Fluorescent sensors to study the interactions of exogenous agents with cells

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The exposure of the cell to exogenous agents, whether from therapy or diet or the environment, has far-reaching consequences on many aspects of cellular homeostasis, including metal ions and redox balance. We are interested in developing molecular imaging tools to understand these interactions. This talk will present progress we have made in the preparation of magnetic resonance (MR) contrast agents and fluorescent sensors to investigate chemical changes in response to external stressors. We have a particular focus on imaging essential and therapeutic metals, and metal-containing nanoparticles within cells using selective fluorescent sensors, and in probing how redox processes are perturbed by these interactions.

Reversible fluorescent sensors enable the imaging of biological systems over time. For the study of redox state in cells, reversibility will enable the monitoring of oxidative bursts in the cell that accompany many essential physiological processes. Utilising flavins as biologically-relevant, reversible redox switches, we have developed cytoplasmic[1] and mitochondrially-localised[2] turn-on fluorescent redox probes, which we have been able to utilise in various biological contexts. In order to minimise probe concentration effects, we have also developed ratiometric probes,[3] which report on oxidative capacity by a change in emission colour rather than intensity (Figure 1). We have demonstrated the applicability of these probes in flow cytometry and fluorescence lifetime imaging microscopy, as well as conventional microscopy experiments. We are also interested in preparing responsive MRI contrast agents that are able to report on their chemical environment *in vivo*. We have developed the first truly off-to-on contrast agents for detecting hypoxia, and have applied these agents to imaging of hypoxic regions of tumour spheroids.[4]

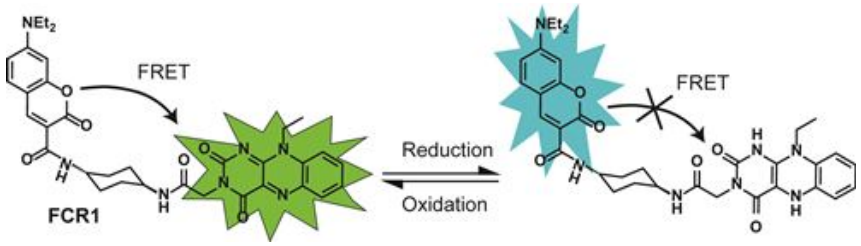

Figure 1: FRET-sensor **FCR1** undergoes a reversible change from green to blue fluorescence upon reduction.

References

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