much needed. Blood cancers are predominantly a disease of old age, so as global longevity continues to increase, the need for improved treatments will only increase further.

[0003] The present invention provides technical advancements to both treatment and diagnosis in blood cancer. The underlying technical problem is thus to address these aspects.

SUMMARY

[0004] The technical problem is solved by the subject-matter as defined in the claims, described in the claims, demonstrated in the examples, and illustrated in the figures. The inventors surprisingly found that serine/arginine repetitive matrix protein 2 (SRRM2; UniProt Q9UQ35), typically localized to the nucleus, is expressed on the surface of blood cancer cells, but not on healthy, non-cancer cells. Thus, surface SRRM2 on the cells obtained from a patient is a biomarker for blood cancer. Furthermore, this selective expression of SRRM2 on the surface of blood cancer cells allows the development of novel blood cancer-specific therapies. The utility of the present disclosure was demonstrated by its use in successfully treating blood cancer in two patients, as defined herein. Specifically, a significantly increased number of surface SRRM2-positive (abnormal) plasma cells could be detected in MM patients, when compared to the number of SRRM2-positive cells in a healthy subject. Further, treatment of MM and PCL patients with SRRM2 specific CAR-T cells led to reduction of cancer-associated plasma cells. Moreover, surface SRRM2 was also found to be significantly elevated on leukemia cells, specifically leukemic blast cells of AML and MM patients, when compared to the expression on normal blood cells and HSC. Notably, AML patients with FMS-like tyrosine kinase-3 (FLT3) mutation showed a significantly higher expression of surface SRRM2 than AML patients without any genetic mutation or other mutations. Further, SRRM2 was highly expressed on newly diagnosed and previously diagnosed MM patients. Moreover, SRRM2 specific CAR-T cells showed potent killing activity *in vitro* in myeloid leukemia cell lines. Further, leukemia blast elimination could be observed *in vivo* in an AML tumor-bearing mouse model. In addition, significant tumor suppression could be observed in a KMS-11-luc CDX MM mouse model. In sum, the data provided herein strongly point to SRRM2 as an optimal and promising target for immunotherapy in blood cancer patients, particularly AML, PCL or MM patients, as well as diagnosing blood cancer, particularly AML, PCL or MM, based on SRRM2 located at the cell surface.

[0004a] In one aspect, the disclosure provides a use of an antibody that binds to human serine/arginine repetitive matrix protein 2 (SRRM2) present on the cell surface of a target cell in the manufacture of a medicament for treating blood cancer in a human patient.

[0004b] In another aspect, the disclosure provides a method for determining whether a patient may suffer from blood cancer, comprising determining in a sample obtained from said patient

whether SRRM2 is present on the cell surface of cells comprised by said sample and/or whether SRRM2 is present on the surface of extracellular vesicles.

[0005] Accordingly, the present disclosure provides an antibody that binds to human serine/arginine repetitive matrix protein 2 (SRRM2) present on the cell surface of a target cell, for use in a method for the treatment of blood cancer in a human patient, in which the patient to be treated has a weight of between 16 and 150 kilograms.

[0024] It is further envisaged in the context of the present disclosure that the blood cancer patient to be treated with the antibody binding to human SRRM2 is refractory to previous cancer therapy and/or in relapse after previous cancer therapy.

[0025] The antibody that binds to human SRRM2 may be used in a method of treatment wherein the route of antibody administration is parenteral, including, but not limited to, intravenous, intradermal, intramuscular, intrathecal, epidural, intracerebral, or intraperitoneal administration.

[0026] The antibody that binds to human SRRM2 present on the cell surface of a target cell may be conjugated with a cytotoxic substance.

[0027] The antibody that binds to human SRRM2 present on the cell surface of a target cell may bind to non-permeabilised cells.

[0028] The antibody that binds to human SRRM2 present on the cell surface of a target cell may bind to living cells.

