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POLYUNSATURATED FATTY ACID MONOGLYCERIDES, COMPOSITIONS, METHODS AND USES THEREOF

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] The present application claims priority to US 62/666,375 filed on May 3, 2018. This document is hereby incorporated by reference in its entirety.

FIELD OF THE DISCLOSURE

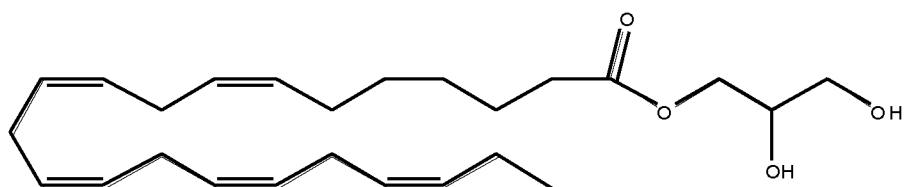
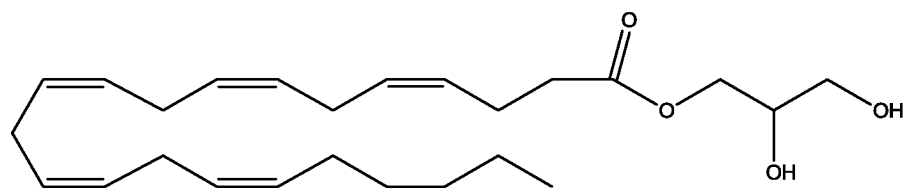
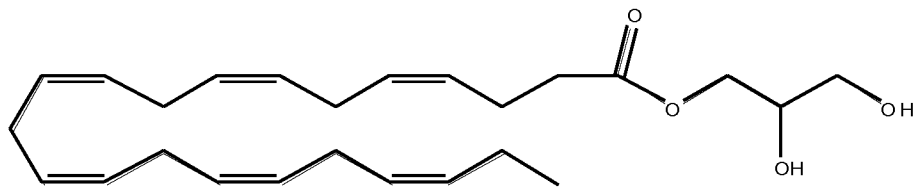
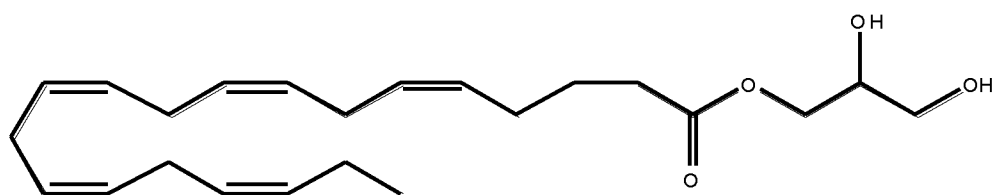
[0002] The present document relates to the field of microbiota. More particularly, it relates to polyunsaturated fatty acid monoglyceride compounds and combinations thereof. It also provided a use as prebiotic and/or a method for modulate the microbiota composition and/or for enhancing the population of at least one probiotic strain. There is also provided a method for enhancing the efficacy of cancer immunotherapy of a subject.

BACKGROUND OF THE DISCLOSURE

[0003] The human gut microbiota is not static and can be rapidly modulated by several factors (Faith and al., The long-term stability of the human gut microbiota 2013. *Science* **341** **6141**: 1237439). Changes in diet and long-chain omega-3 (LCn3) can modulate the gut microbiota of both healthy and prostate cancer (PCa) patients (Costantini, L. and al., Impact of Omega-3 Fatty Acids on the Gut Microbiota 2017. *Int J Mol Sci* **18**, 12). Daily intake of 4g LCn3 for 8 weeks was associated with a reversible bacterial signature and eicosapentanoic acid (EPA) promotes prevalence of anti-inflammatory bacteria like *Lactobacillus* and *Akkermansia* species from the gut microbiota (Piazzi, G. and al., Eicosapentaenoic acid free fatty acid prevents and suppresses colonic neoplasia in colitis-associated colorectal cancer acting on Notch signaling and gut microbiota 2014. *Int J Cancer* **135**(9): 2004-2013).

SUMMARY OF THE DISCLOSURE

[0004] According to one aspect there is provided at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV):

**(I)****(II)****(III)**

(IV)

for use as prebiotic in a subject in need thereof.

[0005] According to another aspect there is provided at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV) for the modulation of the microbiota composition of a subject in need thereof.

[0006] According to another aspect there is provided at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV) for enhancing the population of at least one probiotic strain of a subject in need thereof.

