irinotecan, oxaliplatin, Camptosar (Pharmacia & Upjohn), and Celebrex. Oftentimes, chemotherapy with radiation in adjunct to surgery is used. In general, chemotherapy can achieve long-term survival rates of up to 15% to 20%, even in patients with recurrent or metastatic disease. Unfortunately, the high initial response rate to first line chemotherapy does not appear to translate into a survival benefit. Moreover, there are many undesirable side effects associated with chemotherapy such as temporary hair loss, mouth sores, anemia (decreased numbers of red blood cells that may cause fatigue, dizziness, and shortness of breath), leukopenia (decreased numbers of white blood cells that may lower resistance to infection), thrombocytopenia (decreased numbers of platelets that may lead to easy bleeding or bruising), and gastrointestinal symptoms like nausea, vomiting, and diarrhea.

[0007] While surgery, chemotherapeutic agents, and radiation are useful in the treatment of colorectal cancer, there is a continued need to find better treatment modalities and approaches to manage the disease that are more effective and less toxic, especially when clinical oncologists are giving increased attention to the quality of life of cancer patients.

SUMMARY

[0008] In one aspect, there is provided a recombinant, probiotic lactic acid bacterium, wherein the bacterium comprises a non-replicating plasmid vector comprising (a) a tumor suppressor gene ~~or anti-inflammatory gene~~ operably linked to a first promoter that directs expression of the tumor suppressor gene ~~or anti-inflammatory gene~~ in a mammalian cell, and (b) an adhesin gene operably linked to a second promoter that directs expression of the adhesin gene in the bacterium.

[0009] In another aspect, there is provided the use of the recombinant, probiotic lactic acid bacterium as disclosed herein in the manufacture of a medicament for treating a gastrointestinal cancer ~~or reducing inflammation~~ in a subject~~, wherein the cancer or inflammation is a cancer or inflammation of the gastrointestinal tract~~. In one example, there is provided a method of treating cancer or reducing inflammation in a subject, wherein the method comprises administering a pharmaceutically effective amount of the recombinant, probiotic lactic acid bacterium of the present invention into the gastrointestinal tract of the subject, and wherein the cancer or inflammation is a cancer or inflammation of the gastrointestinal tract.

[0010] In another aspect, there is provided the use of a recombinant, probiotic lactic acid bacterium in the manufacture of a medicament for treating a gastrointestinal cancer in a subject, wherein the bacterium comprises a non-replicating plasmid vector comprising a tumor suppressor gene operably linked to a first promoter that directs expression of the tumor suppressor gene in a mammalian cell, and an adhesin gene operably linked to a second promoter that directs expression of the adhesin gene in the bacterium. In another example, there is provided a method of treating cancer in a subject, wherein the method comprises administering a pharmaceutically effective amount of a recombinant, probiotic lactic acid bacterium, wherein the bacterium comprises a non-replicating plasmid vector comprising an adhesin gene operably linked to a promoter that directs expression of the adhesin gene in the bacterium.

CLAIMS

1. A recombinant, probiotic lactic acid bacterium, wherein the bacterium comprises a non-replicating plasmid vector comprising (a) a tumor suppressor gene ~~or anti-inflammatory gene~~ operably linked to a first promoter that directs expression of the tumor suppressor gene ~~or anti-inflammatory gene~~ in a mammalian cell, and (b) an adhesin gene operably linked to a second promoter that directs expression of the adhesin gene in the bacterium.

2. The recombinant, probiotic lactic acid bacterium of claim 1, wherein the bacterium is a lactic-acid producing bacterium.

3. The recombinant, probiotic lactic acid bacterium of claim 1 or 2, wherein the bacterium is of the Lactococcus genus.

4. The recombinant, probiotic lactic acid bacterium of any one of claims 1 to 3, wherein the bacterium is *Lactococcus lactis*.

5. The recombinant, probiotic lactic acid bacterium of any one of claims 1 to 4, wherein the adhesin is fibronectin-binding protein or internalin.

6. The recombinant, probiotic lactic acid bacterium of any one of claims 1 to 5, wherein the tumor suppressor gene ~~or anti-inflammatory gene~~ has tumor-suppressing ~~or anti-inflammatory effects~~ on cells of the gastrointestinal tract.

7. The recombinant, probiotic lactic acid bacterium of claim 6, wherein the tumor suppressor gene is selected from the group consisting of *DUSP10*, *TP53*, *APC*, *CD95*, *PTEN*, *TRAIL*, *MDA7*, and *PMAIP1*~~, and/or the anti-inflammatory gene is selected from the group consisting of *DUSP10*, *IL10*, *IL11*, *IL13*, *IL1-ra*, and *TGFb*~~.

8. The recombinant, probiotic lactic acid bacterium of claim 7, wherein the tumor suppressor gene ~~or anti-inflammatory gene~~ is *DUSP10* gene.

9. Use of the recombinant, probiotic lactic acid bacterium of any one of claims 1 to 9 in the manufacture of a medicament for treating a gastrointestinal cancer ~~or reducing inflammation~~ in a subject~~, wherein the cancer or inflammation is a cancer or inflammation of the gastrointestinal tract~~.

10. Use of a recombinant, probiotic lactic acid bacterium in the manufacture of a medicament for treating a gastrointestinal cancer in a subject, wherein the bacterium comprises a non-replicating plasmid vector comprising a tumor suppressor gene operably linked to a first promoter that directs expression of the tumor suppressor gene in a mammalian cell, and an adhesin gene operably linked to a second promoter that directs expression of the adhesin gene in the bacterium.

11. The use of claim 10, wherein the bacterium is a lactic-acid producing bacterium.

12. The use of claim 10 or 11, wherein the bacterium is of the Lactococcus genus.

13. The use of any one of claims 10 to 12, wherein the bacterium is *Lactococcus lactis*.

14. The use of any one of claims 10 to 13, wherein the adhesin is fibronectin-binding protein or internalin.

15. The use of claim 9 or 10, wherein the medicament further comprises a pharmaceutically effective amount of immune checkpoint inhibitor, optionally wherein the immune checkpoint inhibitor is anti-programmed death ligand-1 (PDL-1).

16. The use of any one of claims 9 to 15, wherein the gastrointestinal cancer is selected from the group consisting of esophageal cancer, gastric cancer, colorectal cancer and anal cancer.

17. The use of claim 16, wherein the gastrointestinal cancer is colorectal cancer.

18. The use of claim 9, wherein the use reduces gastrointestinal inflammation.

19. The use of claim 18, wherein the gastrointestinal inflammation is the inflammation of the esophagus, the stomach, the small intestine, the casum, the large instestine, or the anus.

~~19~~20. The use of any one of claims 9 to ~~18~~19, wherein the recombinant, probiotic lactic acid bacterium is to be administered orally.

~~20~~21. The use of any one of claims 9 to ~~19~~20, wherein the subject is a human.