CLAIMS

1. An isolated or synthetic dinucleotide analogue, its salt or ester, comprising one 5-aza-cytosine as a base residue in the sequence of the dinucleotide analogue, wherein the dinucleotide is linked with a phospholinker consisting of one phosphorus and wherein the dinucleotide analogue has a general formula of:

~~a. Z-L-G, or G-L-Z,wherein Z is 5-aza-cytosine; G is guanine; and L is a chemical linker covalently linking Z and G; or~~

~~b.~~ 5'-DpG-3' or 5'GpD-3', wherein D is decitabine; p is a phospholinker; and G is deoxyguanosine.

~~2. The dinucleotide analogue of claim 1 , wherein the oligonucleotide analogue is 5 '-DpG-3 ' or 5 '-GpD-3 ', wherein D is decitabine; p is a phospholinker; and G is deoxyguanosine.~~

~~3. The dinucleotide analogue of claim 1, wherein the dinucleotide analogue has a general formula of: Z-L-G, or G-L-Z, wherein Z is 5-aza-cytosine; G is guanine; and L is a chemical linker covalently linking Z and G.~~

42. The dinucleotide analogue of claim 1, wherein the ~~linker L or a~~ phospholinker p is a sugar phosphorodiester linker.

53. The dinucleotide analogue of claim 1, wherein the ~~linker L or a~~ phospholinker p is a ~~ribose or~~ 2'-deoxyribose phosphorodiester linker.

64. The dinucleotide analogue of claim 1, wherein the ~~linker L or a~~ phospholinker p is a ~~ribose or~~ 2'-deoxyribose phosphorothioate linker.

75. The dinucleotide analogue of claim 1, wherein the ~~linker L or a~~ phospholinker p is a ~~ribose or~~ 2'-deoxyribose boranophosphate linker.

86. The dinucleotide analogue of claim 1, wherein the ~~linker L or a~~ phospholinker p is a ~~ribose or~~ 2'-deoxyribose methylphosphonate linker.

~~9. The dinucleotide analogue of claim 1, wherein the linker L or a phospholinker p is 2'-methoxy ribose phosphorodiester linker.~~

~~10. The dinucleotide analogue of claim 1, wherein the linker L or the phospholinker p is 2'-methoxyethyl ribose phosphorodiester linker.~~

~~11. The dinucleotide analogue of claim 1, wherein the linker L or a phospholinker p is 2'-fluoro ribose phosphorodiester linker.~~

~~12. The dinucleotide analogue of claim 1, wherein the linker L is a protein nucleotide (PNA) backbone.~~

~~13~~7. The dinucleotide analogue of claim 1, wherein the salt is formed with an acid selected from the group consisting of hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, carboxylic, sulfonic, sulfo or phospho acids, acetic acid, propionic acid, glycolic acid, succinic acid, maleic acid, hydroxymaleic acid, methylmaleic acid, fumaric acid, malic acid, tartaric acid, lactic acid, oxalic acid, gluconic acid, glucaric acid, glucuronic acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, salicylic acid, 4-aminosalicylic acid, 2-phenoxybenzoic acid, 2-acetoxybenzoic acid, embonic acid, nicotinic acid, isonicotinic acid, amino acid, glutamic acid, aspartic acid, phenylacetic acid, methanesulfonic acid, ethanesulfonic acid, 2-hydroxyethanesulfonic acid, ethane- 1,2-disulfonic acid, benzenesulfonic acid, 4-methylbenzenesulfonic acid, naphthalene-2-sulfonic acid, naphthalene-l,5-disulfonic acid, 2- or 3-phosphoglycerate, glucose-6-phosphate, N-cyclohexylsulfamic acid, and ascorbic acid.

~~14~~8. The dinucleotide analogue of claim 1, wherein the salt is hydrochloride, mesylate, EDTA, sulfite, L-Aspartate, maleate, phosphate, L-Glutamate, (+)-L-Tartrate, citrate, L-Lactate, succinate, acetate, hexanoate, butyrate, or propionate salt.

