CLAIMS

1. A method of treating a patient with a tumor, comprising:

administering, to the patient, a substance which activates cytoplasmatic sensors for intracellular pathogen in the tumor; and

treating the tumor with intra-tumoral alpha-emitter radiotherapy within two weeks of administering the substance which activates cytoplasmatic sensors for intracellular pathogen in the tumor.

2. The method of claim 1, wherein administering the substance comprises administering an agent which induces production within the cell of molecules, which stimulate cytoplasmatic sensors for an intracellular pathogen.

3. The method of claim 2, wherein administering the agent comprises administering a DNA methyltransferase (DNMT) inhibitor.

4. The method of claim 3, wherein administering the DNA methyltransferase (DNMT) inhibitor comprises administering Decitabine.

5. The method of claim 3, wherein administering the DNA methyltransferase (DNMT) inhibitor comprises administering Azacytidine.

6. The method of claim 3, wherein administering the DNA methyltransferase (DNMT) inhibitor comprises administering Guadecitabine.

7. The method of claim 2, wherein administering the agent comprises administering a histone deacetylase (HDAC) inhibitor.

8. The method of claim 7, wherein administering the histone deacetylase (HDAC) inhibitor comprises administering Entinostat.

9. The method of claim 7, wherein administering the histone deacetylase (HDAC) inhibitor comprises administering vorinostat.

10. The method of claim 1, wherein administering the substance comprises administering a pathogen mimic with a delivery agent suitable for cytoplasmic delivery of the pathogen mimic.

11. The method of claim 10, wherein administering the pathogen mimic together with a delivery agent comprises administering a single dose of the intracellular pathogen mimic in a single session.

~~12. The method of claim 10, wherein administering the pathogen mimic together with a delivery agent comprises administering at least three doses of the intracellular pathogen mimic in respective separate sessions.~~

~~13. The method of any of claims 1-12, wherein administering the substance comprises administering the substance with a delivery agent suitable for targeted delivery.~~

~~14. The method of claim 13, wherein the delivery agent comprises a lipid based delivery agent.~~

~~15. The method of claim 13, wherein the delivery agent comprises a polymer based delivery agent.~~

~~16. The method of claim 13, wherein the delivery agent comprises a cationic polymer complex or a cationic lipid.~~

~~17. The method of claim 13, wherein the delivery agent comprises a liposome or a lipoplex.~~

~~18. The method of claim 13, wherein the delivery agent comprises a polymeric micelles.~~

~~19. The method of claim 13, wherein the delivery agent comprises a dendrimer.~~

~~20. The method of claim 13, wherein the delivery agent comprises a solid nanoparticle.~~

~~21. The method of claim 20, wherein the delivery agent comprises a solid lipid nanoparticle or a solid polymeric nanoparticle.~~

~~22. The method of claim 13, wherein the delivery agent comprises a metal-based nanoparticle system.~~

~~23. The method of claim 13, wherein the delivery agent comprises polyethylenimine (PEI).~~

~~24. The method of claim 13, wherein administering the pathogen mimic comprises administering a bacteria mimic~~.

~~25. The method of claim 13, wherein administering the pathogen mimic comprises administering a viral mimic~~.

~~26. The method of claim 25, wherein administering the viral mimic comprises administering double stranded RNA (dsRNA).~~

~~27. The method of claim 26, wherein administering the dsRNA comprises administering polyIC.~~

~~28. The method of claim 27, wherein the delivery agent comprises polyethylenimine (PEI).~~

~~29. The method of claim 28, wherein administering the viral mimic comprises administering BO-112.~~

~~30. The method of claim 26, wherein administering the dsRNA comprises administering 5' ppp-dsRNA.~~

~~31. The method of claim 26, wherein administering the dsRNA comprises administering 3p-hpRNA.~~

~~32. The method of claim 26, wherein administering the dsRNA comprises administering Poly(dA:dT).~~

~~33. The method of claim 26, wherein administering the dsRNA comprises administering poly-ICLC.~~

~~34. The method of claim 26, wherein administering the dsRNA comprises administering poly(A:U).~~

~~35. The method of claim 26, wherein administering the dsRNA comprises administering CpG rich RNA.~~

