

Claims

1. A bispecific molecule comprising at least one anti-CD38 domain and at least one anti-PD-L1 domain, which are capable of simultaneous binding to CD38 and PD-L1 antigens, respectively, wherein the bispecific molecule is a full length antibody comprising two heavy chains and four light chains, wherein each heavy chain comprises
 - a. a Fc region comprising Hinge-CH2-CH3 domains,
 - b. which Fc region is linked to Fab heavy chain (CH1-VH) of antibody 1 (Ab1), wherein the Fc region is linked to the C-terminus of the CH1 domain of Ab1,
 - c. which in turn is linked to the Fab heavy chain (CH1-VH) of antibody 2 (Ab2), by a hinge-derived polypeptide linker sequence, wherein said polypeptide linker sequence links the N-terminus of said Fab heavy chain VH domain of Ab1 with the C-terminus of said CH1 domain of Ab2,and the four light chains comprise Fab light chains (CL-VL) of Ab1 and Fab light chains (CL-VL) of Ab2 associated with their cognate heavy chain domains; Ab1 and Ab2 being different and selected from the group consisting of anti-CD38 antibodies and anti-PD-L1 antibodies.
2. The bispecific molecule of claim 1, wherein Ab1 is an anti-CD38 antibody, and Ab2 is an anti-PD-L1 antibody.
3. The bispecific molecule of claim 1, wherein Ab1 is an anti-PD-L1 antibody, and Ab2 is an anti-CD38 antibody.
4. The bispecific molecule of any of claims 1 to 3, wherein the anti-CD38 antibody is selected from the group consisting of daratumumab, isatuximab, or MOR-202 .
5. The bispecific molecule of any of claims 1 to 4, wherein the anti-PD-L1 antibody is selected from the group consisting atezolizumab, durvalumab, avelumab, or MDX-1105.
6. The bispecific molecule of any of claims 1 to 5, wherein the CH1 and CL domains of Ab1 have a sequence different from the CH1 and CL domains of Ab2.

7. The bispecific molecule of any of claims 1 to 5, wherein the Fab CH1 domain of one of Ab1 or Ab2 is a mutated domain that derives from the CH1 domain of an immunoglobulin by substitution of the threonine residue at position 192 of said CH1 domain with an aspartic acid and the cognate CL domain is a mutated domain that derives from the CL domain of an immunoglobulin by substitution of the asparagine residue at position 137 of said CL domain with a lysine residue and substitution of the serine residue at position 114 of said CL domain with an alanine residue, and/or wherein the Fab CH1 domain of the other of Ab1 or Ab2 is a mutated domain that derives from the CH1 domain of an immunoglobulin by substitution of the leucine residue at position 124 of said CH1 domain with a glutamine and substitution of the serine residue at position 188 of said CH1 domain with a valine residue, and the cognate CL domain is a mutated domain that derives from the CL domain of an immunoglobulin by substitution of the valine residue at position 133 of said CL domain with a threonine residue and substitution of the serine residue at position 176 of said CL domain with a valine residue, wherein the amino acid numbering is according to Kabat numbering.
8. The bispecific molecule of any of claims 1 to 7, which comprises a) two heavy chains, each comprising SEQ ID NO:10 and b) four light chains, two comprising SEQ ID NO:11 and the two others comprising SEQ ID NO: 12.
9. The bispecific molecule of any of claims 1 to 8, wherein the bispecific molecule consists of a) two heavy chains, each consisting of, SEQ ID NO:10 and b) four light chains, two consisting of, SEQ ID NO:11 and the two others consisting of SEQ ID NO: 12.
10. A method for producing the bispecific molecule of any of claims 1 to 9, said method comprising the following steps:
 - a. Culturing in suitable medium and culture conditions a host cell expressing the antibody heavy chain(s) as defined in any of claims 1 to 9, and the antibody light chain(s) as defined in any of claims 1 to 9, and
 - b. Recovering said produced antibodies from the culture medium or from said cultured cells.
11. The bispecific molecule of any of claims 1 to 9, for use as a medicament.

12. The bispecific molecule of any of claims 1 to 9, for use in treating a cancer .
13. The bispecific molecule of claim 12, for use in treating a multiple myeloma, lymphoma or leukemia.
14. Use of the bispecific molecule according to any of claim 1 to 9, in the preparation of a medicament for treating a cancer.
15. The use according to claim 14, wherein the medicament is for treating multiple myeloma, lymphoma or leukemia.