

CLAIMS

1. An anti-PD1 antibody molecule comprising:
 - (a) heavy chain CDRs comprising the amino acid sequence of SEQ ID NO:1 (hcCDR1), SEQ ID NO:2 (hcCDR2) and SEQ ID NO:3 (hcCDR3) and has light chain CDRs comprising the amino acid sequence of SEQ ID NO:4 (lcCDR1), SEQ ID NO:5 (lcCDR2) and SEQ ID NO:6 (lcCDR3); or,
 - (b) heavy chain CDRs comprising the amino acid sequence of SEQ ID NO:7 (hcCDR1), SEQ ID NO:8 (hcCDR2) and SEQ ID NO:9 (hcCDR3) and has light chain CDRs comprising the amino acid sequence of SEQ ID NO:10 (lcCDR1), SEQ ID NO:11 (lcCDR2) and SEQ ID NO:12 (lcCDR3); or,
 - (c) heavy chain CDRs comprising the amino acid sequence of SEQ ID NO:13 (hcCDR1), SEQ ID NO:14 (hcCDR2) and SEQ ID NO:15 (hcCDR3) and has light chain CDRs comprising the amino acid sequence of SEQ ID NO:16 (lcCDR1), SEQ ID NO:17 (lcCDR2) and SEQ ID NO:18 (lcCDR3).
2. The anti-PD1 antibody molecule of claim 1 wherein said antibody molecule is a humanized antibody molecule.
3. The anti-PD1 antibody molecule of claim 1 or 2 wherein said antibody molecule is a monoclonal antibody molecule, Fab, F(ab')₂, Fv or scFv.
4. The anti-PD1 antibody molecule of any of the previous claims which comprises a heavy chain constant region selected from the group consisting of IgG1, IgG2, IgG3, IgG4, IgM, IgA and IgE constant regions.
5. The anti-PD1 antibody molecule of claim 4 wherein the heavy chain constant region is IgG4, preferably IgG4 with a S241P mutation.
6. The anti-PD1 antibody molecule of any of the previous claims wherein the light chain constant region is kappa or lambda.

7. The anti-PD1 antibody molecule of any of the previous claims wherein said antibody molecule has a heavy chain variable domain comprising an amino acid sequence at least 85% identical to any of SEQ ID NOs: 19, 21, 23, 25 and 27.
- 5 8. The anti-PD1 antibody molecule of any of the previous claims wherein said antibody molecule has a heavy chain variable domain comprising an amino acid sequence of any of SEQ ID NOs: 19, 21, 23, 25 and 27.
9. The anti-PD1 antibody molecule of any of the previous claims wherein said
10 antibody molecule has a light chain variable domain comprising an amino acid sequence at least 85% identical to any of SEQ ID NOs: 20, 22, 24, 26 and 28.
10. The anti-PD1 antibody molecule of any of the previous claims wherein said antibody molecule has a light chain variable domain comprising the amino acid
15 sequence of SEQ ID NOs: 20, 22, 24, 26 and 28.
11. The anti-PD1 antibody molecule of any of the previous claims wherein said antibody molecule has a heavy chain comprising the amino acid sequence of
20 SEQ ID NO: 29, 31, 33, 35 or 37.
12. The anti-PD1 antibody molecule of any of the previous claims wherein said antibody molecule has a light chain comprising the amino acid sequence of SEQ
ID NO: 30, 32, 34, 36 or 38.
- 25 13. The anti-PD1 antibody molecule of any of the previous claims wherein said antibody molecule has a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 19 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 20, or a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 21 and a light chain variable
30 domain comprising the amino acid sequence of SEQ ID NO: 22, or a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 23 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO:

24, or a heavy chain variable domain comprising the amino acid sequence of
SEQ ID NO: 25 and a light chain variable domain comprising the amino acid
sequence of SEQ ID NO: 26, or a heavy chain variable domain comprising the
amino acid sequence of SEQ ID NO: 27 and a light chain variable domain
5 comprising the amino acid sequence of SEQ ID NO: 28.

14. The anti-PD1 antibody molecule of any of the previous claims wherein said
antibody molecule has a heavy chain comprising the amino acid sequence of
SEQ ID NO: 29 and a light chain comprising the amino acid sequence of SEQ ID
10 NO: 30 or a heavy chain comprising the amino acid sequence of SEQ ID NO: 31
and a light chain comprising the amino acid sequence of SEQ ID NO: 32, or a
heavy chain comprising the amino acid sequence of SEQ ID NO: 33 and a light
chain comprising the amino acid sequence of SEQ ID NO: 34, or a heavy chain
comprising the amino acid sequence of SEQ ID NO: 35 and a light chain
15 comprising the amino acid sequence of SEQ ID NO: 36, or a heavy chain
comprising the amino acid sequence of SEQ ID NO: 37 and a light chain
comprising the amino acid sequence of SEQ ID NO: 38.

