

Claims

1. A multivalent programmed death ligand 1 (PD-L1) binding compound comprising,

a recombinant Adenovirus (Ad) comprising capsid hexon polypeptides of an Adenovirus strain Ad6 and at least one capsid hexon hypervariable region (HVR) polypeptide from Adenovirus strain Ad57,

wherein the recombinant Ad comprises a plurality of amino acid chains bound to the surface of the recombinant Ad,

wherein each amino acid chain comprises at least one programmed cell death protein 1 (PD-1) polypeptide.
2. The PD-L1 binding compound of Claim 1, wherein the capsid hexon polypeptides of the Adenovirus strain Ad6 comprise HVR polypeptides 1-7 from Adenovirus strain Ad57.
3. The PD-L1 binding compound of Claim 1, wherein the capsid hexon polypeptides of the Adenovirus strain Ad6 comprise HVR polypeptides 2-7 from Adenovirus strain Ad57.
4. The PD-L1 binding compound of Claim 1, wherein the recombinant Ad is a conditionally-replicating Adenovirus (CRAd) which has been modified in an E1A gene encoding an E1A polypeptide, wherein the CRAd exhibits amino acid substitutions in the E1A polypeptide relative to wild-type E1A polypeptide of an Ad strain.
5. The PD-L1 binding compound of Claim 4, wherein the recombinant Ad is a conditionally-replicating Adenovirus (CRAd) wherein the N-terminal portion of the E1A polypeptide comprises an amino acid sequence set forth in SEQ ID NO:32, SEQ ID NO:33 or SEQ ID NO:34.

6. The PD-L1 binding compound of Claim 1, wherein the PD-1 polypeptide is in the form of a fusion protein with a heterologous polypeptide selected from targeting polypeptides, therapeutic polypeptides and/or antigens.
7. The PD-L1 binding compound of Claim 1, wherein the PD-1 polypeptide is a human PD-1 or a murine PD-1.
8. The PD-L1 binding compound of Claim 1, wherein the PD-1 polypeptide exhibits higher affinity interactions with PD-L1 relative to a wild-type PD-1 protein.
9. The PD-L1 binding compound of Claim 1, wherein the PD-1 polypeptide is a fragment of a human PD-1 polypeptide, wherein the fragment of the human PD-1 polypeptide comprises one or more amino acid changes relative to a wild type PD-1, which changes cause an increased affinity for human PD-L1.
10. The PD-L1 binding compound of Claim 1, wherein the recombinant Ad comprises an expression cassette comprising a promoter operably linked to nucleic acids encoding a PD-1 polypeptide which allows for expression of the PD-1 polypeptide in eukaryotic cells.
11. The PD-L1 binding compound of Claim 1, wherein the recombinant Ad comprises nucleic acids which encode one or more therapeutic polypeptides.
12. The PD-L1 binding compound of Claim 11, wherein the recombinant Ad comprises nucleic acids which encode an antibody.
13. The PD-L1 binding compound of Claim 1, wherein the recombinant Ad comprises an expression cassette comprising a promoter operably linked to nucleic acids encoding a therapeutic polypeptide which allows for expression of therapeutic polypeptides in eukaryotic cells.

14. The PD-L1 binding compound of Claim 13, wherein the therapeutic polypeptides are selected from a 4-1BB ligand polypeptide, a OX40 ligand polypeptide, a CD40 ligand polypeptide, and a granulocyte-macrophage colony-stimulating factor polypeptide.
15. The PD-L1 binding compound of Claim 6, wherein the PD-1 polypeptide is fused to a heterologous polypeptide which is a Vitamin K-dependent gamma-carboxyglutamic domain of a factor X single-chain antibody polypeptide (a GLA domain of an FX polypeptide).
16. A pharmaceutical composition comprising the multivalent PD-L1 binding compound of any one of Claims 1 to 15 and a pharmaceutically acceptable carrier.
17. Use of the multivalent PD-L1 binding compound of any one of Claim 1 to 15 in the preparation of a medicament for treating cancer in a subject, wherein cancer cells of the cancer are positive for PD-L-1 expression.
18. The use of claim 17, wherein the subject is identified as having a cancer selected from the group consisting of breast cancer, lung cancer, melanoma and renal cancer.
19. The use of Claim 17 or Claim 18, further comprising one or more cancer therapeutics to be administered to the subject.
20. The use of Claim 19, wherein the cancer therapeutic is an immunotherapy which targets PD-1/PD-L1 pathways.
21. The use of Claim 20, wherein the immunotherapy is selected from the group consisting of nivolumab, pembrolizumab, atezolizumab, avelumab, cemiplimab, and durvalumab.

22. Use of

a multivalent programmed death ligand 1 (PD-L1) binding compound comprising a recombinant Adenovirus (Ad) comprising capsid hexon polypeptides of an Adenovirus strain Ad6 and at least one capsid hexon hypervariable region (HVR) polypeptide from Adenovirus strain Ad57,

wherein the recombinant Ad comprises a plurality of amino acid chains displayed on the surface of the recombinant Ad, and

wherein each amino acid chain comprises at least one programmed cell death protein 1 (PD-1) polypeptide,

in the preparation of a medicament for treating cancer in a subject, wherein cancer cells of the cancer are positive for PD-L1 expression.