[0007] According to another aspect there is provided at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV) for enhancing the efficacy of cancer immunotherapy of a subject in need thereof.

[0008] According to another aspect there is provided the use of at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV) for use as prebiotic in a subject in need thereof.

[0009] According to another aspect there is provided the use of at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV) for the modulation of the microbiota composition of a subject in need thereof.

[0010] According to another aspect there is provided the use of at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV) for enhancing the population of at least one probiotic strain of a subject in need thereof.

[0011] According to another aspect there is provided the use of at least one compound chosen from compound of formula (I), compound of formula

(II), compound of formula (III) and compound of formula (IV) for enhancing the efficacy of cancer immunotherapy of a subject in need thereof.

[0012] According to another aspect there is provided the use of at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV) in the manufacture of a medicament for use as prebiotic in a subject in need thereof.

[0013] According to another aspect there is provided the use of at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV) in the manufacture of a medicament for the modulation of the microbiota composition of a subject in need thereof.

[0014] According to another aspect there is provided the use of at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV) in the manufacture of a medicament for enhancing the population of at least one probiotic strain of a subject in need thereof.

[0015] According to another aspect there is provided the use of at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV) in the manufacture of a medicament for enhancing the efficacy of cancer immunotherapy of a subject in need thereof.

[0016] According to another aspect there is provided a method for use as prebiotic in a subject in need thereof comprising administering an effective amount of at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV).

[0017] According to another aspect there is provided a method for modulating a microbiota composition of a subject in need thereof comprising administering to the subject an effective amount of at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV).

[0018] According to another aspect there is provided a method for enhancing the population of at least one probiotic strain of a subject in need thereof comprising administering to the subject an effective amount of at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV).

[0019] According to another aspect there is provided a method for enhancing efficacy of a cancer immunotherapy of a subject in need thereof comprising administering to the subject an effective amount of at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV).

[0020] According to another aspect, there is provided a composition comprising:

(i) at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV);

(ii) at least one lipid.

[0021] According to another aspect, there is provided a composition comprising (i) at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV) and (ii) at least one lipid for use as prebiotic in a subject in need thereof.

[0022] According to another aspect, there is provided a composition comprising (i) at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV) and (ii) at least one lipid for the modulation of the microbiota composition of a subject in need thereof.

[0023] According to another aspect, there is provided a composition comprising (i) at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV) and (ii) at least one lipid for enhancing the population of at least one probiotic strain of a subject in need thereof.

[0024] According to another aspect, there is provided a composition comprising (i) at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV) and (ii) at least one lipid for enhancing the efficacy of cancer immunotherapy of a subject in need thereof.

BRIEF DESCRIPTION OF THE FIGURES

[0025] Further features and advantages will become more readily apparent from the following description of specific embodiments as illustrated by way of examples in the appended figures wherein:

[0026] Fig. 1 represents the effect of composition **1** (Eicosapentaenoic acid monoglyceride, MAG-EPA) on gut-derived microbiota (A) and tumor-derived microbiota (B). 16S rDNA was extracted from stool samples and tumors of mice fed with composition **1** or control HOSO (higholeic sunflower oil, n=12/group) for 4 weeks before injection of TRAMP-C2 prostate cancer cells. Daily gavage was continued until animal sacrifice.

[0027] Fig. 2 represents the 16S rDNA sequencing of gut-derived microbiota. N=45 participating to a clinical trial comparing daily composition **1** supplementation (MAG-EPA) versus placebo for 6-8 weeks. Relative abundance of bacteria enriched in both groups +/- SEM are represented. Most bacteria overrepresented in gut-derived microbiota of composition **1** group compared to placebo (arrows) have already been associated with favorable clinical response.

DETAILED DESCRIPTION OF THE DISCLOSURE

[0028] Further features and advantages of the previously-mentioned compounds will become more readily apparent from the following description of non-limiting examples.

[0029] The term "microbiota" as used herein refers to an "ecological community of commensal, symbiotic and pathogenic microorganisms" found in and on all multicellular organisms. For example, in human the microbiota

can refers to whole body microbiota or organ specific microbiota like gut microbiota, prostate microbiota, skin microbiota, etc.

[0030] The term “prebiotic” as used herein refers to a food ingredient that induces the growth or activity of beneficial microorganisms (e.g., bacteria and fungi).