15. The anti-PD1 antibody molecule of any of the previous claims which is
20 capable of reducing the binding of human PD-L1/L2 with human PD1.

16. The anti-PD1 antibody molecule of any of the previous claims which is
capable of enhancing an antigen-specific T cell response.

25 17. An isolated nucleic acid molecule encoding the heavy chain variable
domain and/or the light chain variable domain of an antibody molecule of any of
claims 1 to 16.

18. The nucleic acid molecule of claim 17 which has the nucleotide sequence
30 of SEQ ID NOs: 71, 73, 75, 77 or 79 encoding the heavy chain variable domain of
the antibody molecule defined in claim 8.

19. The nucleic acid molecule of claim 17 which has the nucleotide sequence of SEQ ID NOs: 72, 74, 76, 78 or 80 encoding the light chain variable domain of the antibody molecule defined in claim 10.
- 5 20. An expression vector containing a nucleic acid molecule comprising the nucleotide sequence encoding the heavy chain variable domain and/or the light chain variable domain of an antibody molecule of any one of claims 1 to 16.
21. The expression vector of claim 20 containing a nucleic acid molecule
10 comprising the nucleotide sequence of SEQ ID NO: 71 and/or SEQ ID NO: 72, or comprising the nucleotide sequence of SEQ ID NO: 73 and/or SEQ ID NO: 74, or comprising the nucleotide sequence of SEQ ID NO: 75 and/or SEQ ID NO: 76, or comprising the nucleotide sequence of SEQ ID NO: 77 and/or SEQ ID NO: 78 or comprising the nucleotide sequence of SEQ ID NO: 79 and/or SEQ ID NO: 80.
- 15 22. The expression vector of claim 20 or 21 comprising, in addition, a nucleic acid molecule encoding the heavy chain constant domains and/or the light chain constant domain, respectively, linked to the nucleic acid molecule encoding the heavy chain variable domain and/or the light chain variable domain, respectively.
- 20 23. A host cell having an expression vector encoding a heavy chain of an antibody molecule of any one of claims 1 to 16, and an expression vector encoding a light chain of an antibody molecule of any one of claims 1 to 16.
- 25 24. The host cell of claim 23 wherein the cell is a mammalian cell.
25. A method of manufacturing an antibody molecule of any of claims 1 to 16 comprising the steps of:
- 30 - culturing a host cell according to claim 23 or 24 under conditions that allow formation of an antibody molecule according to any of claims 1 to 16; and,
- recovering said antibody molecule.

26. The method of claim 25, additionally comprising the step of purifying said antibody molecule.
- 5 27. The method of claim 25 or 26, additionally comprising the step of formulating said antibody molecule into a pharmaceutical composition.
28. The antibody molecule of any of claims 1 to 16 for use in medicine.
- 10 29. A pharmaceutical composition comprising an anti-PD1 antibody of any of claims 1 to 16 and a pharmaceutically acceptable carrier.
30. The pharmaceutical composition of claim 29 further comprising an anti-LAG3 antibody molecule.
- 15 31. A kit of parts comprising an anti-PD1 antibody of any of claims 1 to 16 and an anti-LAG3 antibody molecule.
32. The composition of claim 30 or the kit of claim 31 wherein said anti-LAG3 antibody molecule binds an epitope of human LAG3 comprising the amino acid sequence LLRRAGVT (SEQ ID NO: 111) and/or YRAAVHLRDRA (SEQ ID NO: 112).
- 20 33. The composition or the kit of any of claims 30 to 32 wherein said anti-LAG3 antibody molecule comprises:
- 25 (a) heavy chain CDRs comprising the amino acid sequence of SEQ ID NO:39 (hcCDR1), SEQ ID NO:40 (hcCDR2) and SEQ ID NO:41 (hcCDR3) and has light chain CDRs comprising the amino acid sequence of SEQ ID NO:42 (lcCDR1), SEQ ID NO:43 (lcCDR2) and SEQ ID NO:44 (lcCDR3);or,
- 30 (b) heavy chain CDRs comprising the amino acid sequence of SEQ ID NO:45 (hcCDR1), SEQ ID NO:46 (hcCDR2) and SEQ ID NO:47 (hcCDR3) and

has light chain CDRs comprising the amino acid sequence of SEQ ID NO:48 (lcCDR1), SEQ ID NO:49 (lcCDR2) and SEQ ID NO:50 (lcCDR3).

