Development of a Zinc Ion-selective Luminescent Lanthanide Chemosensor for Biological Applications

Kazuya Kikuchi, Kenjiro Hanaoka, Kensuke Komatsu, Eri Kawabata, and Tetsuo Nagano

Graduate School of Pharmaceutical Sciences, University of Tokyo, Japan

Zinc (Zn^{2+}) is the second most abundant heavy metal ion after iron in the human body. Zn^{2+} is an essential component of many enzymes, transcription factors and synaptic vesicles in excitatory nerve terminals, and present in serum at a concentration of ~12 μM (total Zn^{2+}). So, detection of chelatable zinc (Zn^{2+}) in biological studies has attracted much attention recently, because chelatable Zn^{2+} plays important roles in many biological systems. Lanthanide complexes (Eu^{3+}, Tb^{3+}, etc.) have excellent spectroscopic properties for biological applications, such as long luminescence lifetimes of the order of milliseconds, a large Stoke's shift of >200 nm and high water-solubility. Herein, we present the design and synthesis of a novel lanthanide sensor molecule, **[Eu-7]**, for detecting Zn^{2+}. This europium (Eu^{3+}) complex employs a quinolyl ligand as both a chromophore and an acceptor for Zn^{2+}. Upon addition of Zn^{2+} to a solution of **[Eu-7]** the luminescence of Eu^{3+} is strongly enhanced, with high selectivity for Zn^{2+} over other biologically relevant metal cations. One of the important advantages of **[Eu-7]** is that this complex can be excited with longer excitation wavelengths (around 340 nm) as compared with previously reported Zn^{2+}-sensitive luminescent lanthanide sensors, whose excitation wavelength is at too high an energy level for biological applications. The usefulness of **[Eu-7]** for monitoring Zn^{2+} changes in living HeLa cells was confirmed with time resolved imaging microscopy. This novel Zn^{2+}-selective luminescent lanthanide chemosensor **[Eu-7]** should be an excellent lead compound for the development of a range of novel luminescent lanthanide chemosensors for biological applications.