[0005] Recent efforts to increase transfection efficiency and cell viability of differentiated neuron by optimizing protocols using LPEI have met with limited success. Attempts have been made to identify underlying mechanisms limiting high transfection efficiency in non-neuronal cells, primary neurons and neuronal cell-lines. Poor transfection of non-dividing, post-mitotic cells including neuronal cells is often thought to be due to the presumed inability of the pDNA in nuclear translocation. In addition, internalization and intracellular barriers were thought to restrict transfection in differentiated neuronal cell. By increasing uptake, more neuronal cells were found to express transgene, but only marginally (from 2 % to 6 % of total cell population). To date, the goal of attaining high transfection efficiency in differentiated neuron using non-viral carriers remains elusive and efforts to produce even more novel polymers with such properties continues.

[0006] Despite significant improvements in diagnosis and innovations in the treatment for various devastating diseases, such as cancer, autoimmune disease, and neurodegenerative disease, effective treatment of these disorders still presents major challenges. Presently, low transfection and delivery efficiencies limit the application of drug-gene therapeutics. It is this unmet need that requires the development of methods to enhance gene delivery *ex vivo* and *in vivo* and the subsequent development of galenics using this technology.

[0007] Accordingly, it is an aim of the present disclosure to ameliorate the above-mentioned disadvantages and provide an improving transfection efficiency.

SUMMARY ~~OF THE INVENTION~~

[0008] ~~In a first aspect, t~~The present ~~invention~~disclosure provides a composition for transfecting a cell with a genetic material comprising a first agent capable of directing the genetic material away from an acidic compartment in the cell and a second agent capable of stabilizing the microtubule or a network thereof.

[0009] ~~In a second aspect, t~~The present ~~invention~~disclosure also provides a method of delivering a genetic material into a cell comprising the step of administering the genetic material with a composition.

[0010] ~~In a third aspect, t~~The present ~~invention~~disclosure further provides a use of a composition in the manufacture of a medicament for treating a disease, selected from a group consisting of cancer, SMA, bone cancers, leukemia, blood cancers, sickle cell disease, Wiskott-Aldrich Syndrome, HIV, genetic disease, diabetes, cardiac disease and neurodegenerative diseases

[0011] ~~In a fourth aspect, t~~There is provided a composition comprising a first agent, as described herein, and a second agent, as described herein.

[0012] ~~In a fifth aspect, t~~The present ~~invention~~disclosure provides a kit according comprising a composition as described herein and instructions for use.

[0012a] In one aspect, there is provided an in vitro method for enhancing intracellular trafficking of genetic material in a cell, the method comprising:

a) transfecting the cell with the genetic material,

b) adding a first agent and a second agent simultaneously, separately or sequentially to the cell after transfection,

wherein the first agent directs the genetic material away from the acidic compartments in the cell, and wherein the second agent stabilizes the microtubule or a network thereof, wherein the first agent is a lipid and/or peptide fusogenic agent, and wherein the second agent is selected from a group consisting of a histone deacteylase inhibitor (HDACi), a tubulin binding agent (TBA), a siRNA that directly or indirectly affects the microtubule network stability, and combinations thereof.

[0012b] In another aspect, there is provided a method as defined above for use in gene therapy.

BRIEF DESCRIPTION OF THE DRAWINGS

[0013] The invention will be better understood with reference to the detailed description when considered in conjunction with the non-limiting examples and the accompanying drawings, in which:

[0014] **Fig. 1** shows a schematic of the possible effects of TrafEn™. It contains an optimized mix of chemoRe-router that specifically re-directs polyplexes away from the acidic compartment (step 1) and re-routing onto microtubular networks stabilized by the use of chemosensitizers (step 2) (e.g., histone deacetylase inhibitor (HDACi), taxanes). The chemosensitizers synergize with the gene product to achieve beneficial therapeutic effects (step 3). TrafEn™ may also be used to improve intracellular trafficking of therapeutic material.

[0015] **Fig. 2** shows a schematic of the composition of TrafEn™, which contains an optimized mix of chemoRe-router and microtubule targeting chemosensitizer. TrafEn™ is shown to enhance transfection efficiency and synergize\ with the gene product to achieve beneficial therapeutic effects.

[0016] **Fig. 3** shows the effects of a microtubular network modifier. (**A**) shows that microtubule dynamicity is inhibited by tubulin acetylation or tubulin binding agents (TBA). TBA, such as chemotherapeutic taxanes, binds to tubulin while inhibition of HDAC6 and Sirtuin2 prevents deacetylations of microtubules; leading to microtubule stabilization. (**B**) depicts the possible effects of histone deacetylation inhibitors (HDACi). These appear to ease the pathological conditions of heart failure via possible multiple mechanisms, including derepression of protective genes and inhibition of the expression of pro-inflammatory genes. Other non-transcriptional effects of HDACi may include the enhancement of acetylation of sacromeric proteins and the inhibition of pathways for autophagy and apoptosis.

[0017] **Fig. 4** shows a schematic depicting the synergistic effect of TrafEn™ and its use as a novel gene-drug therapy combinatorial therapeutic. As described previously in Fig. 2, the components that make up TrafEn™ are a microtubule targeting chemosensitizer and a