[0029] Furthermore, the present disclosure relates to an antibody that binds to human SRRM2 wherein the antibody is used in a method for determining whether a patient may suffer from blood cancer, comprising determining in a sample obtained from said patient whether SRRM2 is present on the cell surface of cells comprised by said sample and/or whether SRRM2 is present on the surface of extracellular vesicles. In the method for determining whether a patient may suffer from blood cancer, an increased amount of SRRM2 on the cell surface of cells and/or present on the surface of extracellular vesicles comprised by a sample obtained from said patient compared to the amount of SRRM2 on the cell surface and/or extracellular vesicles in a sample obtained from a healthy subject indicates that the patient may suffer from blood cancer. No difference in the amount of SRRM2 on the cell surface of cells and/or present on the surface of extracellular vesicles comprised by a sample obtained from said patient when compared to the amount of SRRM2 on the cell surface and/or extracellular vesicles in a sampled obtained from a healthy subject indicates that the patient may not suffer from blood cancer.

[0030] The antibody that binds to human SRRM2 may preferably be an antibody comprising (a) a heavy chain variable region having the amino acid sequence as set forth in SEQ ID NO: 1, and a light chain variable region having the amino acid sequence as set forth in SEQ ID NO: 2, (b) a heavy chain variable region having the amino acid sequence as set forth in SEQ ID NO: 3,

Claims

1. Use of an antibody that binds to human serine/arginine repetitive matrix protein 2 (SRRM2) present on the cell surface of a target cell in the manufacture of a medicament for treating blood cancer in a human patient.

2. The use of claim 1, wherein the patient has a weight of between 16 and 150kg.

3. The use of any of the preceding claims in which the patient is between 2 and 80 years old.

4. The use of any of the preceding claims, wherein said antibody has cytotoxic activity, preferably antigen-dependent cellular cytotoxicity (ADCC) and/or complement-dependent cytotoxicity (CDC).

5. The use of any of the preceding claims, wherein said antibody is part of a chimeric antigen receptor (CAR).

6. The use of claim 5, wherein said CAR is expressed by a T cell, NK cell, NK-T cell or macrophage.

7. The use of any of the preceding claims, wherein SRRM2 present on the cell surface of a target cell is externalized.

8. The use of any of the preceding claims, wherein said blood cancer is a blood cancer characterized by cells expressing human SRRM2 on their cell surface.

9. The use of any of claims 1 to 8, wherein said blood cancer is multiple myeloma.

10. The use of any of claims 1 to 8, wherein said blood cancer is leukemia, including acute erythroid leukemia, acute lymphoblastic leukemia (ALL), acute megakaryoblastic leukemia, acute myeloid leukemia (AML), acute promyelocytic leukemia (APL), chronic lymphocytic leukemia (CLL), chronic myeloid leukemia (CML), chronic myelomonocytic leukemia (CMML), childhood leukemia, hairy cell leukemia (HCL), large granular lymphocytic leukemia (LGLL), mast cell leukemia (MCL), or plasma cell leukemia (PCL).

11. The use of any of claims 1 to 8, wherein said blood cancer is acute myeloid leukemia (AML).

12. The use of any of claims 1 to 8, wherein said blood cancer is plasma cell leukemia (PCL).

13. The use of claim 12, wherein said PCL is primary or secondary PCL.

14. The use of any of claims 1 to 8, wherein said blood cancer is lymphoma, including Burkitt lymphoma, diffuse large B-cell lymphoma (DLBCL), follicular lymphoma, hodgkin lymphoma, non-Hodgkin lymphoma, MALT lymphoma, mantle cell lymphoma, small lymphocytic lymphoma (SLL), post-transplant lymphoproliferative disorder (PTLD), or Waldenström macroglobulinaemia (WM).

15. The use of any of claims 1 to 8, wherein said blood cancer is a myelodysplastic syndrome, a myeloproliferative neoplasm (including polycthaemia vera, essential thrombocythaemia, or myelofibrosis), Erdheim-Chester disease, Langerhans cell histiocytosis, mastocytosis, or mast cell leukemia.

