Probes and Related Methods

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Patent or Application Serial No.: 10/887,465

Grant/Contract Number(s): 9810378, DK52627, GM38784

Foreign Applications filed/intended in (countries): _____

The invention identified above is a Subject Invention under **35 U.S.C. 200, et seq.**, and the Standard Patent Rights clause at **37 CFR 401.14, FAR 52.227-11** or **FAR 52.227-12** (if applicable) which are included among the terms of the above identified grant or contract award from the United State Government. This document is confirmatory of:

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Signed this 11th day of August, 2004.

By Indrani Mukharji, PhD
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ZINC-CHELATING RATIO-METRIC FLUORESCENT PROBES AND RELATED METHODS

This application claims priority benefit from provisional patent application no. 60/485,587 filed July 8, 2003, the entirety of which is incorporated herein by reference.

The United States government has certain rights to this invention pursuant to Grant Nos. DK52627 and GM38784 from the National Institutes of Health and the National Science Foundation, respectively, to Northwestern University.

Background of the Invention

Zinc is an essential element in both enzymatic and biological systems, and is physiologically the second most abundant transition metal. The inorganic physiology of intracellular zinc is poorly understood but of emerging importance in understanding a variety of human disorders and disease states. Histochemical studies of mammalian tissues including the prostate, the insulin secreting beta cells of pancreatic islets, and the dentate neurons of the hippocampus reveal patterns of Zn(II) accumulation that are disrupted in some types of prostatic cancer, diabetes and neurodegenerative disorders respectively. The function of zinc in these tissues or even within compartments of single cell organisms such as *S. cerevease* remains controversial.

In order to investigate the functions of such spectroscopically silent metal ions (e.g., Ca^{2+} and Zn^{2+}) in biological systems, fluorescent sensor molecules that respond to a specific metal ion in the excitation or emission spectrum have shown to be useful tools. Several kinds of fluorescence probes for Zn^{2+} that can be used under physiological condition have been reported to date, most of these utilize "on-off" fluorescent signaling system, in which fluorescence intensity increases lineally upon increasing Zn^{2+} concentration. In these cases, however, the determination of the accurate Zn^{2+} concentration in the cells should be impossible because the fluorescence intensity depends on many factors such as the cell