34. The composition or the kit of any of claims 30 to 33 wherein said anti-
5 LAG3 antibody molecule has
- a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 51 and has a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 52, or
 - a heavy chain variable domain comprising the amino acid sequence of SEQ ID
10 NO: 53 and has a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 54, or
 - a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 55 and has a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 56, or
 - 15 - a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 57 and has a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 58, or
 - a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 59 and has a light chain variable domain comprising the amino acid
20 sequence of SEQ ID NO: 60.

35. The composition or the kit of any of claims 30 to 34 wherein said anti-
LAG3 antibody molecule has
- a heavy chain comprising the amino acid sequence of SEQ ID NO: 61 and has
25 a light chain comprising the amino acid sequence of SEQ ID NO: 62, or
 - a heavy chain comprising the amino acid sequence of SEQ ID NO: 63 and has a light chain comprising the amino acid sequence of SEQ ID NO: 64, or
 - a heavy chain comprising the amino acid sequence of SEQ ID NO: 65 and has a light chain comprising the amino acid sequence of SEQ ID NO: 66, or
 - 30 - a heavy chain comprising the amino acid sequence of SEQ ID NO: 67 and has a light chain comprising the amino acid sequence of SEQ ID NO: 68, or

- a heavy chain comprising the amino acid sequence of SEQ ID NO: 69 and has a light chain comprising the amino acid sequence of SEQ ID NO: 70.

36. The composition or the kit of any of claims 30 to 35 further comprising one
5 or more additional therapeutic agents.

37. A method of treating cancer comprising administering to a patient in need thereof a therapeutically effective amount of the anti-PD1 antibody molecule of any of claims 1 to 16.
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38. The anti-PD1 antibody molecule of any of claims 1 to 16, for use in a method of treating cancer.

39. Use of the anti-PD1 antibody molecule of any of claims 1 to 16 for
15 preparing a pharmaceutical composition for treating cancer.

40. The method or use of an anti-PD1 antibody molecule of any of claims 37 to 39 further comprising an anti-LAG3 antibody molecule.

20 41. The method or use of claim 40 wherein the anti-PD1 antibody molecule is to be administered simultaneously, concurrently, sequentially, successively, alternatively or separately, with the anti-LAG3 antibody molecule.

42. The method or use of claim 40 or 41 wherein said LAG3 antibody molecule
25 binds an epitope of human LAG3 comprising the amino acid sequence LLRRAGVT (SEQ ID NO: 111) and/or YRAAVHLRDRA (SEQ ID NO: 112).

43. The method or use of claims 40 to 42 wherein said LAG3 antibody molecule comprises:

30 (a) heavy chain CDRs comprising the amino acid sequence of SEQ ID NO:39 (hcCDR1), SEQ ID NO:40 (hcCDR2) and SEQ ID NO:41 (hcCDR3) and

has light chain CDRs comprising the amino acid sequence of SEQ ID NO:42 (lcCDR1), SEQ ID NO:43 (lcCDR2) and SEQ ID NO:44 (lcCDR3); or,

(b) heavy chain CDRs comprising the amino acid sequence of SEQ ID NO:45 (hcCDR1), SEQ ID NO:46 (hcCDR2) and SEQ ID NO:47 (hcCDR3) and

5 has light chain CDRs comprising the amino acid sequence of SEQ ID NO:48 (lcCDR1), SEQ ID NO:49 (lcCDR2) and SEQ ID NO:50 (lcCDR3).

44. The method or use of any of claims 20 to 43 wherein said anti-LAG3 antibody molecule has

10 - a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 51 and has a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 52, or

- a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 53 and has a light chain variable domain comprising the amino acid

15 sequence of SEQ ID NO: 54, or

- a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 55 and has a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 56, or

20 - a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 57 and has a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 58, or

- a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 59 and has a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 60.

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45. The method or use of any of claims 40 to 44 wherein said anti-LAG3 antibody molecule has

- a heavy chain comprising the amino acid sequence of SEQ ID NO: 61 and has a light chain comprising the amino acid sequence of SEQ ID NO: 62, or

30 - a heavy chain comprising the amino acid sequence of SEQ ID NO: 63 and has a light chain comprising the amino acid sequence of SEQ ID NO: 64, or

- a heavy chain comprising the amino acid sequence of SEQ ID NO: 65 and has a light chain comprising the amino acid sequence of SEQ ID NO: 66, or
- a heavy chain comprising the amino acid sequence of SEQ ID NO: 67 and has a light chain comprising the amino acid sequence of SEQ ID NO: 68, or
- 5 - a heavy chain comprising the amino acid sequence of SEQ ID NO: 69 and has a light chain comprising the amino acid sequence of SEQ ID NO: 70.

