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The Regulation of Gene Expression in a Breast Cancer Cell Model using Novel Gene Delivery Agents

Adhika Balgobind, Moganavelli Singh and Mario Ariatti
University of KwaZulu-Natal, South Africa

Breast cancer is one of the most common female cancers worldwide and a major cause of cancer death in women. Advances in the understanding of the molecular mechanisms underlying the malignant transformations of breast cancer cells has enabled the possible regulation of the expression of specific genes that are linked to breast cancer. Gene therapy based on small interfering RNA (siRNA) has emerged as an exciting and diverse new therapeutic approach. This molecular tool holds great potential for the treatment of diseases that have until now been considered incurable. However, poor stability and insufficient cellular uptake have limited its usefulness. Therefore, this study focused on the delivery of siRNA to an upregulated breast cancer gene via the use of novel cationic liposomes (non-steric and steric stabilized) which have been synthesized and chemically analyzed. The cholesteryl cytofectin, *N,N*-dimethylaminopropylamidosuccinylcholesterylformylhydrazide (MS09) was synthesized from cholesterol chloroformate. Cationic liposomes were constructed from near equimolar quantities of MS09, dioleoylphosphatidylethanolamine (DOPE) and polyethylene glycol (PEG_{2000}) forming submicron stable unilamellar liposomes. Gel retardation, ethidium displacement and nuclease digestion assays confirmed that siRNA was fully liposome-associated, stable and protected from serum nucleases. Transfection activity of the cationic lipoplexes was determined using the luciferase reporter gene assay and cytotoxicity *in vitro* was evaluated using the cell viability (MTT) assay. Preliminary results suggest that these new cationic liposomal systems have an immense potential to be used for efficient delivery of siRNA therapeutics to bring about silencing of oncogenes associated with breast cancer.