~~15~~9. The dinucleotide analogue of claim 1, wherein the salt is a sodium, calcium, lithium, potassium, ammonium, or trialkylammonium salt.

~~16~~10. The dinucleotide analogue of claim ~~15~~9, wherein the trialkylammonium salt is trimethylammonium, triethylammonium or tripropylammonium salt.

~~17. The dinucleotide analogue of claim 1, wherein the hydroxyl group of the 5'- or 3'-terminus of the oligonucleotide analogue is substituted with a non-hydroxyl protecting group.~~

~~18. The dinucleotide analogue of claim 1, wherein the a non-hydroxyl protecting group is selected from the group consisting of dimethoxytritoxyl (DMTr-O), O-methyl (OMe), ethylene glycol, tetraethylene glycol, hexaethylene glycol, and hexaethylene glycol phosphate.~~

~~19~~11. A pharmaceutical composition comprising ~~an~~ dinucleotide analogue of claim 1 or its pharmaceutically acceptable salt or ester, and a pharmaceutically-acceptable carrier.

~~20~~12. The pharmaceutical composition according to claim ~~19~~11, the dinucleotide analogue of claim 1 or its pharmaceutically acceptable salt or ester is in solid form.

~~21~~13. The pharmaceutical composition according to claim ~~19~~11, wherein the pharmaceutically-acceptable carrier is an aqueous solution.

~~22~~14. The pharmaceutical composition according to claim ~~21~~13, wherein the aqueous solution comprises a water miscible non-aqueous solvent selected from the group consisting of ethanol, glycerin, propylene glycol, polyethylene glycol, and combinations thereof.

~~23.~~15 The pharmaceutical composition according to claim ~~1~~911, wherein the pharmaceutically-acceptable carrier is a solution that has less than 40% of water.

~~24~~16. The pharmaceutical composition according to claim ~~1~~911, wherein the pharmaceutically-acceptable carrier is a solution that has less than 5% of water.

~~25~~17. The pharmaceutical composition according to claim ~~24~~16, wherein the pharmaceutically-acceptable carrier is a solution comprising ethanol, glycerin, propylene glycol, polyethylene glycol, or a combination thereof.

~~26~~18. The pharmaceutical composition according to claim ~~1~~911, wherein the pharmaceutically-acceptable carrier is liposome.

~~27~~19. The pharmaceutical composition according to claim ~~26,~~18 wherein the liposome is cationic liposome.

~~28~~20. The pharmaceutical composition according to claim ~~1~~911, wherein the pharmaceutical composition is in a form of emulsion.

~~29~~21. The pharmaceutical composition according to claim ~~1~~911, wherein the emulsion comprises cationic emulsifier.

~~30~~22. A kit, comprising: a first vessel containing ~~an~~ dinucleotide analogue of claim 1 its salt or ester thereof.

~~31~~23. The kit of claim ~~30~~22, further comprising: a second vessel containing a diluent comprising water, glycerin, propylene glycol, polyethylene glycol or combinations thereof.

~~32~~24. The kit of claim ~~31~~23, further comprising: a written instruction describing how to administer the dinucleotide analogue, its salt or ester thereof to a host in need thereof.

~~33~~25. A method for inhibiting DNA methylation in a cell in vitro, comprising: contacting the cell with the dinucleotide analogue, its salt or ester thereof of claim 1, such that DNA methylation activity of the cell is inhibited.

~~34~~26. The method of claim ~~33~~25, wherein the cell resides in a cell culture in vitro.

~~35~~27. The method of claim ~~33~~25, wherein the cell resides in a tissue section in vitro.

3628. The method of claim 3325, wherein the step of contacting includes contacting the cell with a biologically effective amount of the dinucleotide analogue, its salt or ester thereof of claim 1 such that at least 50% of the DNA methylation activity of the cell is inhibited.