46. The method or use of any of claims 37 to 45 wherein said cancer is a solid tumor cancer or a cancer of the hematopoietic system.

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47. The method or use of any of claims 37 to 46 wherein the antibody molecule(s) is administered in combination with one or more further therapeutic agents or procedures.

15 48. The method or use of claim 47 wherein the one or more further therapeutic agents or procedures is selected from chemotherapy, a targeted anti-cancer therapy, an oncolytic drug, a cytotoxic agent, an immune-based therapy, a cytokine, surgical procedure, a radiation procedure, an activator of a costimulatory molecule, an inhibitor of an inhibitory molecule, a vaccine, or a
20 cellular immunotherapy.

49. An anti-LAG3 antibody molecule which binds to an epitope of human LAG3 comprising the amino acid sequence LLRRAGVT (SEQ ID NO: 111) and/or YRAAVHLRDRA (SEQ ID NO: 112).

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50. The anti-LAG3 antibody molecule of claim 49 wherein said antibody molecule is a humanized antibody molecule.

51. The anti-LAG3 antibody molecule of claim 49 or 50 wherein said antibody
30 molecule is a monoclonal antibody molecule, Fab, F(ab')₂, Fv or scFv.

52. The anti-LAG3 antibody molecule of any of claims 49 to 51 which comprises a heavy chain constant region selected from the group consisting of IgG1, IgG2, IgG3, IgG4, IgM, IgA and IgE constant regions.
- 5 53. The anti-LAG3 antibody molecule of claim 52 wherein the heavy chain constant region is IgG4, preferably IgG4 with a S241P mutation.
54. The anti-LAG3 antibody molecule of any of claims 49 to 53 wherein the light chain constant region is kappa or lambda.
- 10 55. An anti-LAG3 antibody molecule comprising:
(a) heavy chain CDRs comprising the amino acid sequence of SEQ ID NO:39 (hcCDR1), SEQ ID NO:40 (hcCDR2) and SEQ ID NO:41 (hcCDR3) and has light chain CDRs comprising the amino acid sequence of SEQ ID NO:42 (lcCDR1), SEQ ID NO:43 (lcCDR2) and SEQ ID NO:44 (lcCDR3); or
15 (b) heavy chain CDRs comprising the amino acid sequence of SEQ ID NO:45 (hcCDR1), SEQ ID NO:46 (hcCDR2) and SEQ ID NO:47 (hcCDR3) and has light chain CDRs comprising the amino acid sequence of SEQ ID NO:48 (lcCDR1), SEQ ID NO:49 (lcCDR2) and SEQ ID NO:50 (lcCDR3).
- 20 56. The anti-LAG3 antibody molecule of any of claims 49 to 55 wherein said antibody molecule has a heavy chain variable domain comprising an amino acid sequence at least 85% identical to any of SEQ ID NOs: 51, 53, 55, 57 and 59.
- 25 57. The anti-LAG3 antibody molecule of any of claims 49 to 56 wherein said antibody molecule has a heavy chain variable domain comprising an amino acid sequence of any of SEQ ID NOs: 51, 53, 55, 57 and 59.
58. The anti-LAG3 antibody molecule of any of claims 49 to 57 wherein said antibody molecule has a light chain variable domain comprising an amino acid
30 sequence at least 85% identical to any of SEQ ID NOs: 52, 54, 56, 58 and 60.

59. The anti-LAG3 antibody molecule of any of claims 49 to 58 wherein said antibody molecule has a light chain variable domain comprising the amino acid sequence of SEQ ID NOs: 52, 54, 56, 58 and 60.

5 60. The anti-LAG3 antibody molecule of any of claims 49 to 59 wherein said antibody molecule has a heavy chain comprising the amino acid sequence of SEQ ID NO: 61, 63, 65, 67 or 69.

10 61. The anti-LAG3 antibody molecule of any of claims 49 to 60 wherein said antibody molecule has a light chain comprising the amino acid sequence of SEQ ID NO: 62, 64, 66, 68 or 70.

62. The anti-LAG3 antibody molecule of any of claims 49 to 61 wherein said antibody molecule has

15 - a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 51 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 52, or

- a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 53 and a light chain variable domain comprising the amino acid sequence of

20 SEQ ID NO: 54, or

- a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 55 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 56, or

- a heavy chain variable domain comprising the amino acid sequence of SEQ ID

25 NO: 57 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 58, or

- a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 59 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 60.