[0031] The term “lipid” as used herein refers to as any fat-soluble (lipophilic), molecules, such as fats, fat-like substances, oils (such as animal oil, marine oil, vegetable oil, fish oil concentrate, re-esterified fish oil or re-esterified concentrated fish oil), waxes, sterols (such as cholesterol, ergosterol, sitosterol, stigmasterol, fat-soluble vitamins (such as vitamins A, D, E and K), fatty acids, oxidized fatty acid (such as lipoxin, specialized pro-resolving mediators or epoxydes), fatty acids esters thereof, and various derivatives thereof such as monoglycerides, diglycerides, triglycerides, phospholipids, glycolipids, and cerebrosides and pharmaceutically acceptable salts thereof.

[0032] The expression “effective amount” of a compound of the present disclosure is a quantity sufficient to, when administered to the subject, including a mammal, for example a human, effect beneficial or desired results, including clinical results, and, as such, an “effective amount” depends upon the context in which it is being applied. The amount of a given compound of the present disclosure that will correspond to such an amount will vary depending upon various factors, such as the given drug or compound, the pharmaceutical formulation, the route of administration, the identity of the subject or host being treated, and the like, but can nevertheless be routinely determined by one skilled in the art.

[0033] The term “probiotic strain” as used herein refers to any microorganisms that are known to provide health benefits when consumed. The World Health Organization's (WHO) 2001 defines probiotics as live microorganisms that, “...when administered in adequate amounts, confer a health benefit on the host”.

[0034] For example, the subject in need thereof can be a bee, human, cat, dog, etc...

[0035] For example, the at least one compound is said compound of formula (I).

[0036] For example, the at least one compound is said compound of formula (II).

[0037] For example, the at least one compound is said compound of formula (III).

[0038] For example, the at least one compound is said compound of formula (IV).

[0039] For example, the at least one compound is said compound of formula (I), said compound of formula (III) and said compound of formula (IV).

[0040] For example, the at least one compound is said compound of formula (I) and said compound of formula (IV).

[0041] For example, the at least one compound is said compound of formula (I) and said compound of formula (III).

[0042] For example, the at least one compound is said compound of formula (III) and said compound of formula (IV).

[0043] For example, the at least one compound can be for use in combination with at least one lipid.

[0044] For example, the at least one lipid and said at least one compound can be for simultaneous administration.

[0045] For example, the at least one lipid and said at least one compound can be for separate administration.

[0046] For example, the at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV) can be administered in combination with at least one lipid.

[0047] For example, the at least one lipid and said at least one compound can be administered simultaneously.

[0048] For example, the at least one lipid and said at least one compound can be administered separately.

[0049] For example, the at least one lipid can be chosen from animal oil, marine oil, fish oil, fish oil concentrate, re-esterified fish oil, re-esterified concentrated fish oil, vegetable oil, fatty acids, fatty acids ethyl esters, fatty acids esters, monoglycerides, diglycerides, triglycerides and phospholipids.

[0050] For example, the at least one lipid can be chosen from marine oil, fish oil, fish oil concentrate, re-esterified fish oil, re-esterified concentrated fish oil, fatty acids ethyl esters, fatty acids esters, monoglycerides, diglycerides, triglycerides and phospholipids.

[0051] For example, the at least one probiotic strain can be chosen from *Akkermenssia muciniphila*, *Bacillus Coagulans*, *Bifidobacterium Animalis*, *Bifidobacterium Bifidum*, *Bifidobacterium Breve*, *Bifidobacterium longum*, *Lactobacillus Acidophilus*, *Lactobacillus bulgaricus*, *Lactobacillus Rhamnosus*, *Lactobacillus Reuteri*, *Ruminococcus*, *Lactococcus Lactis*, *Streptococcus Thermophilus*, *Streptococcus Salivarius* and *Christensenellaceae* family.

[0052] For example, the at least one probiotic strain can be chosen from *Akkermenssia muciniphila*, *Bifidobacterium Animalis*, *Lactobacillus Acidophilus*, *Lactococcus Lactis*, *Ruminococcus* and *Christensenellaceae* family.

EXAMPLE 1

Preparation of a composition (composition 1) comprising compound IV.

[0053] Composition 1 comprising compound IV, was prepared by reacting 1 kg of EPA concentrated fish oil (ethyl ester form) with 0,27 kg of glycerol with 0,05 kg of Novozym 435 (lipase) in 2 kg of acetone at 50°C for 4h. The lipase was filtered, the acetone was removed in vacuo and the

mixture was allowed to stand for phase separation. The lower unreacted glycerol phase was removed to give 1 kg of the final composition **1** comprising compound **IV**, unreacted ethyl ester and small amount of diglycerides and triglyceride.

