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## Quantifying the effectiveness of drug delivery systems *in vivo*

The ability of a drug molecule to reach the right protein in the correct intracellular compartment of the target cell type, in the desired tissue following a systemic dose, is governed by a complex network of active and passive transport processes. Furthermore, the same biological mechanisms that ensure on-target exposure are also responsible for the delivery of drug to off-target sites, potentially causing negative outcomes. Understanding the concentration of drug at target (D@T) is therefore one of the three pillars of successful drug discovery. While it is possible to tweak the structure of small molecules to increase their uptake into the target environment, this is often at the cost of decreased potency or metabolic stability. Furthermore, macromolecules (proteins and oligos) have less flexibility in their pharmacophores and are often excluded from biological compartments due to their size and charge. This challenge has given rise to the field of targeted drug delivery strategies, ranging from covalent modification to create pro-drugs to complex formulations to encapsulate the payload molecule and deliver it to the target. Each approach has the potential to effect on and off target exposure and will inevitably add to the cost of the final medicine. Finally, the capability to accurately measure the concentration of a drug molecule at the site of action remains a significant challenge, but is crucial to our ability to select the best molecule and evaluate the added benefit of a delivery system. Methodologies that are able to determine drug location and concentration, while preserving the structure of the surrounding tissue, continue to improve in reproducibility and resolution. This presentation will aim to Clarify targeted vs. enhanced uptake; review the formulation options to improve delivery; explore a way to quantify the value of a given delivery system; outline experimental methods available to measure the location and concentration of drugs in a given tissue; share some of the GSK experiences in this challenging field.

### Biography

Steve Hood completed his PhD in Molecular Toxicology at Surrey University and joined Glaxo Group Research as a Post-Doctoral Fellow in 1993. Following the formation of GlaxoSmithKline (GSK) in 2001, he managed a team determining the drug-drug interaction liabilities while developing ADME strategies for the emerging GSK antibody portfolio. In 2010, he led a cross divisional team charged with understanding and overcoming the delivery issues inherent in GSK's diverse oligonucleotide portfolio while helping to develop these molecules from early discovery to file. In 2011, he initiated a project that has grown into the active IMI academic/industry COMPACT collaboration (http://www.compact-research.org/) and he is actively involved in facilitating the interaction between academia, biotech and large industry partners.

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