10^9, more particularly from about 10^6 to about 10^8, most particularly from about 10^6 to about 10^7 colony forming units (CFU).

[0033] In particular embodiments, the attenuated mutant strain of Salmonella is for use in personalized cancer immunotherapy comprising the step of assessing the tumor antigen expression pattern and/or stroma antigen expression pattern of a patient.

[0033a] In one aspect, the present invention relates to an attenuated mutant strain of Salmonella comprising at least one copy of a recombinant DNA molecule comprising a eukaryotic expression cassette encoding Wilms' Tumor Protein (WT1).

[0033b] In one aspect, the present invention relates to the use of an attenuated mutant strain of Salmonella as described herein, in the manufacture of a vaccine.

DETAILED DESCRIPTION OF THE INVENTION

[0034] The present invention may be understood more readily by reference to the following detailed description of the invention and the examples included therein.

[0035] In one aspect, the present invention relates to an attenuated mutant strain of Salmonella comprising at least one copy of a recombinant DNA molecule comprising an expression cassette encoding Wilms' Tumor Protein (WT1).

[0036] According to the invention, the attenuated Salmonella strain functions as the bacterial carrier of the recombinant DNA molecule comprising an expression cassette encoding Wilms' Tumor Protein (WT1) for the delivery of said recombinant DNA molecule into a target cell.

[0037] In the context of the present invention, the term "attenuated" refers to a bacterial strain of reduced virulence compared to the parental bacterial strain, not harboring the attenuating mutation. Attenuated bacterial strains have preferably lost their virulence but retained their ability to induce protective immunity. Attenuation can be accomplished by deletion of various genes, including virulence, regulatory, and metabolic genes. Attenuated bacteria may be found naturally or they may be

CLAIMS

1. An attenuated mutant strain of Salmonella comprising at least one copy of a recombinant DNA molecule comprising an expression cassette encoding Wilms' Tumor Protein (WT1).

2. The attenuated mutant strain of Salmonella of claim 1, wherein the attenuated mutant strain of Salmonella is of the species Salmonella enterica, particularly wherein the attenuated mutant strain of Salmonella is Salmonella typhi Ty21a.

3. The attenuated mutant strain of Salmonella of claim 1 or 2, wherein the expression cassette is a eukaryotic expression cassette.

4. The attenuated mutant strain of Salmonella of any one of claims 1 to 3, wherein WT1 is selected from the group consisting of human WT1 and a protein that shares at least 80% sequence identity therewith, particularly wherein WT1 is truncated, more particularly wherein the zinc finger domain of WT1 is deleted, most particularly wherein the truncated WT1 has the amino acid sequence as found in SEQ ID NO 1.

5. The attenuated mutant strain of Salmonella of claim 3 or 4, wherein the recombinant DNA molecule comprises the kanamycin antibiotic resistance gene, the pMB1 ori, and a eukaryotic expression cassette encoding human WT1 or a protein that shares at least 80% sequence identity therewith, particularly truncated human WT1, under the control of a CMV promoter.

6. The attenuated mutant strain of Salmonella of any one of claims 1 to 5 for use as a medicament.

7. The attenuated mutant strain of Salmonella of claim 6 for use as a vaccine.

8. The attenuated mutant strain of Salmonella of claim 7 for use in cancer immunotherapy.

9. The attenuated mutant strain of Salmonella of claim 8, wherein cancer immunotherapy further comprises administration of one or more further attenuated mutant strain(s) of Salmonella comprising at least one copy of a recombinant DNA molecule comprising an expression cassette encoding a tumor antigen and/or a tumor stroma antigen, particularly wherein said one or more further attenuated mutant strain(s) of Salmonella is/are Salmonella typhi Ty21a comprising a eukaryotic expression cassette, more particularly wherein said one or more further attenuated mutant strain(s) of Salmonella comprise(s) an attenuated mutant strain of Salmonella encoding human VEGFR-2, more particularly wherein said one or more further attenuated mutant strain(s) of Salmonella comprise(s) the attenuated mutant strain of Salmonella designated VXM01.

10. The attenuated mutant strain of Salmonella of any of the preceding claims, in particular according to claim 9, wherein the attenuated mutant strain of Salmonella is co-administered with said one or more further attenuated mutant strain(s) of Salmonella.

11. The attenuated mutant strain of Salmonella of any one of claims 8 to 10, wherein cancer immunotherapy is accompanied by chemotherapy, radiotherapy or biological cancer therapy, particularly wherein the attenuated mutant strain of Salmonella is administered before or during the chemotherapy or the radiotherapy treatment cycle or before or during biological cancer therapy, or before and during the chemotherapy or the radiotherapy treatment cycle or the biological cancer therapy.

12. The attenuated mutant strain of Salmonella of any one of claims 6 to 11, wherein the attenuated mutant strain of Salmonella is administered orally.