~~36. The method of claim 13, wherein administering the pathogen mimic comprises administering a pathogen mimic that is recognized by intracellular receptors as non-self.~~

~~37. The method of any of claims 1-12, wherein administering the substance which activates cytoplasmatic sensors for intracellular pathogen comprises administering a plurality of different substances which activate cytoplasmatic sensors for intracellular pathogen.~~

~~38. The method of claim 37, wherein administering a plurality of different substances which activate cytoplasmatic sensors for intracellular pathogen comprises administering a first agent which induces production within the cell of molecules, which stimulate cytoplasmatic sensors for an intracellular pathogen and a second agent comprising a pathogen mimic with a delivery agent suitable for cytoplasmic delivery of the pathogen mimic~~.

~~39. The method of claim 38, further comprising additionally administering to the patient a supportive treatment of cyclophosphamide.~~

~~40. The method of any of claims 1-12, wherein treating the tumor with alpha-emitter radiotherapy comprises inserting a brachytherapy source carrying alpha-emitting radionuclides into the tumor.~~

41. The method of claim 40, wherein the brachytherapy source releases alpha-emitting radionuclides at a rate of less than 25% of the alpha-emitting radionuclides on the source when inserted to the tumor, per day.

42. The method of claim 40, wherein the brachytherapy source comprises a Radium source.

43. The method of any of claims 1-12, wherein treating the tumor with alpha-emitter radiotherapy is performed only after completing the administering of the substance.

44. The method of any of claims 1-12, wherein administering the substance comprises administering with nanoghosts, which direct the substance to the tumor.

45. The method of any of claims 1-12, wherein administering the substance comprises administering one or more substances in at least two separate sessions separated from each other by at least 12 hours.

46. The method of claim 45, wherein administering the one or more substances comprises administering in at least three separate sessions separated from each other by at least 20 hours.

47. The method of any of claims 1-12, and comprising identifying a primary tumor in the patient and wherein administering the substance comprises administering the substance to the identified primary tumor.

48. The method of any of claims 1-12, wherein treating the tumor with alpha-emitter radiotherapy comprises treating with alpha-emitter radiotherapy less than 80 hours after administering a last dose of the substance.

49. The method of any of claims 1-12, wherein treating the tumor with alpha-emitter radiotherapy comprises treating with alpha-emitter radiotherapy less than 60 hours after administering a last dose of the substance.

50. The method of any of claims 1-12, wherein treating the tumor with alpha-emitter radiotherapy comprises treating with alpha-emitter radiotherapy at least 12 hours after administering a last dose of the substance.

51. The method of any of claims 1-12, wherein treating the tumor with alpha-emitter radiotherapy comprises treating with alpha-emitter radiotherapy at least 24 hours after administering a last dose of the substance.

52. The method of any of claims 1-12 further comprising additionally administering to the patient a supportive treatment which counters accelerated tissue repair induced by the alpha-emitter radiotherapy.

~~53. The method of any of claims 1-12 further comprising additionally administering to the patient a supportive treatment which downregulates inflammation.~~

~~54. The method of any of claims 1-12 further comprising additionally administering to the patient a supportive treatment which downregulates checkpoint expression.~~

~~55. The method of any of claims 1-12 further comprising additionally administering to the patient a supportive treatment of cyclophosphamide.~~

~~56. The method of any of claims 1-12 further comprising additionally administering to the patient a supportive treatment of pomalidomide.~~

~~57. The method of any of claims 1-12 further comprising additionally administering to the patient a supportive treatment of berzosertib.~~

~~58. The method of any of claims 1-12 further comprising additionally administering to the patient a supportive treatment of a checkpoint blockade.~~

~~59. The method of claim 58, further comprising additionally administering to the patient a supportive treatment of anti PD-1.~~

~~60. The method of claim 58, further comprising additionally administering to the patient a supportive treatment of anti-PD-L1.~~

~~61. The method of claim 58, further comprising additionally administering to the patient a supportive treatment of anti-CTLA4.~~

~~62. The method of claim 58, further comprising additionally administering to the patient a supportive treatment of one or more TLR agonists.~~

~~63. The method of claim 58, further comprising additionally administering to the patient a supportive treatment of one or more MSDCs inhibitors.~~

