

Polyplexes and Lipoplexes for mammalian gene delivery: from traditional to Microarray screening

Abstract

Gene therapy requires the development of non-toxic and highly efficient delivery systems for DNA and RNAi. Polycations, especially dendrimers, have shown enormous potential as gene transfer vehicles, displaying minimal toxicity with a broad range of cell lines. In this paper, a total of 13 dendrimers, up to G3.0, were constructed from AB3 type isocyanate monomers using solid phase methodology and evaluated for transfection activity. Among the library of compounds prepared, a G3.0 dendrimer displayed comparable activity to Superfect. Gel retardation assays demonstrated that all of the compounds completely bound plasmid DNA, indicating the efficient formation of complexes between DNA and the dendrimers. A “transfection microarray” approach was developed for screening these compounds as well as a panel of lipoplexes (complexes of DNA with cationic lipids) and polyplexes (complexes of DNA with synthetic polycationic polymers), in 3D solution like micro-assay). Five cationic lipids with a cholesterol tail showed stronger or comparable transfection activity relative to Effectene. The new, micro-array screening method was rapid and miniaturized, offering the potential of high throughput screening of large libraries of transfection candidates, with thousands of library members per array, and the ability to rapidly screen a broad range of cell types.