target antigens, the ability of NK cells to bind to the constant region of antibodies, enables NK cells to specifically kill the cells that are tagged with antibodies. The NK cell's recognition of the antibodies is mediated by Fc receptor (of the NK cell) binding to the Fc portion of the antibody. This type of killing is called, antibody-dependent cell cytotoxicity (ADCC). NK cells can also kill cells independent of the mechanism of ADCC, where this killing requires expression of MHC class I to be lost or deficient in the target cell (see, e.g., Caligiuri (2008) Blood 112:461-469).

[0007] The technique of "delayed type hypersensitivity response" can be used to distinguish between immune responses that mainly involve cellular immunity or mainly involve humoral immunity. A positive signal from the delayed type hypersensitivity response indicates a cellular response (see, e.g., Roychowdhury, et al. (2005) AAPS J. E834-E846).

[0008] Autophagy is a homeostatic process by which cytosolic components and organelles are delivered to the lysosome for degradation. Autophagy is also associated with innate and adaptive immune responses to intracellular pathogens whereby cytosolic antigens are loaded onto major histocompatibility complex (MHC) class II molecules for CD4+ T-cell recognition.

Summary

[0008a] In one aspect, there is provided a population of mammalian dendritic cells comprising:

cancer-specific peptides from cancer cells taken from a subject that has cancer;

wherein the cancer-specific peptides are acquired in vitro by dendritic cells from said cancer cells;

wherein the cancer cells are not treated in vitro with interferon-gamma (IFN-gamma) or with IFN-gamma mimetic;

wherein greater than about 60 percent (%) of said cancer cells that are not treated in vitro with IFN-gamma or IFN-gamma mimetic, are autophagic and non-apoptotic, and,

wherein the dendritic cells and cancer cells are from the same subject.

[0008b] In another aspect, there is provided a vaccine for the subject as defined above, comprising the population of dendritic cells as defined above.

[0008c] In another aspect, there is provided a melanoma vaccine comprising:

at least one mature dendritic cell from a subject that has melanoma;

wherein the at least one mature dendritic cell had been contacted with at least one cancer tumor cell from the same subject,

wherein the at least one cancer tumor cell that is contacted with the at least one mature dendritic cell is non-dividing, autophagic, and non-apoptotic

[0008d] In another aspect, there provided a use of an immune-stimulatory amount of the population of dendritic cells as defined above for the preparation of a

medicament for stimulating an immune response against a cancer-specific antigen, wherein the medicament is to be administered to a subject.

[0008e] In another aspect, there is provided a method for preparing a dendritic cell vaccine, involving cancer cells and dendritic cells from the same subject, the method comprising:

one or more cancer cells is treated with an agent that prevents cell division;

the one or more cancer cells are not treated in vitro with interferon-gamma (IFN-gamma) or with an IFN-gamma mimetic;

cancer cells that are autophagic and non-apoptotic are selected;

cancer cells that are non-autophagic and apoptotic are rejected; and, wherein the cancer cells that are autophagic and non-apoptotic are provided to one or more autologous dendritic cells, or wherein peptides derived from the cancer cells that are autophagic and non-apoptotic are provided to one or more autologous dendritic cells.

[0008f] In another aspect, there is provided a composition comprising:

at least one cancer cell that is not treated with interferon-gamma (IFN-gamma) from a first subject and at least one antigen presenting cell (APC) from the same first subject, wherein the cancer cell is: autophagic; and, non-apoptotic.

[0008g] In another aspect, there is provided a use of an immunology effective amount of the composition as defined above for the preparation of a medicament for stimulating an immune response in a subject having a cancer and comprising cancer cells, wherein the medicament is to be administered to said subject, and wherein the subject is the same subject as the first subject.

[0008h] In another aspect, there is provided a method for manufacturing the vaccine as defined above or the composition as defined above, comprising contacting at least one cancer tumor cell to at least one antigen presenting cell (APC), wherein the at least one cancer tumor cell is from a first human subject, and wherein the at least one APC is from the same first human subject.

[0008i] In another aspect, there is provided a method for preparing a dendritic cell vaccine, comprising: treating cancer cells acquired from a first subject with an agent that prevents cell division; wherein the cancer cells are not treated in vitro with IFN-gamma or an IFN-gamma mimetic; selecting cancer cells that are autophagic and non-apoptotic; and, contacting the selected cancer cells with autologous dendritic cells from the same first subject.

[0008j] In another aspect, there is provided a composition that comprises a dendritic cell vaccine, as prepared by the method as defined above.

[0008k] In another aspect, there is provided a use of the composition as defined above for the preparation of a medicament for stimulating an immune response against a cancer-specific antigen, wherein the medicament is to be administered to a subject that has cancer.

Description

[0009] As used herein, including the appended claims, the singular forms of words such as "a," "an," and "the" include their corresponding plural references unless the context clearly dictates otherwise. All references cited herein are incorporated by reference to the same extent as if each individual publication, patent, published patent application, and sequence listing, as well as figures and drawings in said publications and patent documents, was specifically and individually indicated to be incorporated by reference.

