bypasses the BBB. Therapeutic agents can be delivered into the brain with a minimum of the toxicity, therefore, as well as to normal tissue and to organs commonly accessed by systemic delivery.

SUMMARY

[0009a] In one aspect, there is provided use of a composition for imaging a brain tumor in a subject, wherein the composition comprises a plurality of intact, bacterially derived minicells and wherein: (a) each minicell comprises (i) an antibody that specifically recognizes a tumor cell antigen and (ii) an imaging agent, and (b) the brain tumor has blood vessels with fenestrations in the vessel walls through which the minicells can extravasate passively.

[0010] In view of the drawbacks affecting conventional approaches in this area, a method is provided for administering systemically a therapeutically effective amount of a composition comprised of a plurality of intact, bacterially derived minicells, where each minicell of the plurality encompasses an anti-neoplastic agent. By the same token, the present description contemplates the use of such composition for manufacture of a medicament for the treatment of a brain tumor. The plurality can include at least about 10^8 minicells, including but not limited to at least about 10^{10} minicells. Also, a composition as described here can contain less than about 10 EU free endotoxin and/or at most 1 parent bacterial cell per 10^8 minicells, *e.g.*, per 10^{10} minicells..

[0011] The anti-neoplastic agent encompassed by the minicells can be a radionuclide, for example, such as yttrium-90, technetium-99m, iodine-123, iodine-131, rubidium-82, thallium-201, gallium-67, fluorine-18, xenon-133, or indium-111, which can be attached to a protein or a carbohydrate on the surface of the minicells, or it can be attached on the surface of the tumor targeting ligand attached on the surface of the minicells. In this context, the composition can contain, for instance, between about 30 Gy to about 100 Gy radioactivity. The anti-neoplastic agent also can be a chemotherapy drug, where, for example, the composition contains at most about 1 mg thereof. Moreover, the anti-neoplastic agent can be a functional nucleic acid or a polynucleotide encoding a functional nucleic acid. Thus, the functional nucleic acid can inhibit a gene that promotes tumor cell proliferation, angiogenesis or resistance to chemotherapy and/or that inhibits apoptosis or cell cycle arrest. Illustrative of

Claims

1. Use of a composition for imaging a brain tumor in a subject, wherein the composition comprises a plurality of intact, bacterially derived minicells and wherein:

(a) each minicell comprises (i) an antibody that specifically recognizes a tumor cell antigen and (ii) an imaging agent, and

(b) the brain tumor has blood vessels with fenestrations in the vessel walls through which the minicells can extravasate passively.

2. The use of claim 1, wherein the plurality includes at least 10^8 minicells.

3. The use of claim 2, wherein the plurality includes at least 10^{10} minicells.

4. The use of any one of claims 1-3, wherein the composition comprises less than 10 endotoxin units (EU) free endotoxin.

5. The use of any one of claims 1-4, wherein the composition comprises at most 1 parent bacterial cell per 10^8 minicells.

6. The use of any one of claims 1-5, wherein the imaging agent is a radionuclide.

7. The use of claim 6, wherein the radionuclide is selected from yttrium-90, technetium-99m, iodine-123, iodine-131, rubidium-82, thallium-201, gallium-67, fluorine-18, xenon-133, and indium-111.

8. The use of claim 6 or 7, wherein the radionuclide is attached to a protein or a carbohydrate on the surface of the minicells.

9. The use of claim 6 or 7, wherein the radionuclide is attached to a bispecific antibody that is associated with the surface of the minicells.

10. The use of any one of claims 6 to 9, wherein the composition which comprises 30 Gy to 100 Gy radioactivity.

11. The use of any one of claims 1 to 10, wherein the imaging is performed by single-photon emission computed tomography (SPECT).

12. The use of any one of claims 1-11, wherein the brain tumor is selected from the group consisting of glioblastoma, astrocytic tumor, oligodendroglial tumor, ependymoma, craniopharyngioma, pituitary tumor, primary lymphoma of the brain, pineal gland tumor, primary germ cell tumor of the brain, and combinations thereof.

13. The use of claim 12, wherein the brain tumor is a metastatic brain tumor.

14. The use of claim 12, wherein the brain tumor is glioblastoma.

15. The use of claim 1 or 12, wherein the tumor is a stage II, III, or IV tumor.

16. The use of claim 1 or 12, wherein the tumor is a stage III or IV tumor.

17. The use of claim 1 or 12, wherein angiogenesis has initiated in the tumor.

18. The use of claim 1 or 12, wherein vascularization has initiated in the tumor.

19. The use of claim 1, wherein the minicells are derived from *S. typhimurium* or *E. coli* bacteria.

20. The use of claim 1, wherein the antibody is a bi-specific antibody.

21. The use of claim 1, wherein the tumor cell antigen is EGFR.