[0006] The disclosures of all publications, patents, patent applications, and published patent applications referred to herein are hereby incorporated herein by reference in their entirety.

SUMMARY

[0007] Described herein are nanoparticles comprising (a) a hydrophobic drug, (b) an albumin, and (c) a bioactive polypeptide conjugated to the albumin. In some embodiments, the bioactive polypeptide is an antibody or a fragment thereof. In some embodiments, the bioactive polypeptide is conjugated (either covalently or non-covalently) to the albumin of the nanoparticle. In some embodiments, the bioactive polypeptide is embedded in the nanoparticle. Further described herein are methods of manufacturing such nanoparticle compositions.

[0008] In one aspect, there is provided a composition comprising nanoparticles comprising (a) a hydrophobic drug, (b) an albumin, and (c) a bioactive polypeptide conjugated to the albumin. In some embodiments, the bioactive polypeptide is covalently crosslinked to the albumin. In some embodiments, the bioactive polypeptide is covalently crosslinked to the albumin through a chemical crosslinker. In some embodiments, the bioactive polypeptide is covalently crosslinked to the albumin through a disulfide bond. In some embodiments, the bioactive polypeptide is conjugated to the albumin through a non-covalent crosslinker. In some embodiments, the bioactive polypeptide comprises a first component of the non-covalent crosslinker and the albumin comprises a second component of the non-covalent crosslinker, and wherein the first component specifically binds to the second component. In some embodiments, the non-covalent crosslinker comprises nucleic acid molecules, wherein at least a portion of the nucleic acid molecules are complementary.

[0009] In another aspect, there is provided a composition comprising nanoparticles comprising (a) a solid core comprising a hydrophobic drug, (b) an albumin associated with a surface of the nanoparticle, and (c) a bioactive polypeptide embedded in the surface of the nanoparticle or the solid core. In some embodiments, the bioactive polypeptide is embedded in the surface of the nanoparticles. In some embodiments, the bioactive polypeptide is embedded in the solid core.

[0010] In some embodiments of the nanoparticles described above, at least 75% of the bioactive polypeptide in the composition is associated with the nanoparticles. In some embodiments, the nanoparticles comprise at least about 100 bioactive polypeptides.

high pressure homogenization, thereby forming an emulsion, wherein the organic solution comprises a hydrophobic drug dissolved in one or more organic solvents, and wherein the aqueous solution comprises the albumin, wherein the albumin is derivatized with a crosslinker moiety; (ii) removing at least a portion of the one or more organic solvents from the emulsion to obtain a post-evaporated suspension, and (iii) adding the bioactive polypeptide to the post-evaporated suspension, wherein the bioactive polypeptide is derivatized with a crosslinker moiety, thereby forming the composition. In some embodiments, the method further comprises replacing the derivatized albumin not associated with the nanoparticles with non-derivatized albumin.

[0023] In another aspect, there is provided a method of making a composition comprising nanoparticles comprising a hydrophobic drug, an albumin and a bioactive polypeptide, the method comprising: (i) subjecting a mixture of an organic solution and an aqueous solution to high pressure homogenization, thereby forming an emulsion, wherein the organic solution comprises a hydrophobic drug dissolved in one or more organic solvents, and wherein the aqueous solution comprises the albumin, wherein at least a portion of the albumin is conjugated to the bioactive polypeptide; and (ii) removing at least a portion of the one or more organic solvents from the emulsion, thereby forming the composition. In some embodiments, the method further comprises replacing the bioactive polypeptide-conjugated albumin not associated with the nanoparticles with unconjugated albumin.

[0024] In another aspect, there is provided a method of making a composition comprising nanoparticles comprising a hydrophobic drug, an albumin, and a bioactive polypeptide conjugated to the albumin, comprising conjugating the bioactive polypeptide to nanoparticles comprising the hydrophobic drug and albumin.

[0025] In some embodiments of the methods described above, the method further comprises sterile filtering the composition.

[0026] In some embodiments of the methods described above, the bioactive polypeptide is an antibody or fragment thereof. In some embodiments, the bioactive polypeptide is bevacizumab, trastuzumab, BGB-A317, or tocilizumab.

[0027] Further provided herein is a composition obtained by the method of any one of methods described above.

[0027a] In another aspect, there is provided a composition obtained by the method as described herein.

[0028] Also provided herein, there is a pharmaceutical composition comprising any one of the compositions described above, and a pharmaceutically acceptable excipient.

[0028a] In another aspect, there is provided a pharmaceutical composition comprising the composition as described herein, and a pharmaceutically acceptable excipient.

[0029] Disclosed is a method of treating a disease in an individual, comprising administering to the individual an effective amount of the any of the compositions described above. In some embodiments, the disease is a cancer. In some embodiments, the individual is human.

[0029a] In another aspect, there is provided use of an effective amount of the composition as described herein in the manufacture of a medicament for treating a disease in an individual.

[0030] These and other aspects and advantages of the present disclosure will become apparent from the subsequent detailed description and the appended claims. It is to be understood that one, some, or all of the properties of the various embodiments described herein may be combined to form other embodiments of the present disclosure.

BRIEF DESCRIPTION OF THE DRAWINGS

[0031] FIG. 1 shows a schematic illustrating one embodiment of a method for making a composition comprising nanoparticles described herein by including a bioactive polypeptide and albumin in an aqueous solution.

[0032] FIG. 2 shows a schematic illustrating one embodiment of a method for making a composition comprising nanoparticles described herein by adding a bioactive polypeptide to a crude mixture comprising an aqueous solution (comprising albumin and water) and an organic solution (comprising one or more organic solvents and a hydrophobic drug).

[0033] FIG. 3 shows a schematic illustrating one embodiment of a method for making a composition comprising nanoparticles described herein by adding a bioactive polypeptide to an emulsion comprising an aqueous solution (comprising albumin and water) and an organic solution (comprising one or more organic solvents and a hydrophobic drug).

[0034] FIG. 4 shows a one embodiment of a method for making a composition comprising nanoparticles described herein by adding a bioactive polypeptide to a post-evaporation nanoparticle suspension, wherein the nanoparticles comprise albumin and a hydrophobic drug.

[0035] FIG. 5 shows a schematic illustrating one embodiment of a method for making a composition comprising nanoparticles described herein by adding a bioactive polypeptide to pre-manufactured nanoparticles comprising albumin and a hydrophobic drug.

[0036] FIG. 6 shows a schematic illustrating one embodiment of a method for making a composition comprising nanoparticles described herein by adding a bioactive polypeptide to a nanoparticle suspension, wherein the nanoparticles comprise derivatized albumin and a hydrophobic drug. The bioactive polypeptide conjugates to the derivatized albumin associated with the nanoparticles.

41. Use of an effective amount of the composition of any one of claims 1-25, 39 and 40 in the manufacture of a medicament for treating a disease in an individual.

42. The use of claim 41, where the disease is a cancer.

43. The use of claim 41 or 42, wherein the individual is human.