What is claimed:

1. A hemoglobin-based oxygen carrier pharmaceutical composition configured to target a receptor expressed on the surface of cancer cells within a mass of cancerous tissue or tumors such that the hemoglobin-based oxygen carrier pharmaceutical composition triggers a receptor-mediated mechanism to facilitate the uptake and localization of the hemoglobin-based oxygen carrier into the cancer cells within the mass of the cancerous tissues or tumor for inducing apoptosis in cells of said cancerous tissues or tumors including self-renewing and tumor-initiating cells to prevent cancer recurrence, providing oxidative stress or shock to said cancerous tissues or tumors, and sensitizing the cancerous tissues or tumors to a chemotherapeutic or radiotherapy concurrently or subsequently administered.

2. The pharmaceutical composition of claim 1 further comprising a chemotherapeutic agent which is chemically conjugated with the hemoglobin-based oxygen carrier for synergistically targeting the cancerous tissues or tumors and the cancerous tumor cells including the self-renewing and tumor initiating cells.

3. The pharmaceutical composition of claim 1, wherein said chemotherapeutic agent is selected from 5-fluorouracil, Bortezomib, doxorubicin, cisplatin, or any combination thereof.

4. The pharmaceutical composition of claim 1, wherein said hemoglobin-based oxygen carrier is selected from a heat stable cross-linked tetrameric hemoglobin, a polymerized hemoglobin, or a modified hemoglobin molecule with an undetectable amount of dimer concentration and low concentration of met-hemoglobin.

5. The pharmaceutical composition of claim 1, wherein said receptor-mediated mechanism is Clathrin-mediated endocytosis.

6. The pharmaceutical composition of claim 1 is administered to a subject in need thereof prior to disruption of blood supply and/or during re-establishment of blood supply in a surgical removal of a tumor from said subject.

7. The pharmaceutical composition of claim 6 is administered in a range of approximately 0.2g/kg- 1.2g/kg body weight of said subject.

8. The pharmaceutical composition of claim 1, wherein said cancerous tissues or tumors comprise hepatic, mammary, brain, colon, lung, head and neck, nasopharyngeal, and leukemia.

9. The pharmaceutical composition of claim 1, wherein said cancerous tissues or tumors are hypoxic.

10. The pharmaceutical composition of claim 4, wherein said cross-linked tetrameric hemoglobin has a molecular weight of 60-70kDa and is heat treated with the addition of N-acetyl cysteine at a concentration of 0.05-0.4%.

11. The pharmaceutical composition of claim 4 is free of vasoconstricting impurities and protein impurities, non-pyrogenic, endotoxin-free, phospholipid-free, stroma-free and a met-hemoglobin level of less than 5%.

12. The pharmaceutical composition of claim 1, wherein said hemoglobin-based oxygen carrier is modified having a longer half life to penetrate into the mass of said cancerous tissues or tumors and to provide oxidative stress or shock to said cancerous tissues or tumors such that apoptosis in cells of said cancerous tissues or tumors including said self-renewing and tumor-initiating cells is induced.

13. The pharmaceutical composition of claim 1, wherein said self-renewing and tumor-initiating cells are cancer stem cells and/or progenitor cells.

14. The pharmaceutical composition of claim 12, wherein said hemoglobin-based oxygen carrier is administered alone or in combination with at least one chemotherapeutic agent and/or radiotherapy, and wherein said hemoglobin-based oxygen carrier is administered as an adjunctive therapy.

15. The pharmaceutical composition of claim 4, wherein said modified hemoglobin molecule is pegylated hemoglobin molecule.

16. Use of a hemoglobin-based oxygen carrier in preparation of a pharmaceutical composition for treating cancerous tissues and preventing recurrence of cancerous tumors, wherein said composition is administered alone or in combination with at least one chemotherapeutic agent to a subject in need thereof.

17. The use of claim 16, wherein said composition is administered to said subject during or after removal of cancerous tissues or tumors.

18. The use of claim 16, wherein the cancerous tissues or tumors are hepatic, nasopharyngeal, brain, colon, lung, head and neck, mammary and leukemia.

19. The use of claim 16, wherein the cancerous tissues or tumor are hypoxic.

20. The use of claim 16, wherein said hemoglobin-based oxygen carrier is cross-linked tetrameric hemoglobin having a molecular weight of 60-70kDa and is heat stable after heat treatment and addition of N-acetyl cysteine at a concentration of 0.05-0.4%.

21. The use of claim 20, wherein said composition is free of vasoconstricting impurities and protein impurities, non-pyrogenic, endotoxin-free, phospholipid-free, stroma-free and a met-hemoglobin level of less than 5% after said heat treatment and reaction with the added N-acetyl cysteine.

22. The use of claim 16, wherein said composition is administered by infusion in a range of approximately 0.2-1.2g/kg body weight and at a rate of less than 10ml/hour/kg body weight.

23. The use of claim 16, wherein said at least one chemotherapeutic agent is selected from 5-fluorouracil, Bortezomib, doxorubicin, cisplatin, or any combination thereof.

