demonstrated that Acute Myeloid Leukemia (AML) blasts show an arginase-dependent ability to inhibit T-cell proliferation and hematopoietic stem cells. Furthermore, arginase and iNOS inhibitors reduce the suppressive activity of AML.

In mammals, two arginase isoenzymes exist: Arginase1 and Arginase2. The two isoenzymes catalyse the same biochemical reaction (and thus cannot be disntinguished by enzymatic assays) but differ in cellular expression, regulation and subcellular localisation.

Summary

The present inventors have previously identified a 50 amino acid region of Arginase1 and Arginase2 which is a "hot spot" for immunogenicity. This region corresponds to positions 161-210 of full length human Arginase1 (SEQ ID NO: 53) or positions 180 – 229 of full length human Arginase2 (SEQ ID NO: 51), or corresponding positions in murine Arginases. The region and peptides derived from it are described in WO2018065563. The present inventors have also identified that a specific sub-set of polypeptides derived from the "hot spot" region of Arginase1 are particularly effective at stimulating immune responses. These peptides correspond to positions 169-206 of full length human Arginase1, positions 169-200 of full length human Arginase1 or positions 169-210 of full length human Arginase1 (or corresponding positions in human Arginase2 or murine Arginase1). This sub-set of polypeptides is described in PCT/EP2019/075731 and its priority application GB1815549.9.

The present inventors have now identified that polypeptides derived from an entirely different region of human Arginase2 are particularly effective at stimulating immune responses. Surprisingly, the region spans the C-terminus of the transit peptide of human Arginase2 (position 22 of SEQ ID NO: 51 – see schematic diagram in Figure 7). Sequence identity to human Arginase1 is relatively low in this region.

The polypeptides of the present disclosure are expected to be particularly effective at stimulating a beneficial immune response against Arginase2 and Arginase2-expressing cells. The development of novel immune therapies for cancer requires a thorough understanding of the molecules that are involved in the pathogenesis as well as the specific proteins recognized by the immune system. In the clinical setting the induction of Arginase specific immune responses could in addition to the killing of cancer cells support anti-cancer immune responses in general by suppressing the immune suppressive function of Arginase expressing cells especially MDSC and tumor-associated macrophages (TAMs). Hence, since Arginase-expressing cells antagonize the desired effects of other immunotherapeutic approaches targeting myeloid dendritic cells e.g. by vaccination with the polypeptides of the present disclosure, would consequently be highly synergistic with additional anti-cancer immunotherapy.

The present disclosure provides a polypeptide which is an immunogenic fragment of human Arginase2 (SEQ ID NO: 51) that consists of a sequence of at least 20 and up to 50 consecutive amino acids of SEQ ID NO: 51 which (i) include at least the amino acids at positions 21, 22 and 23 of SEQ ID NO: 51, or (ii) are selected from positions 180 – 229 of SEQ ID NO: 51. The polypeptide may comprise or consist of up to 15, 20, 25, 30, 35, 40, 45 or 50 consecutive amino acids of SEQ ID NO: 51 as defined in (i) or (ii). The polypeptide may comprise or consist of the amino acid sequence of any one of SEQ ID NOs: 59, 58, 57, 54, 55,

CLAIMS

1. A polypeptide which is an immunogenic fragment of human Arginase2 (SEQ ID NO: 51) that consists of a sequence of at least 20 and up to 50 consecutive amino acids of SEQ ID NO: 51 which include at least the amino acids at positions 21, 22 and 23 of SEQ ID NO: 51.

2. The polypeptide of claim 1 which consists of up to 25, 30, 35, 40 or 45 consecutive amino acids of SEQ ID NO: 51.

3. The polypeptide of claim 1 or 2 which comprises the amino acid sequence of any one of SEQ ID NOs: 59, 58, 57, 54, 55, 56, 2 or 3, or which consists of the amino acid sequence of any one of SEQ ID NOs: 59, 58, 57, 2 or 3.

4. The polypeptide of any one of the preceding claims, which has a maximum length of 20, 25, 30, 35, 40, 45 or 50 amino acids and/or in which the C terminal amino acid is replaced with the corresponding amide.

5. A composition comprising the polypeptide of any one of the preceding claims and an adjuvant.

6. A composition according to claim 5, comprising at least one pharmaceutically acceptable diluent, carrier or preservative.

7. A composition according to claim 5 or 6 wherein the adjuvant is selected from the group consisting of bacterial DNA based adjuvants, oil/surfactant based adjuvants, viral dsRNA based adjuvants, imidazoquinolines, and a Montanide ISA adjuvant.

8. The polypeptide of any one of claims 1 to 4 or the composition of any one of claims 5 to 7 for use in therapy.

9. Use of the polypeptide of any one of claims 1 to 4 or the composition of any one of claims 5 to 7 in the manufacture of a medicament for treating a cancer.

10. The use of claim 9, wherein the use further comprises the simultaneous or sequential administration of an additional cancer therapy.

11. The use of claim 10 wherein the additional cancer therapy is an immune system checkpoint inhibitor.

12. The use of claim 11, wherein the immune system checkpoint inhibitor is an antibody.

13. The use of claim 12 wherein the antibody is an anti-PD1 antibody.

14. The use of any one of claims 9 to 13 wherein said cancer is cancer of the kidney, prostate, breast, brain, head and neck, or small intestine, or is a colorectal or gastric cancer, or is a melanoma, or is a leukemia.

15. The use of claim 14, wherein the leukemia is acute myeloid leukemia (AML).

16. A method of stimulating arginase2-specific T cells, the method comprising contacting the cells with the polypeptide of any one of claims 1 to 4 or the composition of claim 5 to 7, wherein the method is performed *ex vivo*.

17. The method of claim 16, wherein the cells are present in a sample taken from a healthy subject or from a cancer patient.

18. The method of claim 16, wherein the cells are present in a tumour sample.

19. A nucleic acid encoding a polypeptide according to any one of claims 1 to 4.