DISCLOSURE

[0010] The present disclosure provides a population of mammalian dendritic cells comprising: cancer-specific peptides from cancer cells taken from a subject that has a cancer; wherein the cancer-specific peptides are acquired in vitro by dendritic cells from said cancer cells; wherein the cancer cells are not treated in vitro with interferon-gamma (IFN-gamma) or with IFN-gamma mimetic; wherein the majority of the cancer cells are not treated in vitro with a interferon-gamma (IFN-gamma) or

Claim 14. A melanoma vaccine comprising:

at least one mature dendritic cell from a subject that has melanoma;

wherein the at least one mature dendritic cell had been contacted with at least one cancer tumor cell from the same subject,

wherein the at least one cancer tumor cell that is contacted with the at least one mature dendritic cell is non-dividing, autophagic, and non-apoptotic.

Claim 15. ~~A method~~ Use an immune-stimulatory amount of the population of dendritic cells of claim 1 for the preparation of a medicament for stimulating an immune response against a cancer-specific antigen, wherein ~~comprising administering an immune-stimulatory amount of the dendritic cells of claim 1~~ the medicament is to be administered to ~~the~~a subject.

Claim 16. The ~~method~~ use of claim 15, wherein the immune response that is stimulated comprises one or more of $CD4^+$ T cell response, $CD8^+$ T cell response, and B cell response.

Claim 17. The ~~method~~ use of claim 16, wherein the $CD4^+$ T cell response, $CD8^+$ T cell response, or B cell response, can be measured by ELISPOT assays, by intracellular cytokine staining assays, by tetramer assays, or by detecting antigen-specific antibody production.

Claim 18. The ~~method~~ use of claim 15, wherein the immune response comprises a survival time that comprises 2-year overall survival (OS), and where the 2-year overall survival is at least about 60%.

Claim 19. The ~~method~~ use of claim 15, wherein the administration comprises subcutaneous injections of the vaccine.

Claim 20. The ~~method~~ use of claim 15, wherein the administration comprises injections of the vaccine given weekly for three months and then monthly for five months.

Claim 21. A method for preparing a dendritic cell vaccine, involving cancer cells and dendritic cells from the same subject, the method comprising:

one or more cancer cells is treated with an agent that prevents cell division;

the one or more cancer cells are not treated in vitro with interferon-gamma (IFN-gamma) or with an IFN-gamma mimetic;

cancer cells that are autophagic and non-apoptotic are selected;

cancer cells that are non-autophagic and apoptotic are rejected; and, wherein the cancer cells that are autophagic and non-apoptotic are provided to one or more autologous dendritic cells, or wherein peptides derived from the cancer cells that are autophagic and non-apoptotic are provided to one or more autologous dendritic cells.

Claim 22. A composition comprising:

at least one cancer cell that is not treated with interferon-gamma (IFN-gamma) from a first subject and at least one antigen presenting cell (APC) from the same first subject, wherein the cancer cell is:

autophagic; and,

non-apoptotic.

Claim 23. The composition of claim 22, wherein the cancer cell is MHC class II-expressing.

Claim 24. The composition of claim 22, wherein the APC is a dendritic cell, a macrophage, or a B cell.

Claim 25. The composition of claim 22, wherein the at least one cancer cell comprises cancer-specific peptides, and wherein the ~~cancer-specific-peptides~~ cancer-specific peptides are substantially not contained in said APCs and are substantially not processed by said APCs.

Claim 26. The composition of claim 22, wherein the cancer cells comprise melanoma-specific peptides, and wherein the ~~cancer-specific-peptides~~ cancer-specific peptides are substantially contained in said APCs and are partially or substantially processed in said APCs.

Claim 27. The composition of claim 22, wherein the cancer cell is loaded into the APC.

Claim 28. The composition of claim 22, wherein the cancer cell is not loaded into the APC.

Claim 29. The composition of claim ~~19~~22, wherein the autophagy is demonstrated by a test that assays microtubule-associated protein light chain 3 (LC3).

Claim 30. The composition of claim 22, wherein the cells are demonstrated to be non-apoptotic using at least one of the reagent, 7-aminoactinomycin D (7-ADD), or the reagent annexin.

Claim 31. ~~A method of~~Use of an immunology effective amount of the composition of claim 22 for the preparation of a medicament for stimulating an immune response in a subject having a cancer and comprising cancer cells, wherein the medicament is to be administered to said subject, and wherein the subject is the same subject as the first subject~~, comprising administering an immunology effective amount of the composition of claim 22~~.

Claim 32. The composition of claim 22, wherein at least 90% of the cancer cells are not treated in vitro with IFN-gamma, and less than 10% of the cancer cells are treated in vitro with IFN-gamma.

Claim 33. A method for manufacturing the vaccine of claim 1 or the composition of claim 19, comprising contacting at least one cancer tumor cell to at least one antigen presenting cell (APC), wherein the at least one cancer tumor cell is from a first human subject, and wherein the at least one APC is from the same first human subject.

Claim 34. A method for preparing a dendritic cell vaccine, comprising: treating cancer cells acquired from a first subject with an agent that prevents cell division; wherein the cancer cells are not treated in vitro with IFN-gamma or an IFN-gamma mimetic; selecting cancer cells that are autophagic and non-apoptotic; and, contacting the selected cancer cells with autologous dendritic cells from the same first subject.

Claim 35. A composition that comprises a dendritic cell vaccine, as prepared by the method of claim 34.

Claim 36. ~~A method~~Use of the composition of claim 35 for the preparation of a medicament for stimulating an immune response against a cancer-specific antigen, wherein the medicament is to be administered ~~comprising administering the composition of claim 34~~ to a subject that has cancer.