EXAMPLE 2

Composition 1 increase the amount of *akkermansia muciniphila* in gut microbita

[0054] Data from a prostate cancer mouse model showed increased of *Akkermansia muciniphila* in fecal samples of a lipid formulation containing composition **1**-fed animals (Fig 1B). The presence of *Akkermansia* is believed to stimulate immunotherapy response in cancer patients. In addition, mouse prostate tumor-derived as well as gut-derived microbiota from lipid formulation containing composition **1**-treated animals showed reduced *Bacteroides fragilis* (Fig. 1C, 1D). *B. fragilis* can produce a toxin that damages host epithelial cells.

EXAMPLE 2

Composition 1 modulate the gut microbita in a phase II human clinical trial.

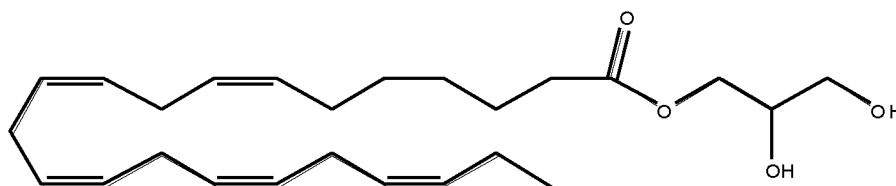
[0055] 45 patients were randomized to either composition **1** or a placebo for 6-8 weeks before prostatectomy for prostate cancer. 16srRNA analyses showed striking changes in the composition of the gut microbiota of the lipid formulation containing composition **1**-treated patients (Fig. 2), in particular an increased abundance of *Ruminococcus* and *Alistipes*, associated in other studies with favourable response to immunotherapy

[0056] While the compounds, compositions, methods and uses thereof have been described in connection with specific embodiments thereof, it will be understood that they can be further modified and this application is intended to cover any variations, uses, or adaptations of the compounds,

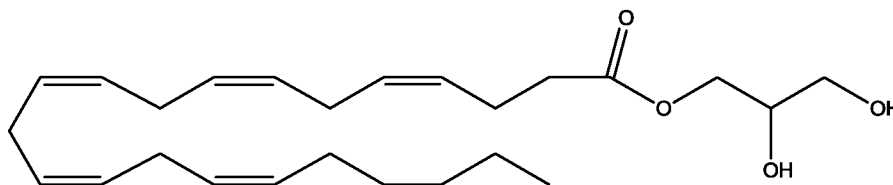
compositions, methods and uses thereof following, in general, the principles described in the present document and including such departures from the present disclosure as come within known or customary practice within the art to which the present document pertains and as may be applied to the features hereinbefore set forth, and as follows in the scope of the appended claims.

WHAT IS CLAIMED IS:

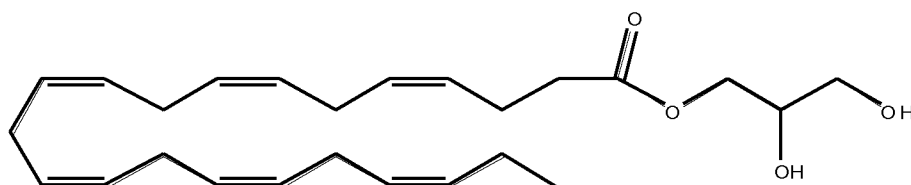
1. At least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV):



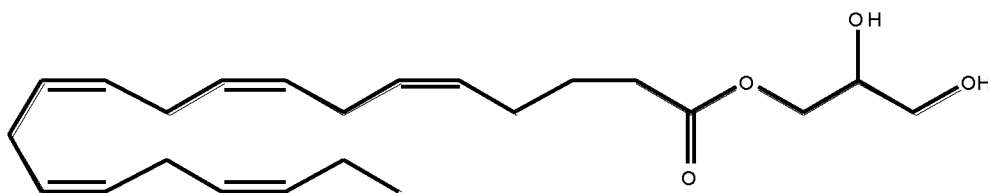
(I)



(II)



(III)



(IV)

for use as prebiotic in a subject in need thereof.

