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Activating endocytosis for enhancing cellular delivery and modifying intracellular targeting of therapeutics

Targeting disease processes inside cells with biopharmaceuticals represents a major challenge, not least in overcoming biological barriers such as those posed by the plasma membrane and endolysosomal organelles. Investment in this approach is justified when one considers the number individual intracellular targets now available to us as we continue to understand disease processes at the gene, protein and signaling level. This is true for many high-burden diseases such as cancer, infectious diseases and inherited genetic defects such as cystic fibrosis. Our research at Cardiff University is focused on studying endocytosis and specifically on designing methods to analyze individual endocytic pathways to characterize how Drug Delivery Vectors (DDVs) and associated therapeutics bind to and gain access to cells. As vectors, we have paid particular attention to natural ligands, cell penetrating peptides, antibodies and polymer conjugates. We have made significant contributions to the current understanding of the way DDVs interact with cells, enter cells and traffic on endocytic pathways that critically govern their intracellular fate. This lecture consists of work we have performed focusing on technologies and *in vitro* models, we have exploited to study cell binding and endocytosis of DDVs including cell penetrating peptides, exosomes, ligand decorated nanoparticles and antibodies targeting plasma membrane receptors on cancer cells. Mainly highlights will be on how we recently demonstrated that Internalisation of receptors, and associated ligands, can be significantly enhanced through manipulating ligand and receptor association, and how normal endocytic routes can be modified to reach a desired intracellular location. Our involvement in a €30M FP7 Innovative Medicine Initiative (IMI-EFPIA) consortium (COMPACT www.compact-research.org) will also be discussed. This represents public-private collaboration between 14 European academic institutes and pharmaceutical companies aiming to improve the cellular delivery of biopharmaceuticals across major biological barriers of the intestine, lung, blood-brain barrier and skin.

Biography

Arwyn T Jones obtained a PhD in protein-crystallography at Birkbeck College, University of London and undertook postdoctoral endocytosis research at the University of Liverpool, Harvard University, and EMBL-Heidelberg as EMBO and Alexander von Humboldt fellow. Appointed as a lecturer at the Cardiff University School of Pharmacy and Pharmaceutical Sciences in 2001 he is now Professor of Membrane Traffic and Drug Delivery. His research falls within cancer cell biology, endocytosis, and drug delivery. A major objective understands endocytosis to improve the cellular delivery efficiency of drug delivery vectors including peptides, natural and synthetic nanoparticles and antibodies targeting plasma membrane receptors. Recent work has concentrated on strategic approaches to plasma membrane targeting to stimulate endocytosis and intracellular targeting. He has published widely within these fields and his group has made significant contributions to the current understanding of the way drug delivery vectors interact with cells and enter endocytic pathways that govern their intracellular fate.

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