Emissive Lanthanide Complexes as Cellular Probes and Diagnostic Agents

Abstract: A series of over 75 lanthanide(III) complexes has been prepared, designed to report on the local environment by modulation of emission spectral form, lifetime or circular polarisation. These responsive complexes have been used for the in vitro analysis of key bioactive species (pH, pO2, urate, lactate, citrate) in various biological fluids and for real time microscopy applications in viable living cells. Their design is based on a mechanistic appreciation of the salient issues in probe design: affinity for the target species, probe localisation and competitive quenching phenomena. A key aspect has been the use of ratiometric methods, analysing the relative intensity of two emission spectral bands, or examining mixtures of Eu and Tb complexes of a common ligand [1,2].

The emission spectral form of Eu(III) complexes is sensitive to changes in the local coordination environment. This can arise from reversible coordination of certain anions to the metal centre in aqueous media. The affinity of the anion for the metal centre can be modulated in several ways including variation of overall complex charge, altering the steric demand at the metal centre, or by the introduction of competitive intramolecular ligation. Complexes have been defined that can signal changes in bicarbonate, lactate and citrate based on this approach [3,4]. For example, citrate analyses of <1μL samples of prostatic or seminal fluid samples have been made and results compared with enzymatic or 1H NMR measurements, allowing correlation of the reduction of citrate with progression of prostate adenocarcinoma.

These emissive complexes may also be used as cellular probes and have been shown by inhibition, promotion and co-staining experiments to enter the cell by macropinocytosis [5]; the probes are trafficked to different cell compartments following protein recognition. It is the constitution and linkage mode of the sensitising moiety that determines the cell uptake profile [1,6]. Use of a pH or bicarbonate responsive probe may allow changes in local pH or [HCO3−] to be followed, in real time, within the mitochondria of living cells by multi-photon microscopy.

References:

Gäste sind herzlich willkommen – Guests are most welcome!

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