rapid and robust upregulation of numerous inflammatory mediators, including cytokines, chemokines and interferons. Co-incident with the expression of these genes is the migration of DCs to draining lymph nodes (dLN) and the upregulation of factors important for T cell activation, such as MHC and co-stimulatory molecules. Thus, the process of PRR signaling leads to a shift in DC activities from a non-stimulatory (naïve) state to an "activated" state (K. Inaba, *et al*. *J. Exp. Med*., vol. 191, no. 6, pp. 927–36, Mar. 2000 I. Mellman and R. M. Steinman, *Cell*, vol. 106, no. 3, pp. 255–8, Aug. 2001).

SUMMARY

There is a need to diversify current approaches to cancer immunotherapy. Accordingly, described herein are methods of inducing or enhancing an adaptive immune response to a cancer in a subject and methods of treating cancer in a subject. In one aspect, the present disclosure provides a use of a Toll-Like Receptor (TLR) ligand in the manufacture of a first medicament, use of a non-canonical inflammasome-activating lipid in the manufacture of a second medicament, and use of a cancer immunogen in the manufacture of a third medicament, wherein the first, second, and third medicaments are to be used in combination therapy to induce or enhance an adaptive immune response to a cancer in a subject, wherein said non-canonical inflammasome-activating lipid comprises [(2R)-2-(4-carboxybutanoyloxy)-3-hexadecanoyloxy propyl] 2- (trimethylazaniumyl)ethyl phosphate (**PGPC**). In another aspect, the present disclosure provides a use of (i) a Toll-Like Receptor (TLR) ligand; (ii) a non-canonical inflammasome-activating lipid; and (iii) a cancer immunogen in the manufacture of a medicament for inducing or enhancing an adaptive immune response to a cancer in a subject, wherein said non-canonical inflammasome-activating lipid comprises [(2R)-2-(4-carboxybutanoyloxy)-3-hexadecanoyloxy propyl] 2-(trimethylazaniumyl)ethyl phosphate (**PGPC**). In another aspect, the present disclosure provides a use of a Toll-Like Receptor (TLR) ligand in the manufacture of a first medicament, use of a non-canonical inflammasome-activating lipid in the manufacture of a second medicament, and use of a cancer immunogen in the manufacture of a third medicament, wherein the first, second, and third medicaments are to be used in combination therapy to treat cancer in a subject, wherein said non-canonical inflammasome-activating lipid comprises [(2R)-2-(4-carboxybutanoyloxy)-3-hexadecanoyloxy propyl] 2-(trimethylazaniumyl)ethyl phosphate (**PGPC**).

In another aspect, the present disclosure provides a use of (i) a Toll-Like Receptor (TLR) ligand; (ii) a non-canonical inflammasome-activating lipid and (iii) a cancer immunogen in the manufacture of a medicament for treating cancer in a subject, wherein said non-canonical inflammasome-activating lipid comprises [(2R)-2-(4-carboxybutanoyloxy)-3-hexadecanoyloxy propyl] 2- (trimethylazaniumyl)ethyl phosphate (**PGPC**). In some examples, the methods hyperactivate dendritic cells (DCs), which induce T helper type I (TH1) and cytotoxic T lymphocyte (CTL) responses in the absence of TH2 immunity. Hyperactivating stimuli drive T cell responses that protect against tumors that are sensitive or resistant to PD-1 inhibition. These protective responses depend on inflammasomes in DCs and can be generated using tumor lysates as immunogens.

Thus, provided herein are methods of inducing or enhancing an adaptive immune response to a cancer in a subject that comprise administering an effective amount of (i) a Toll-Like Receptor (TLR) ligand;, (ii) a non-canonical inflammasome-activating lipid,; and (iii) an cancer immunogen to the subject.

Also provided herein are methods of treating cancer in a subject that comprise administering an effective amount of (i) a Toll-Like Receptor (TLR) a TLR ligand;, (ii) a non-canonical inflammasome-activating lipid, and (iii) a cancern immunogen to the subject.

In some examples of the methods described herein, the cancer immunogen is an infectious agent immunogen, wherein an infection with the infectious agent is associated with development of cancer.

In some examples of the methods described herein, the cancer immunogen is from a cancer immunogen cell.

In some examples of the methods described herein, the cancer immunogen is or comprises whole tumor cell lysate.

What is claimed:

1. Use of a Toll-Like Receptor (TLR) ligand in the manufacture of a first medicament, use of a non-canonical inflammasome-activating lipid in the manufacture of a second medicament, and use of a cancer immunogen in the manufacture of a third medicament, wherein the first, second, and third medicaments are to be used in combination therapy to induce or enhance an adaptive immune response to a cancer in a subject, wherein said non-canonical inflammasome-activating lipid comprises [(2R)-2-(4-carboxybutanoyloxy)-3-hexadecanoyloxy propyl] 2- (trimethylazaniumyl)ethyl phosphate (**PGPC**).

2. Use of (i) a Toll-Like Receptor (TLR) ligand; (ii) a non-canonical inflammasome-activating lipid; and (iii) a cancer immunogen in the manufacture of a medicament for inducing or enhancing an adaptive immune response to a cancer in a subject, wherein said non-canonical inflammasome-activating lipid comprises [(2R)-2-(4-carboxybutanoyloxy)-3-hexadecanoyloxy propyl] 2- (trimethylazaniumyl)ethyl phosphate (**PGPC**).

