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BV 2010-04 - Coupled to Human UDP-glucuronosyltransferase Genes: Enhanced Tissue and Cellular Delivery of Therapeutic Levels of DNA.

APPLICATION: Accelerated delivery of DNA for control of cancer and other proliferative disorders.

SUMMARY: The utility of gene therapy has not been fully realized because the level of expression of therapeutic DNA in most cases does not meet the thresholds that are required for efficacy. The present invention is a composition of matter which involves targeted nanotubes and genetic elements in combination and novel methods of treating tumor cells. In general this combination of materials has demonstrated enhanced delivery and efficacy of these compositions on target cells.

This invention is a composition comprising a targeting moiety, a nanoparticle delivery material and a UDP-glucuronosyltransferase (UGT) or a DNA vector encoding a UGT. The UGT's catalyze the covalent modification of a variety of bioactive substrates by attaching carbohydrate moieties to them. The most biologically significant substrates of the UGT's are retinoic acid, poly unsaturated fatty acids, prostaglandins, steroids, and steroid hormones. It is recognized that UGT's possess the ability to interfere with the synthesis of lipids through the glucuronidation of these compounds. Thus these enzymes are proposed to play a major role in regulating cancer cell growth. Therefore, more effectively delivered UGT's can play an essential role in growth control of a variety of cell types.

The invention further includes improved methods for delivery of nucleic acids encoding a UGT to a tumor cell using carbon nanotubes. The introduction of UGT genes into cancer cells in a targeted manner using various nanoparticles is a novel and non-obvious invention.

In vitro experiments demonstrate that incubation of carbon nanotube/plasmid particles with pancreatic cancer cells, arrested growth and promoted cell death within 24 hours. *In vivo* models studies are currently being conducted to establish the therapeutic index that is possible with these compositions.