2. At least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV), for use in modulating a microbiota composition of a subject in need thereof.
3. At least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV), for use in enhancing the population of at least one probiotic strain of a subject in need thereof.
4. At least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV), for use in enhancing efficacy of cancer immunotherapy of a subject in need thereof.
5. The at least one compound of any one of claims 1 to 4, wherein said at least one compound is said compound of formula (I).
6. The at least one compound of any one of claims 1 to 4, wherein said at least one compound is said compound of formula (II).
7. The at least one compound of any one of claims 1 to 4, wherein said at least one compound is said compound of formula (III).
8. The at least one compound of any one of claims 1 to 4, wherein said at least one compound is said compound of formula (IV).
9. The at least one compound of any one of claims 1 to 4, wherein said at least one compound is said compound of formula (I), said compound of formula (III) and said compound of formula (IV).
10. The at least one compound of any one of claims 1 to 4, wherein said at least one compound is said compound of formula (I) and said compound of formula (IV).

11. The at least one compound of any one of claims 1 to 4, wherein said at least one compound is said compound of formula (I) and said compound of formula (III).
12. The at least one compound of any one of claims 1 to 4, wherein said at least one compound is said compound of formula (III) and said compound of formula (IV).
13. The at least one compound of any one of claims 1 to 12, for use in combination with at least one lipid.
14. The at least one compound of claim 13, wherein said at least one lipid and said at least one compound are for simultaneous administration.
15. The at least one compound of claim 13, wherein said at least one lipid and said at least one compound are for separate administration.
16. The at least one compound of claim 3, wherein at least one probiotic strain is chosen from from *Akkermenssia muciniphila*, *Bacillus Coagulans*, *Bifidobacterium Animalis*, *Bifidobacterium Bifidum*, *Bifidobacterium Breve*, *Bifidobacterium longum*, *Lactobacillus Acidophilus*, *Lactobacillus bulgaricus*, *Lactobacillus Rhamnosus*, *Lactobacillus Reuteri*, *Lactococcus Lactis*, *Ruminococcus Streptococcus Thermophilus*, *Streptococcus Salivarius* and *Christensenellaceae* family.
17. The at least one compound of claim 3, wherein at least one probiotic strain is chosen from *Akkermenssia muciniphila*, *Bifidobacterium Animalis*, *Lactobacillus Acidophilus*, *Lactococcus Lactis*, *Ruminococcus* and *Christensenellaceae* family.
18. Use of at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV), as prebiotic in a subject in need thereof.

19. Use of at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV), for the modulation of the microbiota composition of a subject in need thereof.
20. Use of at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV), for enhancing the population of at least one probiotic strain of a subject in need thereof.
21. Use of at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV), for enhancing the efficacy of cancer immunotherapy of a subject in need thereof.
22. Use of at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV), in the manufacture of a medicament for use as prebiotic in a subject in need thereof.
23. Use of at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV), in the manufacture of a medicament for the modulation of the microbiota composition of a subject in need thereof.
24. Use of at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV), in the manufacture of a medicament for enhancing the population of at least one probiotic strain of a subject in need thereof.
25. Use of at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV), in the manufacture of a medicament for enhancing the efficacy of cancer immunotherapy of a subject in need thereof.

26. The use of any one of claims 18 to 25, wherein said at least one compound is said compound of formula (I).
27. The use of any one of claims 18 to 25, wherein said at least one compound is said compound of formula (II).
28. The use of any one of claims 18 to 25, wherein said at least one compound is said compound of formula (III).
29. The use of any one of claims 18 to 25, wherein said at least one compound is said compound of formula (IV).
30. The use of any one of claims 18 to 25, wherein said at least one compound is said compound of formula (I), said compound of formula (III) and said compound of formula (IV).
31. The use of any one of claims 18 to 25, wherein said at least one compound is said compound of formula (I) and said compound of formula (IV).
32. The use of any one of claims 18 to 25, wherein said at least one compound is said compound of formula (I) and said compound of formula (III).
33. The use of any one of claims 21 to 25, wherein said at least one compound is said compound of formula (III) and said compound of formula (IV).
34. The use of any one of claims 21 to 33, for use in combination with at least lipid.
35. The use of claim 34, wherein said at least one lipid and said at least one compound are for simultaneous administration.
36. The use of claim 34, wherein said at least one lipid and said at least one compound are for separate administration.

