

Claims

1. An artificial antigen presenting cell (aAPC) comprising a polymeric nanoparticle having attached polypeptide ligands suitable for activating or inhibiting antigen-specific T cells, the nanoparticle having a size in the range of 20 to 200 nm, the nanoparticle comprising:

5 a poly(lactic-co-glycolic acid) (PLGA) or polylactic acid (PLA) polymer core (PLGA/PLA), and

a hydrophilic shell formed of polyethylene glycol (PEG),

wherein the polymeric nanoparticle comprises PLGA/PLA-PEG and PLGA/PLA-methoxyPEG (mPEG) block co-polymers with the PLGA/PLA portion having
10 molecular weights of from about 10 kDa to about 30 kDa and the PEG portion having molecular weight(s) of from about 2 kDa to about 10 kDa,

wherein a portion of the PLGA/PLA-PEG polymers have a terminal attachment of a polypeptide ligand, and

wherein the polypeptide ligands comprise HLA ligands presenting one or more peptide
15 antigens.

2. The aAPC of claim 1, wherein the PEG portions of the block co-polymers have a molecular weight of from about 3000 and/or about 5000 Da.

20 3. The aAPC of claim 1, wherein the PLGA/PLA portions of the block co-polymers have a molecular weight of about 20,000 Da.

4. The aAPC of claim 1, wherein the polymer core is based on a 20:1 to 1:20 Lactic Acid:Glycolic Acid ratio.

25 5. The aAPC of claim 1, wherein the polymer core comprises PLA.

6. The aAPC of claim 1, wherein the polypeptide ligands are attached to PEG through primary amines on the polypeptides.

7. The aAPC of claim 1, wherein the polypeptide ligands are attached to PEG maleimide functional groups through an unpaired cysteine side chain.
- 5 8. The aAPC of claim 1, wherein the aAPC has a surface charge of about 0 to -20 mV.
9. The aAPC of claim 1, wherein the aAPC has a surface charge of from about -5 to about -10 mV.
- 10 10. The aAPC of claim 1, having less than about 500 polypeptide ligands per particle.
11. The aAPC of claim 1, having less than about 300 polypeptide ligands per particle.
12. The aAPC of claim 1, wherein the polypeptide ligands further comprise a co-stimulatory or inhibitory ligand.
- 15 13. The aAPC of claim 12, wherein the polypeptide ligands comprise an anti-CD28 agonistic antibody or an antigen-binding portion thereof.
14. The aAPC of claim 12, wherein the polypeptide ligands comprise an antibody that binds to Fas.
- 20 15. The aAPC of claim 1, wherein the HLA ligands are dimeric.
16. The aAPC of claim 15, wherein the HLA polypeptide ligands are fused with co-stimulatory or inhibitory ligands.
- 25 17. The aAPC of claim 15, wherein the HLA comprises a fusion with immunoglobulin sequences.
- 30 18. The aAPC of claim 17, wherein the aAPC comprises an anti-CD28 antibody ligand, and each of the HLA immunoglobulin fusion polypeptide ligands and the anti-CD28 antibody ligands

have an IgG4 constant region with mutations at codons S241 and L248, and an unpaired cysteine at codon 473.

19. The aAPC of claim 17, wherein the HLA ligands comprise an extracellular domain of HLA
5 fused to an immunoglobulin hinge region, without immunoglobulin variable domain sequences.