One aspect as reported herein is a disulfide-linked multivalent multi-function protein, characterized in that it comprises

- one or two antigen presenting domains,
- one antibody Fc-region, and
- one or more antigen binding sites,

wherein the antigen presenting domain comprises in N- to C-terminal direction

(i) a T-cell response eliciting peptide,

(ii) a β2-microglobulin, and

(iii) an extracellular domains α1, α2, and α3 of a class I MHC molecule with a relative frequency of 1 % or more,

wherein the antigen binding site binds to a cancer cell surface antigen,

wherein the antigen presenting domain comprises an intrachain/interdomain disulfide bond which is formed between a first cysteine residue that is arranged in a linker connecting the T-cell response eliciting peptide and β2-microglobulin and a second cysteine residue that is introduced in the extracellular domains α1, α2, and α3 of the class I MHC molecule.

In one embodiment one non-naturally occurring cysteine residue in the antigen presenting domain is in the linker between T-cell response eliciting peptide and one

Patent Claims

1. A disulfide-linked multivalent multi-function protein, characterized in that it comprises

- one or two antigen presenting domains,

- one antibody Fc-region, and

- one or more antigen binding sites,

wherein the antigen presenting domain comprises in N- to C-terminal direction

(i) a T-cell response eliciting peptide,
(ii) a β2-microglobulin, and
(iii) an extracellular domains α1, α2, and α3 of a class I MHC molecule with a relative frequency of 1 % or more,

wherein the antigen binding site binds to a cancer cell surface antigen,

wherein the antigen presenting domain comprises an intrachain/interdomain disulfide bond which is formed between a first cysteine residue that is arranged in a linker connecting the T-cell response eliciting peptide and β2-microglobulin and a second cysteine residue that is introduced in the extracellular domains α1, α2, and α3 of the class I MHC molecule.

2. The disulfide-linked multivalent multi-function protein according to claim 1, characterized in that the antigen binding site comprises i) a pair of an antibody heavy chain and an antibody light chain, or ii) a scFv fusion polypeptide comprising in N- to C-terminal direction a scFv antibody fragment and an antibody Fc-region polypeptide, or iii) a scFab fusion polypeptide comprising in N- to C-terminal direction a scFab and an antibody Fc-region polypeptide,

or

the antigen binding sites comprise independently of each other i) a (cognate) pair of an antibody heavy chain and an antibody light chain, whereby the individual chains can be wild-type chains or modified chains (substituted, mutated or domain exchanged), or ii) a scFv fusion polypeptide comprising in N- to C-terminal direction a scFv antibody fragment and an antibody Fc-region polypeptide, or iii) a scFab fusion polypeptide comprising in N- to C-terminal direction a scFab and an antibody Fc-region polypeptide.

3. The disulfide-linked multivalent multi-function protein according to any one of claims 1 or 2, characterized in that i) an antigen presenting domain is linked to the N-terminus of the heavy chain or to the N-terminus of the light chain of an antigen binding site, or ii) one antigen presenting domain is linked to each N-terminus of the heavy chain or to each N-terminus of the light chain of each antigen binding site, or iii) an antigen presenting domain is linked to the C-terminus of the heavy chain or to the C-terminus of the light chain of the antigen binding site, or vi) one antigen presenting domain is linked to each C-terminus of the heavy chain or to each C-terminus of the light chain of each antigen binding site, or v) an antigen presenting domain is linked to the N- or C-terminus of an scFv fusion polypeptide, or vi) one antigen presenting domain is linked to each N- or C-terminus of each scFv fusion polypeptide, or vii) an antigen presenting domain is linked to the N- or C-terminus of a scFab fusion polypeptide, or viii) one antigen presenting domain is linked to each N- or C-terminus of each scFab fusion polypeptide, or ix) an antigen presenting domain is linked to the N- or C-terminus of the second Fc-region polypeptide, or x) one antigen presenting domain is linked to the N- or C-terminus of the first Fc-region polypeptide and one antigen presenting domain is linked to the N- or C-terminus of the second Fc-region polypeptide.

4. The disulfide-linked multivalent multi-function protein according to any one of claims 1 to 3, characterized in that the T-cell response eliciting peptide is a human cytomegalovirus-derived peptide.

5. The disulfide-linked multivalent multi-function protein according to any one of claims 1 to 4, characterized in that the virus-derived peptide has the amino acid sequence of SEQ ID NO: 01.

6. The disulfide-linked multivalent multi-function protein according to any one of claims 1 to 5, characterized in that the class I MHC molecule with a relative frequency of 1 % or more is selected from the group comprising HLA-A*0201, HLA-A*1101, HLA-A*2402, HLA-A*340101, HLA-C*0304, HLA-C*0401, and HLA-C*0702.

7. The disulfide-linked multivalent multi-function protein according to any one of claims 1 to 6, characterized in that the class I MHC molecule with a relative frequency of less than 1 % is selected from the group comprising HLA-B*4201, HLA-B*5901, HLA-B*6701, and HLA-B*7802.

8. A pharmaceutical formulation comprising the disulfide-linked multivalent multi-function protein according to any one of claims 1 to 7 and optionally a pharmaceutically acceptable carrier.

9. The disulfide-linked multivalent multi-function protein according to any one of claims 1 to 7 for use as a medicament.

10. The disulfide-linked multivalent multi-function protein according to any one of claims 1 to 7 for use in treating cancer.

11. The disulfide-linked multivalent multi-function protein according to any one of claims 1 to 7 for use in attracting virus-specific cytotoxic T-cells of an individual to a target.

12. The disulfide-linked multivalent multi-function protein according to any one of claims 1 to 7 for use in removal of cancer cells or virus infected cells.