37. The use of claim 20 or 24, wherein the at least one probiotic strain is chosen from *Akkermenssia muciniphila*, *Bacillus Coagulans*, *Bifidobacterium Animalis*, *Bifidobacterium Bifidum*, *Bifidobacterium Breve*, *Bifidobacterium longum*, *Lactobacillus Acidophilus*, *Lactobacillus bulgaricus*, *Lactobacillus Rhamnosus*, *Lactobacillus Reuteri*, *Lactococcus Lactis*, *Ruminococcus*, *Streptococcus Thermophilus*, *Streptococcus Salivarius* and *Christensenellaceae* family.
38. The use of claim 20 or 24, wherein the at least one probiotic strain is chosen from *Akkermenssia muciniphila*, *Bifidobacterium Animalis*, *Lactobacillus Acidophilus*, *Lactococcus Lactis*, *Ruminococcus* and *Christensenellaceae* family.
39. A method of using at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV), said method comprising administering an effective amount of said at least one compound as a prebiotic.
40. A method for modulating a microbiota composition of a subject in need thereof comprising administering to the subject an effective amount of at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV).
41. A method for enhancing population of at least one probiotic strain of a subject in need thereof comprising administering to the subject an effective amount of at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV).
42. A method for enhancing the efficacy of cancer immunotherapy of a subject in need thereof comprising administering to the subject an effective amount of at least one compound chosen from compound of

formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV).

43. The method of any one of claims 39 to 42, wherein said at least one compound is said compound of formula (I).
44. The method of any one of claims 39 to 42, wherein said at least one compound is said compound of formula (II).
45. The method of any one of claims 39 to 42, wherein said at least one compound is said compound of formula (III).
46. The method of any one of claims 39 to 42, wherein said at least one compound is said compound of formula (IV).
47. The method of any one of claims 39 to 42, wherein said at least one compound is said compound of formula (I), said compound of formula (III) and said compound of formula (IV).
48. The method of any one of claims 39 to 42, wherein said at least one compound is said compound of formula (I) and said compound of formula (IV).
49. The method of any one of claims 39 to 42, wherein said at least one compound is said compound of formula (I) and said compound of formula (III).
50. The method of any one of claims 39 to 42, wherein said at least one compound is said compound of formula (III) and said compound of formula (IV).
51. The method of any one of claims 39 to 50, wherein said at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV) is administered in combination with at least one lipid.

52. The method of any one of claims claim 39 to 51, wherein said at least one lipid and said at least one compound are administered simultaneously.
53. The method of any one of claims claim 39 to 51, wherein said at least one lipid and said at least one compound are administered separately.
54. The method of claim 41, wherein the at least one probiotic strain is chosen from *Akkermenssia muciniphila*, *Bacillus Coagulans*, *Bifidobacterium Animalis*, *Bifidobacterium Bifidum*, *Bifidobacterium Breve*, *Bifidobacterium longum*, *Lactobacillus Acidophilus*, *Lactobacillus bulgaricus*, *Lactobacillus Rhamnosus*, *Ruminococcus*, *Lactobacillus Reuteri*, *Lactococcus Lactis*, *Streptococcus Thermophilus*, *Streptococcus Salivarius* and *Christensenellaceae* family.
55. The method of claim 41, wherein the at least one probiotic strain is chosen from *Akkermenssia muciniphila*, *Bifidobacterium Animalis*, *Lactobacillus Acidophilus*, *Lactococcus Lactis*, *Ruminococcus* and *Christensenellaceae* family.
56. A composition comprising:
- (i) at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV); and
- (ii) at least one lipid.
- for use as prebiotic in a subject in need thereof.
57. A composition comprising:
- (i) at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV); and

(ii) at least one lipid.

for use in the modulation of the microbiota composition of a subject in need thereof.

58. A composition comprising:

(i) at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV); and

(ii) at least one lipid.

for use in enhancing the population of at least one probiotic strain of a subject in need thereof.

59. A composition comprising:

(i) at least one compound chosen from compound of formula (I), compound of formula (II), compound of formula (III) and compound of formula (IV); and

(ii) at least one lipid.

for use in enhancing efficacy of cancer immunotherapy of a subject in need thereof.

60. The composition of any one of claims 56 to 59, wherein said at least one lipid is chosen from marine oil, fish oil, fish oil concentrate, re-esterified fish oil, re-esterified concentrated fish oil, fatty acids ethyl esters, fatty acids esters, monoglycerides, diglycerides, triglycerides and phospholipids.

61. The composition of any one of claims 56 to 60, wherein said at least one compound is said compound of formula (I).

62. The composition of any one of claims 56 to 60, wherein said at least one compound is said compound of formula (II).

63. The composition of any one of claims 56 to 60, wherein said at least one compound is said compound of formula (III).
64. The composition of any one of claims 56 to 60, wherein said at least one compound is said compound of formula (IV).
65. The composition of any one of claims 56 to 60, wherein said at least one compound is said compound of formula (I), said compound of formula (III) and said compound of formula (IV).
66. The composition of any one of claims 56 to 60, wherein said at least one compound is said compound of formula (I) and said compound of formula (IV).
67. The composition of any one of claims 56 to 60, wherein said at least one compound is said compound of formula (I) and said compound of formula (III).
68. The composition of any one of claims 56 to 60, wherein said at least one compound is said compound of formula (III) and said compound of formula (IV).