16. The use of any of the preceding claims, wherein said antibody is conjugated with a cytotoxic substance.

17. The use of any of the preceding claims, wherein said antibody binds to non-permeabilised cells.

18. The use of any of the preceding claims, wherein said antibody binds to living cells.

19. The use of any of the preceding claims, wherein said antibody is an antibody comprising
(a) a heavy chain variable region comprising heavy chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 9, heavy chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 10, and heavy chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 11, and
a light chain variable region comprising light chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 12, light chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 13, and light chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 14;
(b) a heavy chain variable region comprising heavy chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 15, heavy chain CDR2 having the amino acid

sequence as set forth in SEQ ID NO: 16, and heavy chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 17, and

a light chain variable region comprising light chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 18, light chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 19, and light chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 20;

(c) a heavy chain variable region comprising heavy chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 21, heavy chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 22, and heavy chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 23, and

a light chain variable region comprising light chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 24, light chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 25, and light chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 26; or

(d) a heavy chain variable region comprising heavy chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 21, heavy chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 22, and heavy chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 23, and

a light chain variable region comprising light chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 27, light chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 28, and light chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 29.

20. The use of any of the preceding claims, wherein said antibody is an antibody comprising

(a) a heavy chain variable region having the amino acid sequence as set forth in SEQ ID NO: 1 and a light chain variable region having the amino acid sequence as set forth in SEQ ID NO: 2,

(b) a heavy chain variable region having the amino acid sequence as set forth in SEQ ID NO: 3, and a light chain variable region having the amino acid sequence as set forth in SEQ ID NO: 4,

(c) a heavy chain variable region having the amino acid sequence set forth in SEQ ID NO: 5, and light chain variable region having the amino acid sequence as set forth in SEQ ID NO: 6, or

(d) a heavy chain variable region having the amino acid sequence set forth in SEQ ID NO: 5, and light chain variable region having the amino acid sequence as set forth in SEQ ID NO: 7.

21. A method for determining whether a patient may suffer from blood cancer, comprising determining in a sample obtained from said patient whether SRRM2 is present on the cell surface of cells comprised by said sample and/or whether SRRM2 is present on the surface of extracellular vesicles.

22. The method of claim 21, wherein an increased amount of SRRM2 on the cell surface of cells comprised by said sample and/or present on the surface of extracellular vesicles when compared to the amount of SRRM2 on the cell surface of cells comprised by said sample and/or present on the surface of extracellular vesicles in a sample obtained from a healthy subject indicates that the patient may suffer from blood cancer.

23. The method of claim 21, wherein no difference in the amount of SRRM2 on the cell surface of cells and/or present on the surface of extracellular vesicles comprised by a sample obtained from said patient when compared to the amount of SRRM2 on the cell surface and/or extracellular vesicles in a sampled obtained from a healthy subject indicates that the patient may not suffer from blood cancer.

24. The method of any of claims 21 to 23, wherein said antibody is an antibody comprising (a) a heavy chain variable region comprising heavy chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 9, heavy chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 10, and heavy chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 11, and
a light chain variable region comprising light chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 12, light chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 13, and light chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 14;
(b) a heavy chain variable region comprising heavy chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 15, heavy chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 16, and heavy chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 17, and
a light chain variable region comprising light chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 18, light chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 19, and light chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 20;
(c) a heavy chain variable region comprising heavy chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 21, heavy chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 22, and heavy chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 23, and

a light chain variable region comprising light chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 24, light chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 25, and light chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 26; or

(d) a heavy chain variable region comprising heavy chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 21, heavy chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 22, and heavy chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 23, and

a light chain variable region comprising light chain CDR1 having the amino acid sequence as set forth in SEQ ID NO: 27, light chain CDR2 having the amino acid sequence as set forth in SEQ ID NO: 28, and light chain CDR3 having the amino acid sequence as set forth in SEQ ID NO: 29.

25. The method of any of claims 21 to 24, wherein said antibody is an antibody comprising

(a) a heavy chain variable region having the amino acid sequence as set forth in SEQ ID NO: 1 and a light chain variable region having the amino acid sequence as set forth in SEQ ID NO: 2,

(b) a heavy chain variable region having the amino acid sequence as set forth in SEQ ID NO: 3, and a light chain variable region having the amino acid sequence as set forth in SEQ ID NO: 4,

(c) a heavy chain variable region having the amino acid sequence set forth in SEQ ID NO: 5, and light chain variable region having the amino acid sequence as set forth in SEQ ID NO: 6, or

(d) a heavy chain variable region having the amino acid sequence set forth in SEQ ID NO: 5, and light chain variable region having the amino acid sequence as set forth in SEQ ID NO: 7.