by normal cells, but are broadly upregulated by a variety of different cancers secondary to genomic damage. MIC is an important ligand for the NKG2D receptor on cytotoxic lymphocytes, specifically NK cells, CD8 T cells and gamma-delta T cells. Expression of MIC targets such cells for elimination by the immune system. However, many tumors are found to escape this important immune surveillance pathway by shedding MIC from the cell surface, a process in which the MIC alpha3 domain is unfolded by the disulfide isomerase ERp5 rendering it sensitive to cleavage by matrix metalloproteases such as ADAM 10 and ADAM 17. Shed MIC causes downregulation of the NKG2D receptor on NK cells and CD8 T cells. Proteolytic cleavage thus turns an immune-stimulatory protein into an immunosuppressive substance.

[0007] Thus a need exists for compounds to inhibit MICA shedding.

SUMMARY

[0007a] In one aspect, the present disclosure provides a fusion protein comprising a monomeric ferritin subunit protein joined to a MIC alpha 3-domain protein , wherein the MIC alpha 3-domain protein comprises the amino acid sequence of SEQ ID NO: 3 or SEQ ID NO: 4 or an amino acid sequence at least 90% identical thereto, and wherein the monomeric ferritin subunit protein comprises a domain that allows the fusion protein to self-assemble into nanoparticles.

[0007b] In another aspect, the present disclosure provides a nanoparticle comprising the fusion protein disclosed herein.

[0007c]In yet another aspect, the present disclosure provides a vaccine composition comprising the nanoparticle disclosed herein.

[0007d] In yet another aspect, the present disclosure provides use of a fusion protein, a nanoparticle or a vaccine composition disclosed herein in the manufacture of a medicament for treating cancer in a subject.

[0008] Disclosed are vaccine compositions including as an immunogenic component, an effective amount of a peptide including the MIC alpha 3-domain. By effective amount means an amount effective to elicit an immune response against the MIC alpha 3-domain.

[0009] The MIC alpha 3-domain is a MICA or MICB alpha 3-domain. Optionally, the MIC alpha 3-domain is non glycosylated. Preferably, the peptide includes amino acid sequence of SEQ ID NO: 3 or SEQ ID NO: 4. Also disclosed is that the vaccine composition comprises a plurality of peptides. Also disclosed is that the peptide is conjugated to a carrier protein.

[00010] Also disclosed is a fusion protein having a monomeric ferritin subunit protein joined to a MIC alpha 3-domain protein. The monomeric ferritin subunit protein has a domain that allows the fusion protein to self-assemble into nanoparticles. In a preferred example, the monomeric subunit is a Helicobacter pylori ferritin protein. Optionally, the fusion protein is further conjugated to a CpG oligonucleotide.

[00011] Also disclosed is a nanoparticle including the fusion protein according to the disclosure. The nanoparticle includes a plurality of MIC alpha 3-domain peptides.

We Claim:

1. A fusion protein comprising a monomeric ferritin subunit protein joined to a MIC alpha 3-domain protein, wherein the MIC alpha 3-domain protein comprises the amino acid sequence of SEQ ID NO: 3 or SEQ ID NO: 4 or an amino acid sequence at least 90% identical thereto, and wherein the monomeric ferritin subunit protein comprises a domain that allows the fusion protein to self-assemble into nanoparticles.

2. The fusion protein of claim 1, wherein the monomeric ferritin subunit is a monomeric subunit of a Helicobacter pylori ferritin protein.

3. A nanoparticle comprising the fusion protein of claim 1 or 2.

4. A vaccine composition comprising the nanoparticle of claim 3.

5. Use of a fusion protein of claim 1 or 2; or a nanoparticle of claim 3; or a vaccine composition of claim 4 in the manufacture of a medicament for treating cancer in a subject.

6. The use of claim 5, wherein the vaccine composition is to be administered as part of a therapeutic regimen.

7. The use of claim 6, wherein the therapeutic regimen is radiation therapy, targeted therapy, immunotherapy, or chemotherapy.

8. The use of any one of claims 5-7, wherein said subject has tested positive for shed MIC in their serum.

9. The use of any one of claims 5-8, wherein one or more vaccines specific for an antigen other than a MIC alpha 3-domain antigen is/are to be administered to the subject.

10. The vaccine composition of claim 4, further comprising an adjuvant.

11. The vaccine composition of claim 10, wherein the adjuvant is selected from: aluminum phosphate, benzyalkonium chloride, ubenimex, QS21, IL-2, granulocyte macrophage colony-stimulating factor (GM-CSF), IL-18, chemokine (C--C motif) ligand 21 (CCL21), IL-6, CpG, LPS, TLR agonists, cationic liposomes, N3 (cationic lipid), monophosphoryl lipid A (MPL1), cholera toxin, enterotoxin, Fms-like tyrosine kinase-3 ligand (Flt-3L), bupivacaine, marcaine, and levamisole.

12. The fusion protein of claim 1, wherein the fusion protein is further conjugated to a CpG oligonucleotide sequence.