

P040 Organising Nano-sized Gene Delivery Vectors for Targeting the Urokinase Plasminogen Activator Receptor.
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In the engineering of vectors for cancer gene therapy, the Urokinase Plasminogen Activator Receptor (uPAR) appears a suitable receptor for targeting, due to its over-expression in certain tumours. Having shown the high receptor-affinity of the peptide sequence, U11, we propose that the self-insertion of an U11-lipopeptide onto liposomal/ DNA assemblies can render their selectivity for cancer cells.

The lipopeptide was synthesised on solid phase, and incorporated onto the liposomal surface by the method of *post-insertion*. Its secondary structure as part of a liposomal assembly was firstly monitored by circular dichroism, followed by examination of the integrity of targeted systems by aggregation studies in buffered and serum-rich solutions. Transfection and fluorescence microscopy studies were then conducted to examine cell internalisation and subsequent gene delivery.

The conformation of the lipopeptide was found to be in the form of a β -sheet, either alone or part of the liposomal structure. In comparison to non-targeted systems, the targeted vectors were found to resist aggregation in buffer and serum-rich solutions. An important finding includes the 3-fold increase in gene expression of targeted systems, giving indication of receptor-mediated endocytosis. Fluorescence microscopy further suggested an increased rate of internalisation of uPAR-targeted systems by cancer cells.