13. The attenuated mutant strain of Salmonella of any one of claims 8 to 12, wherein the cancer is selected from leukemia, particularly from acute myeloid leukemia (AML) and acute lymphoid leukemia (ALL), and from solid tumors, particularly from lung cancer, breast cancer, esophageal, colon, colorectal, gastric, cholangioductal, pancreatic cancer, glioblastoma, head and neck cancer, synovial sarcoma, angiosarcoma, osteosarcoma, thyroid cancer, cervical, endometrial, ovarian cancer, neuroblastoma, rhabdomyosarcoma, prostate cancer.

14. The attenuated mutant strain of Salmonella of any one of claims 6 to 13, wherein the single dose comprises from about 10^5 to about 10^{11}, particularly from about 10^6 to about 10^{10}, more particularly from about 10^6 to about 10^9 , more particularly from about 10^6 to about 10^8, most particularly from about 10^6 to about 10^7 colony forming units (CFU).

15. The attenuated mutant strain of Salmonella of any one of claims 8 to 14 for use in individualized cancer immunotherapy comprising the step of assessing the tumor antigen expression pattern and/or stroma antigen expression pattern of a patient.

CLAIMS

1. An attenuated mutant strain of Salmonella comprising at least one copy of a recombinant DNA molecule comprising a eukaryotic expression cassette encoding Wilms' Tumor Protein (WT1).

2. The attenuated mutant strain of Salmonella of claim 1, wherein the attenuated mutant strain of Salmonella is of the species Salmonella enterica, particularly wherein the attenuated mutant strain of Salmonella is Salmonella typhi Ty21a.

3. The attenuated mutant strain of Salmonella of claim 1 or 2, wherein WT1 is selected from the group consisting of human WT1 and a protein that shares at least 80% sequence identity therewith, particularly wherein the zinc finger domain of WT1 is deleted, more particularly wherein WT1 has the amino acid sequence as found in SEQ ID NO 1.

4. The attenuated mutant strain of Salmonella of any one of claims 1 to 3, wherein the recombinant DNA molecule comprises the kanamycin antibiotic resistance gene, the pMB1 ori, and a eukaryotic expression cassette encoding human WT1 or a protein that shares at least 80% sequence identity therewith, particularly wherein the zinc finger domain of WT1 is deleted, under the control of a CMV promoter.

5. The attenuated mutant strain of Salmonella of any one of claims 1 to 4 for use as a medicament.

6. Use of an attenuated mutant strain of Salmonella of any one of claims 1 to 4, in the manufacture of a vaccine.

7. The use of claim 6, wherein the vaccine is for cancer immunotherapy.

8. The use of claim 7, wherein the vaccine is to be further administered with one or more further attenuated mutant strain(s) of Salmonella comprising at least one copy of a recombinant DNA molecule comprising an expression cassette encoding a tumor antigen and/or a tumor stroma antigen, particularly wherein said one or more further attenuated mutant strain(s) of Salmonella is/are Salmonella typhi Ty21a comprising a eukaryotic expression cassette, more particularly wherein said one or

more further attenuated mutant strain(s) of Salmonella comprise(s) an attenuated mutant strain of Salmonella encoding human VEGFR-2, more particularly wherein said one or more further attenuated mutant strain(s) of Salmonella comprise(s) the attenuated mutant strain of Salmonella designated VXM01.

9. The use of claim 8, wherein the vaccine is to be co-administered with said one or more further attenuated mutant strain(s) of Salmonella.

10. The use of any one of claims 7 to 9, wherein the vaccine is to be accompanied by chemotherapy, radiotherapy or biological cancer therapy, particularly wherein the attenuated mutant strain of Salmonella is to be administered before or during the chemotherapy or the radiotherapy treatment cycle or before or during biological cancer therapy, or before and during the chemotherapy or the radiotherapy treatment cycle or the biological cancer therapy.

11. The use of any one of claims 6 to 10, wherein the vaccine is to be administered orally.

12. The use of any one of claims 7 to 11, wherein the cancer is selected from leukemia, particularly from acute myeloid leukemia (AML) and acute lymphoid leukemia (ALL), and from solid tumors, particularly from lung cancer, breast cancer, esophageal, colon, colorectal, gastric, cholangioductal, pancreatic cancer, glioblastoma, head and neck cancer, synovial sarcoma, angiosarcoma, osteosarcoma, thyroid cancer, cervical, endometrial, ovarian cancer, neuroblastoma, rhabdomyosarcoma, prostate cancer.

13. The attenuated mutant strain of Salmonella of claim 5 or use in any one of claims 6 to 12, wherein the attenuated mutant strain of Salmonella or the vaccine is to be administered in a single dose, wherein the single dose comprises from about 10^5 to about 10^{11}, particularly from about 10^6 to about 10^{10}, more particularly from about 10^6 to about 10^9, more particularly from about 10^6 to about 10^8, most particularly from about 10^6 to about 10^7 colony forming units (CFU).

14. The use of any one of claims 7 to 13 in individualized cancer immunotherapy wherein the tumor antigen expression pattern and/or stroma antigen expression pattern of a patient is to be assessed.