24. The use of claim 16, wherein said combination of the hemoglobin-based oxygen carrier and at least one chemotherapeutic agent are configured to synergistically target cells with expression of a receptor in said cancerous tissues or tumors, triggering a receptor-mediated mechanism, thereby sensitizing the cells in the cancerous tissues or tumors such that more hemoglobin-based oxygen carriers and chemotherapeutic agent are selectively taken up by the cells and localized in the cytoplasm of the cells while said cells become more sensitive to said chemotherapeutic agent.

25. The use of claim 16, wherein said hemoglobin-based oxygen carrier is administered as an adjunctive therapy with said at least one chemotherapeutic agent for providing oxidative stress or shock to a mass of the cancerous tissues or tumors and for sensitizing said cancerous tissues or tumors to said chemotherapeutic agent such that apoptosis of cells in said cancerous tissues or tumors including self-renewing and tumor-initiating cells is induced.

26. The use of claim 25, wherein said self-renewing and tumor-initiating cells are cancer stem cells and/or cancerous progenitor cells.

27. The use of claim 16, wherein said cancerous tissues or tumors comprise hepatic, mammary, brain, colon, lung, head and neck, nasopharyngeal, and leukemia.

28. The use of claim 24, wherein said receptor-mediated mechanism is Clathrin-mediated endocytosis.

Claims

1. A method for reducing recurrence of cancerous tumors and minimizing local and distant metastasis comprising administering a composition comprising a hemoglobin-based oxygen carrier at a concentration of 9.5 to 10.5 g/dL in combination with at least one chemotherapeutic agent or radiotherapy to facilitate uptake and localization of the hemoglobin-based oxygen carrier into cancer cells within a mass of cancerous tissues or tumors for inducing apoptosis in cells of said cancerous tissues or tumors including self-renewing and tumor-initiating cells, providing oxidative stress or shock to said cancerous tissues or tumors, and sensitizing the cancerous tissues or tumors to the at least one chemotherapeutic agent or radiotherapy, said composition being either administered to a subject in need thereof concurrently with or subsequently to the at least one chemotherapeutic agent.

2. The method of claim 1, wherein said composition is administered to said subject during or after removal of the cancerous tissues or tumors.

3. The method of claim 1, wherein the cancerous tissues or tumors are hypoxic.

4. The method of claim 3, wherein the hypoxic cancerous tissues or tumors comprise hepatic, nasopharyngeal, brain, colon, lung, head and neck, mammary and leukemia.

5. The method of claim 1, wherein said hemoglobin-based oxygen carrier is selected from modified or recombinant hemoglobin molecule which is either chemically conjugated with or surface modified with at least one compound.

6. The method of claim 5, wherein said hemoglobin-based oxygen carrier is cross-linked tetrameric hemoglobin having a molecular weight of 60-70 kDa and is heat stable after heat treatment and addition of N-acetyl cysteine at a concentration of 0.05-0.4% and said at least one compound is the chemotherapeutic agent.

7. The method of claim 6, wherein said composition is non-pyrogenic, endotoxin-free, phospholipid-free, stroma-free and has a met-hemoglobin level of less than 5% after said heat treatment and reaction with the added N-acetyl cysteine.

8. The method of claim 1, wherein said composition is administered by infusion or intravenous injection of the hemoglobin-based oxygen carrier in a range of approximately 0.2-1.2 g/kg body weight of the subject.

9. The method of claim 1, wherein said at least one chemotherapeutic agent is selected from 5-fluorouracil, doxorubicin, cisplatin, or any combination thereof.

10. The method of claim 1, wherein said hemoglobin-based oxygen carrier and at least one chemotherapeutic agent are administered concurrently to synergistically target cells with expression of a receptor in said cancerous tissues or tumors, thereby triggering a receptor-mediated mechanism, and sensitizing the cells in the cancerous tissues or tumors such that more hemoglobin-based oxygen carriers and chemotherapeutic agent are selectively taken up by the cells and localized in the cytoplasm of the cells while said cells become more sensitive to said chemotherapeutic agent.

11. The method of claim 1, wherein said hemoglobin-based oxygen carrier is administered to said subject as an adjunctive therapy subsequently to said at least one chemotherapeutic agent for providing oxidative stress or shock to a mass of the cancerous tissues or tumors and for sensitizing said cancerous tissues or tumors to said chemotherapeutic agent such that apoptosis of cells in said cancerous tissues or tumors including self-renewing and tumor-initiating cells is induced.

12. The method of claim 1, wherein said self-renewing and tumor-initiating cells comprise cancer stem cells and/or cancerous progenitor cells.

13. The method of claim 10, wherein said receptor-mediated mechanism is Clathrin-mediated endocytosis or said receptor is Clathrin.

14. The method of claim 5, wherein said at least one compound is poly(ethylene) glycol.

15. The method of claim 10, wherein said hemoglobin-based oxygen carrier is chemically conjugated with the chemotherapeutic agent in order to have the synergic effects on cancerous tissues or tumors.

16. The method of claim 3, wherein said hemoglobin-based oxygen carrier inhibits expression of hypoxic response elements comprising HIF1α, VEGF, ET1, and VHL in the hypoxic cancerous tissues or tumor.