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63. The anti-LAG3 antibody molecule of any of claims 49 to 62 wherein said antibody molecule has

- a heavy chain comprising the amino acid sequence of SEQ ID NO: 61 and a light chain comprising the amino acid sequence of SEQ ID NO: 62, or
- a heavy chain comprising the amino acid sequence of SEQ ID NO: 63 and a light chain comprising the amino acid sequence of SEQ ID NO: 64, or
- 5 - a heavy chain comprising the amino acid sequence of SEQ ID NO: 65 and a light chain comprising the amino acid sequence of SEQ ID NO: 66, or
- a heavy chain comprising the amino acid sequence of SEQ ID NO: 67 and a light chain comprising the amino acid sequence of SEQ ID NO: 68, or
- a heavy chain comprising the amino acid sequence of SEQ ID NO: 69 and a
- 10 light chain comprising the amino acid sequence of SEQ ID NO: 70.

64. The anti-LAG3 antibody molecule of any of claims 49 to 63 for use in medicine.

- 15 65. A pharmaceutical composition comprising an anti-LAG3 antibody of any of claims 49 to 63 and a pharmaceutically acceptable carrier.

66. The pharmaceutical composition of claim 65 further comprising
- an anti-PD1 antibody molecule, preferably an anti-PD1 antibody molecule of any
 - 20 of claims 1 to 16, pembrolizumab, or nivolumab, or
 - an anti-PDL-1 antibody molecule, preferably atezolizumab, avelumab or durvalumab.

67. A kit of parts comprising
- 25 - an anti-LAG3 antibody molecule of any of claims 49 to 63 and
 - an antibody molecule selected from the group consisting of anti-PD1 antibody molecules of any of claims 1 to 16, pembrolizumab, nivolumab, atezolizumab, avelumab and durvalumab.

- 30 68. The composition or the kit of parts of any of claims 65 to 67 further comprising one or more additional therapeutic agents.

69. A method of treating cancer comprising administering to a patient in need thereof a therapeutically effective amount of the anti-LAG3 antibody molecule of any of claims 49 to 63.

5 70. The anti-LAG3 antibody molecule of any of claims 49 to 63 for use in a method of treating cancer.

71. Use of an anti-LAG3 antibody molecule of any of claims 49 to 63 for preparing a pharmaceutical composition for treating cancer.

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72. The method or use of any of claims 69 to 71 further comprising an anti-PD1 antibody molecule or an anti-PDL1 antibody molecule.

15 73. The method or use of claim 72 wherein said anti-PD1 antibody molecule is an anti-PD1 antibody molecule of any of claims 1 to 16, pembrolizumab, or nivolumab, or wherein said anti-PDL-1 antibody molecule is atezolizumab, avelumab or durvalumab.

20 74. The method or use of claim 72 or claim 73 wherein the anti-LAG3 antibody molecule is to be administered simultaneously, concurrently, sequentially, successively, alternatively or separately, with the anti-PD1 or anti-PDL1 antibody molecule.

25 75. An isolated nucleic acid molecule encoding the heavy chain variable domain and/or the light chain variable domain of an antibody molecule of any of claims 49 to 63.

30 76. An expression vector containing a nucleic acid molecule encoding the heavy chain variable domain and/or the light chain variable domain of an antibody molecule of any one of claims 49 to 63.

77. The expression vector of claim 76 containing a nucleic acid molecule encoding the heavy chain and/or the light chain of an antibody molecule of any one of claims 49 to 63.

5 78. A host cell transfected with an expression vector of claim 76 or 77.

79. A method of manufacturing an antibody molecule of any of claims 49 to 63 comprising the steps of:

- culturing a host cell according to claim 78 under conditions that allow formation
- 10 of an antibody molecule according to any of claims 49 to 63 and
- recovering said antibody molecule.

80. The method of claim 79, additionally comprising the step of purifying said antibody molecule.

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81. The method of claim 80, additionally comprising the step of formulating said antibody molecule into a pharmaceutical composition.

82. A pharmaceutical combination comprising an anti-PD1 antibody molecule

20 according to any one of claims 1 to 16 and an anti-LAG3 antibody molecule according to any one of claims 49 to 63.

83. A pharmaceutical combination comprising an anti-PD1 antibody molecule selected from the group consisting of anti-PD1 antibody molecules PD1-1, PD1-2,

25 PD1-3, PD1-4, and PD1-5, and an anti-LAG3 antibody molecule selected from the group consisting of anti-LAG3 antibody molecules LAG3-1, LAG3-2, LAG3-3, LAG3-4, and LAG3-5.