~~64. The method of claim 58, further comprising additionally administering to the patient a supportive treatment of one or more Tregs inhibitors.~~

~~65. The method of claim 58, further comprising additionally administering to the patient a supportive treatment of one or more DNA repair inhibitors.~~

~~66. The method of claim 58, further comprising additionally administering to the patient a supportive treatment of one or more Antiangiogenic factors.~~

~~67. The method of any of claims 1-12, further comprising performing surgery to remove the tumor, at least a week after beginning treating the tumor with alpha-emitter radiotherapy.~~

68. The method of any of claims 1-12, wherein treating the tumor with intra-tumoral alpha-emitter radiotherapy comprises treating the tumor with intra-tumoral alpha-emitter radiotherapy less than a week after administering the substance which activates cytoplasmatic sensors for intracellular pathogen in the tumor.

69. A kit for treatment of a patient, comprising:

at least one source for being at least partially introduced into a body of a subject, having alpha-emitting atoms mounted thereon;

at least one substance which activates cytoplasmatic sensors for intracellular pathogen; and

a sterile package containing the at least one source and the at least one substance.

70. The kit of claim 69, wherein the alpha-emitting atoms are mounted on the source in a manner which allows controllable release of the alpha-emitting atoms or their daughter radionuclides from the source.

71. The kit of claim 69, wherein the alpha-emitting atoms comprise radium atoms.

72. The kit of any of claims 69-71, wherein the at least one substance comprises a DNA methyltransferase (DNMT) inhibitor.

73. The kit of claim 72, wherein the DNA methyltransferase (DNMT) inhibitor comprises Decitabine.

74. The kit of claim 72, wherein the at least one substance further comprises a pathogen mimic with a delivery agent suitable for cytoplasmic delivery of the pathogen mimic.

75. The kit of any of claims 69-71, wherein the at least one substance comprises a pathogen mimic with a delivery agent suitable for cytoplasmic delivery of the pathogen mimic.

76. The kit of any of claims 69-71, further comprising in the sterile package, a supportive treatment drug which counters accelerated tissue repair induced by the alpha-emitter radiotherapy.

77. The kit of claim 76, wherein the supportive treatment drug comprises a drug which downregulates inflammation.

78. The use of polyIC^{PEI} in the production of a medicament for administering to a tumor of a patient wherein the administration pattern of the medicament comprises administering a therapeutically effective amount of polyIC^{PEI} to the tumor, in one or more sessions, followed by treating the tumor with intra-tumoral alpha-emitter radiotherapy less than a week after administering the polyIC^{PEI}.

~~79. The use of a DNA methyltransferase (DNMT) inhibitor in the production of a medicament for administering to a tumor of a patient wherein the administration pattern of the medicament comprises administering a therapeutically effective amount of the DNMT inhibitor.~~

CLAIMS

1. Use of a substance including an RNA pathogen mimic with a delivery agent comprising polyethylenimine (PEI), in the manufacture of a medicament for the treatment of a tumor of a patient, wherein the administration pattern of the medicament comprises administration of a therapeutically effective amount of the substance to the patient, in one or more sessions, followed by treatment of the tumor with intra-tumoral alpha-emitter radiotherapy less than two weeks after administration of the substance, and at least 12 hours after administration of a last dose of the substance.

2. The use of claim 1, wherein the substance comprises polyIC with polyethylenimine (PEI).

3. The use of claim 1, wherein the substance comprises poly-ICLC.

4. The use of claim 1, wherein the substance comprises an oncolytic virus.

5. The use of claim 1, wherein the substance comprises BO-112.

6. The use of any one of claims 1-5, wherein the administration pattern of the medicament further comprises administration of a supportive treatment drug for checkpoint inhibition.

7. The use of claim 6, wherein the supportive treatment drug comprises a checkpoint blockade.

8. The use of any one of claims 1-7, wherein the intra-tumoral alpha-emitter radiotherapy is provided by a source carrying radium atoms.

9. The use of any one of claims 1-8, wherein the intra-tumoral alpha-emitter radiotherapy is provided by a source carrying alpha-emitting atoms mounted on the source in a manner which allows controllable release of the alpha-emitting atoms or their daughter radionuclides from the source.