3729. Use of a pharmaceutical composition comprising a therapeutically-effective amount of the dinucleotide analogue, its salt or ester thereof of claim 1, and a pharmaceutically-acceptable carrier, in the manufacture of a medicament for treating a disease associated with aberrant DNA methylation.

3830. The use according to claim 3729, wherein the medicaement is to be administered orally, parenterally, topically, intraperitoneally, intravenously, intraarterially, transdermally, sublingually, intramuscularly, rectally, transbuccally, intranasally, liposomally, via inhalation, vaginally, intraoccularly, via local delivery, subcutaneously, intraadiposally, intraarticularly, or intrathecally.

3931. The use according to claim 3729, wherein the medicament is to be administered intravenously.

4032. The use according to claim 3729, wherein the medicament is to be administered subcutaneously.

4133. The use according to claim 3729, wherein a second therapeutic agent is to be administered in combination with the medicament.

4234. The use according to claim 4133, wherein the second therapeutic agent is selected from the group consisting of histone deacetylase inhibitors, antibiotic agents, alkylating agents, retinoids, hormonal agents, plant-derived agents, biologic agents, interleukins, interferons, cytokines, immuno-modulating agents, and monoclonal antibodies.

4335. The use according to claim 4234, wherein the histone deacetylase inhibitor is selected from the group consisting of trichostatin A, suberoylanilide hydroxamic acid, oxamflatin, suberic bishydroxamic acid, m-carboxy-cinnamic acid bishydroxamic acid, pyroxamide, trapoxin A, apicidin, depsipeptide, N-(2-amimophenyl)-4-[N-(pyridin-3-ylmethoxycarbonyl)aminomethyl] benzamide, butyric acid, phenylbutyrate and arginine butyrate.

4436. The use according to claim 3729, wherein the disease associated with aberrant DNA methylation is selected from the group consisting of hematological disorders, benign tumor and cancer.

45 37. The use according to claim 4436, wherein the hematological disorder is selected from the group consisting of acute myeloid leukemia, acute promyelocyte leukemia, acute lymphoblastic leukemia, chronic myelogenous leukemia, myelodysplastic syndromes, and sickle cell anemia.

4638. The use according to claim 4436, wherein the cancer is selected from group consisting of breast cancer, skin cancer, bone cancer, prostate cancer, liver cancer, lung cancer, non-small cell lung cancer, brain cancer, cancer of the larynx, gall bladder, pancreas, rectum, parathyroid, thyroid, adrenal, neural tissue, head and neck, colon, stomach, bronchi, and kidney cancer, basal cell carcinoma, squamous cell carcinoma of both ulcerating and papillary type, metastatic skin carcinoma, osteo sarcoma, Ewing's sarcoma, veticulum cell sarcoma, myeloma, giant cell tumor, small-cell lung tumor, gallstones, islet cell tumor, primary brain tumor, acute and chronic lymphocytic and granulocytic tumors, hairy-cell tumor, adenoma, hyperplasia, medullary carcinoma, pheochromocytoma, mucosal neuronms, intestinal ganglioneuromas, hyperplastic corneal nerve tumor, marfanoid habitus tumor, Wilm's tumor, seminoma, ovarian tumor, leiomyomater tumor, cervical dysplasia and in situ carcinoma, neuroblastoma, retinoblastoma, soft tissue sarcoma, malignant carcinoid, topical skin lesion, mycosis fungoide, rhabdomyosarcoma, Kaposi's sarcoma, osteogenic sarcoma, malignant hypercalcemia, renal cell tumor, polycythemia vera, adenocarcinoma, glioblastoma multiforma, leukemias, lymphomas, malignant melanomas, and epidermoid carcinomas.

4739. The dinucleotide analogue of claim 1, wherein the dinucleotide analogue is 5'-DpG-3', wherein D is decitabine; p is a phospholinker; and G is deoxyguanosine.