Title: Illuminating Ligand-Receptor Interactions: New Insights into GPCR Pharmacology using Fluorescent Ligands

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G protein-coupled receptors (GPCRs) represent the largest family of transmembrane signaling proteins in the human genome and are estimated to be the target of approximately 40% of all currently marketed drugs. Using fluorescence as a means to study these important medicinal targets allows entry to a large range of pharmacological techniques that can capture dynamic processes involving unmodified receptors in live cells. As such, many fluorescently labeled agonists or antagonists have now been developed to target numerous GPCRs, and permitted pharmacological measurements to be made down to the single cell and single molecule level.

The major attraction of this approach is that detailed kinetic studies can be undertaken with the receptor in its native environment within the cell membrane. Furthermore the increased resolution and temporal capability of these techniques can also be applied to native cells endogenously expressing the receptor of interest. In this presentation, examples will be given of the development of fluorescent agonists and antagonists for the adenosine A1 and A3 receptors, and the β1- and β2-adrenoceptors as well as the various approaches that can be used to visualise their binding in single living cells. This will be illustrated with quantitative approaches to study ligand-binding properties using high content screening and its application to fragment-based drug discovery.