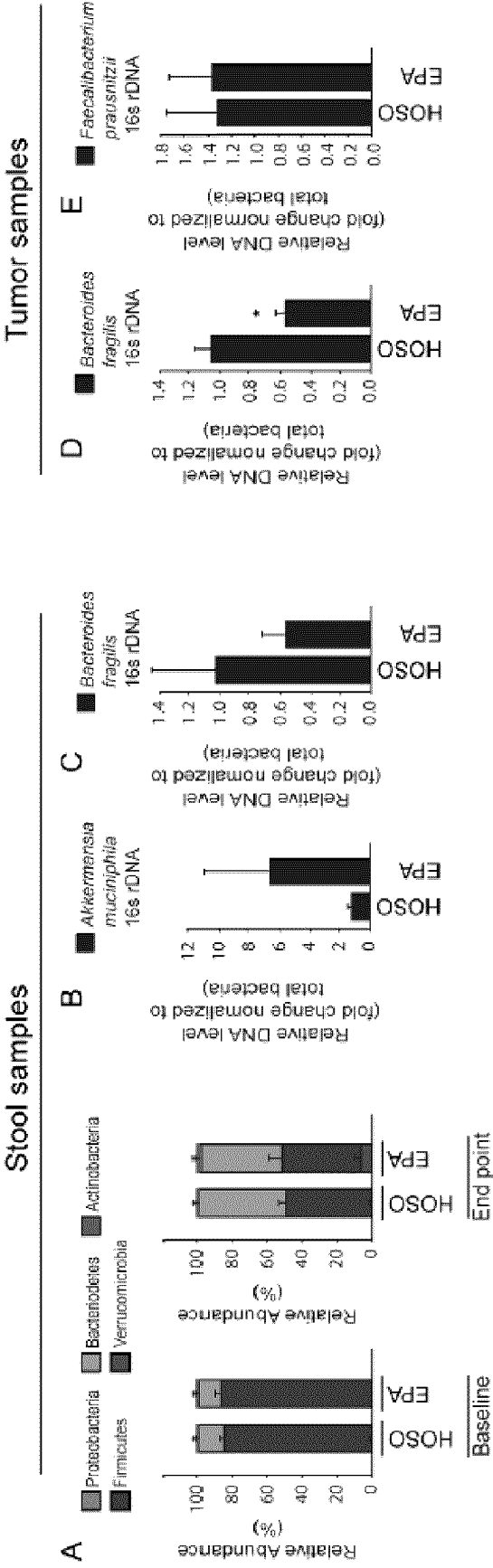


Fig. 1

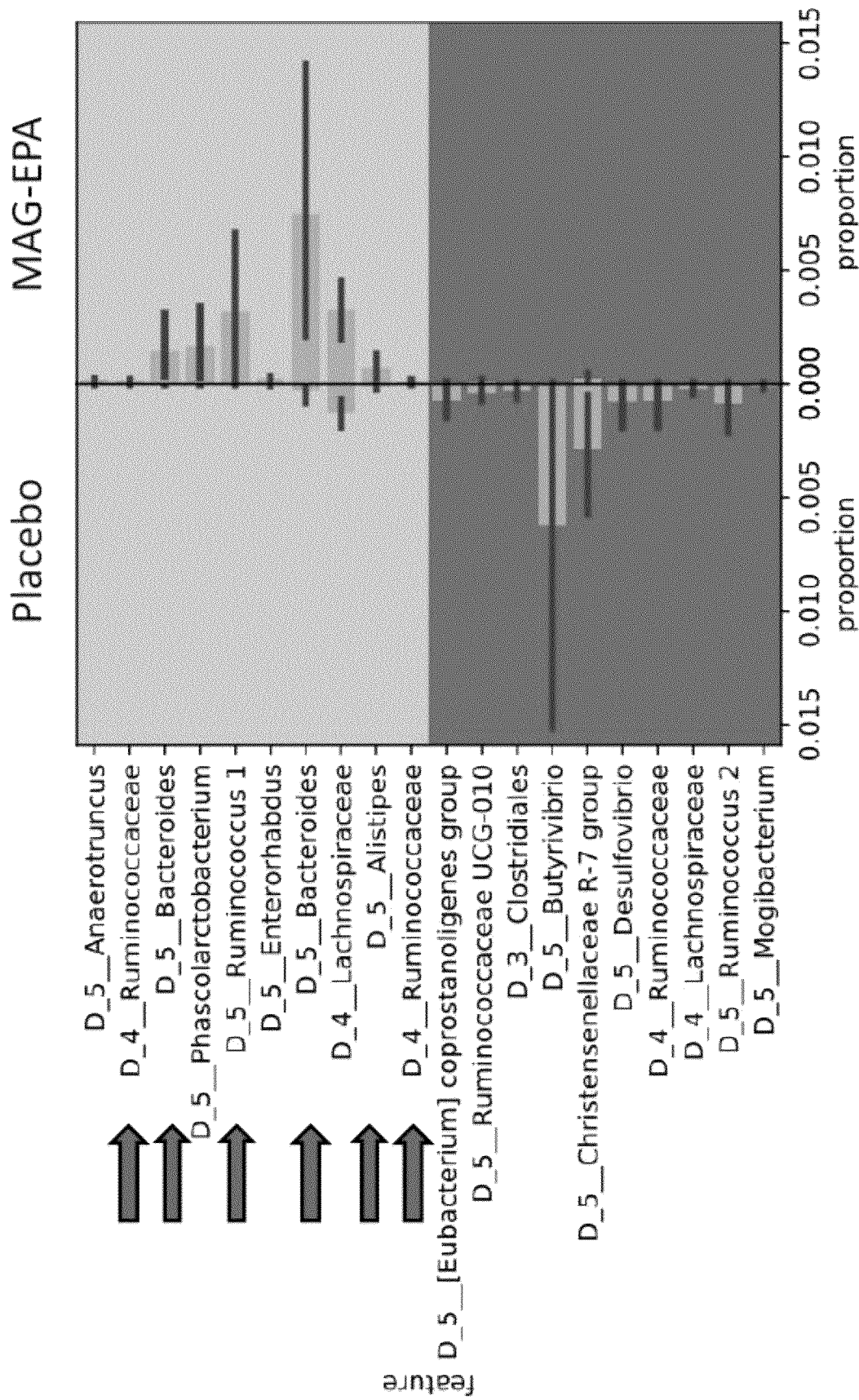


Fig. 2

INTERNATIONAL SEARCH REPORT

International application No.

PCT/CA2019/050587

A. CLASSIFICATION OF SUBJECT MATTER
 IPC: **A61K 31/232** (2006.01), **A61P 1/00** (2006.01), **C07C 69/587** (2006.01)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
 IPC (A61K-31/23)

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic database(s) consulted during the international search (name of database(s) and, where practicable, search terms used)
 Questel Orbit (IPC and monoglyceride+, fatty acid+, polyunsatur+), Questel Orbit (IPC and prebiotic+)
 Canadian Patent Database (CPD) (IPC and polyunsaturated "fatty acid" monoglyceride)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	US 2009/0291102 (FORTIN, S.) 26 November 2009 (26-11-2009) Page 1, paragraph 4-8; page 3, paragraph 33-34; page 5, paragraph 62	1-68
A	CA 2.538.382 (HOBBS et al.) 17 March 2005 (17-03-2005) Pages 3-5, 22-23	1-68
A	CA 2.599.473 (SCHOLZ et al.) 21 September 2016 (21-09-2006) Pages 1-2, 10-11	1-68

☐ Further documents are listed in the continuation of Box C.

☒ See patent family annex.

* "A" "E" "L" "O" "P"	Special categories of cited documents: document defining the general state of the art which is not considered to be of particular relevance earlier application or patent but published on or after the international filing date document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) document referring to an oral disclosure, use, exhibition or other means document published prior to the international filing date but later than the priority date claimed	"T" "X" "Y" "&"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art document member of the same patent family
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Date of the actual completion of the international search
 15 May 2019 (15-05-2019)

Date of mailing of the international search report
 26 July 2019 (26-07-2019)

Name and mailing address of the ISA/CA
 Canadian Intellectual Property Office
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 Gatineau, Quebec K1A 0C9
 Facsimile No.: 819-953-2476

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INTERNATIONAL SEARCH REPORT
Information on patent family members

International application No.
PCT/CA2019/050587

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		EP2136844A4	25 July 2012 (25-07-2012)
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		ES2704439T3	18 March 2019 (18-03-2019)
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