3. Use of a Toll-Like Receptor (TLR) ligand in the manufacture of a first medicament, use of a non-canonical inflammasome-activating lipid in the manufacture of a second medicament, and use of a cancer immunogen in the manufacture of a third medicament, wherein the first, second, and third medicaments are to be used in combination therapy to treat cancer in a subject, wherein said non-canonical inflammasome-activating lipid comprises [(2R)-2-(4-carboxybutanoyloxy)-3-hexadecanoyloxy propyl] 2-(trimethylazaniumyl)ethyl phosphate (**PGPC**).

4. Use of (i) a Toll-Like Receptor (TLR) ligand; (ii) a non-canonical inflammasome-activating lipid and (iii) a cancer immunogen in the manufacture of a medicament for treating cancer in a subject, wherein said non-canonical inflammasome-activating lipid comprises [(2R)-2-(4-carboxybutanoyloxy)-3-hexadecanoyloxy propyl] 2- (trimethylazaniumyl)ethyl phosphate (**PGPC**).

5. The use of any one of claims 1-4, wherein the cancer immunogen is an infectious agent immunogen, wherein an infection with the infectious agent is associated with development of cancer.

6. The use of any one of claims 1-4, wherein the cancer immunogen is from a cancer cell.

7. The use of claim 6, wherein the cancer immunogen is or comprises whole tumor cell lysate.

8. The use of any one of claims 1–7, wherein the TLR ligand is selected from a TLR1 ligand, a TLR2 ligand, a TLR3 ligand, a TLR4 ligand, a TLR5 ligand, a TLR6 ligand, a TLR7 ligand, a TLR8 ligand, a TLR9 ligand, a TLR10 ligand, a TLR11 ligand, a TLR12 ligand, a TLR13 ligand, and combinations thereof.

9. The use of any one of claims 1–7, wherein the TLR ligand is a TLR4 ligand.

10. The use of claim 9, wherein the TLR4 ligand is selected from monophosphoryl lipid A (MPLA), lipopolysaccharide (LPS), or combinations thereof.

11. The use of any one of claims 1-10, wherein the TLR ligand is a TLR agonist.

12. The use of any one of claims 1–11, wherein the non-canonical inflammasome-activating lipid further comprises 2-[[(2R)-2-[(E)-7-carboxy-5-hydroxyhept-6-enoyl]oxy-3-hexadecanoyloxypropoxy]-hydroxyphosphoryl]oxyethyl-trimethylazanium (**HOdiA-PC**), [(2R)-2-[(E)-7-carboxy-5-oxohept-6-enoyl]oxy-3-hexadecanoyloxypropyl] 2-(trimethylazaniumyl)ethyl phosphate (**KOdiA-PC**), 1-palmitoyl-2-(5-hydroxy-8-oxo-octenoyl)-*sn*-glycero-3-phosphorylcholine (**HOOA-PC**), 2-[[(2R)-2-[(E)-5,8-dioxooct-6-enoyl]oxy-3-hexadecanoyloxypropoxy]-hydroxyphosphoryl]oxyethyl-trimethylazanium (**KOOA-PC**), [(2R)-3-hexadecanoyloxy-2-(5-oxopentanoyloxy)propyl] 2-(trimethylazaniumyl)ethyl phosphate (**POVPC**), [(2R)-3-hexadecanoyloxy-2-[4-[3-[(E)-[2-

[(Z)-oct-2-enyl]-5-oxocyclopent-3-en-1-ylidene]methyl]oxiran-2-yl]butanoyloxy]propyl] 2-(trimethylazaniumyl)ethyl phosphate (**PECPC**), [(2R)-3-hexadecanoyloxy-2-[4-[3-[(E)-[3-hydroxy-2-[(Z)-oct-2-enyl]-5-oxocyclopentylidene]methyl]oxiran-2-yl]butanoyloxy]propyl] 2-(trimethylazaniumyl)ethyl phosphate (**PEIPC**), or a combination thereof.

13. The use of any one of claims 1–12, wherein the subject is a mammal.

14. The use of claim 13, wherein the subject is a human.

15. The use of any one of claims 2, 4, or 5-14, wherein the TLR ligand, non-canonical inflammasome-activating lipid, and cancer immunogen are to be administered as part of a pharmaceutical composition.

16. The use of any one of claims 1, 2, or 5-15, wherein the adaptive immune response is a prophylactic immune response.

17. The use of any one of claims 1, 2, or 5-15, wherein the adaptive immune response is a therapeutic immune response.

18. The use of any one of claims 1, 2, or 5-17, wherein the adaptive immune response comprises T-cell activation.

19. The use of any one of claims 1–18, further comprising one or more therapeutic interventions.

20. The use of claim 19, wherein the TLR ligand, non-canonical inflammasome-activating lipid, and cancer immunogen, and the one or more therapeutic interventions are to be co-administered or to be sequentially administered.

21. The use of claim 19 or claim 20, wherein the one or more therapeutic interventions comprises: radiation, chemotherapy, surgery, therapeutic antibodies, immunomodulatory agents, proteasome inhibitors, pan-deacetylase (DAC) inhibitors, histone deacetylase

(HDAC) inhibitors, checkpoint inhibitors, adoptive cell therapies, vaccines or combinations thereof.

22. The use of claim 21, wherein the adoptive cell therapies comprise: CAR-T cell therapy, CAR- NK cell therapy, T cells, dendritic cells or combinations thereof.