

P008 siRNA inhibition of endocytic pathways for studying cellular uptake of cell penetrating peptides

Al-Soraj M; Watkins C; Jones A T

Welsh School of Pharmacy, Cardiff University, Cardiff, Wales, UK, CF10 3NB

The plasma membrane represents an impermeable barrier for most macromolecules. Peptides classified as cell-penetrating peptides (CPPs), however, efficiently translocate into the cytoplasm either directly across the plasma membrane or through endolysosomal membranes following endocytic uptake. CPPs can also deliver macromolecular cargo thus generating huge interest in their application as delivery vectors for therapeutic macromolecules such as genes and proteins. There is currently little consensus regarding the type of endocytic pathway used by different CPPs, alone or attached to cargo, to gain access to cells as uptake via clathrin vesicles, caveolae and macropinocytosis have been proposed. This knowledge is however, important if we are to maximise their use as drug delivery agents. In this study, we have used siRNA to silence critical endocytic proteins such as clathrin heavy chain and dynamin to inhibit distinct endocytic pathways. We will present functional characterisation of these cells with respects of endocytic capacity of marker ligands such as transferrin and dextran, and assess their capacity to internalise the CPPs octaarginine (R8) and HIV-Tat peptide.