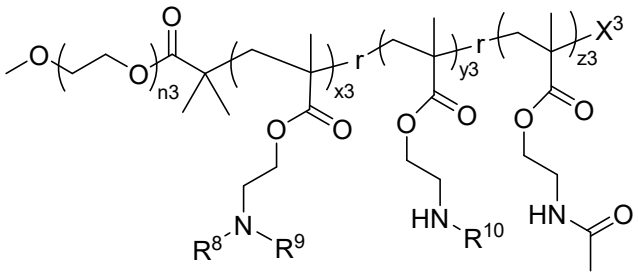
~~WHAT IS~~ CLAIM~~ED IS~~:

1. A micelle comprising:

(i) a block copolymer of Formula (III), or a pharmaceutically acceptable salt, solvate, or hydrate thereof:



Formula (III),

wherein:

n_3 is an integer from 10-200;

x_3 is an integer from 40-300;

y_3 is an integer from 0-6;

z_3 is an integer from 0-10;

X^3 is a halogen, -OH, or -C(O)OH;

R^8 and R^9 are each independently an optionally substituted C_1-C_6 alkyl, C_3-C_{10} cycloalkyl or aryl;

or R^8 and R^9 are taken together with the corresponding nitrogen to which they are attached to form an optionally substituted 5 to 7-membered ring; and

each R^{10} is independently hydrogen or ICG; and

(ii) a therapeutic agent encapsulated by the block copolymer,

wherein the therapeutic agent is a protein conjugated to a fluorescent dye.

2. The micelle of claim 1, wherein R^8 and R^9 are each independently an optionally substituted C_1-C_6 alkyl.

3. The micelle of claim 1 or 2, wherein R^8 and R^9 are each independently -CH_2CH_3, -$CH_2CH_2CH_3$, or -$CH_2CH_2CH_2CH_3$.

4. The micelle of any one of claims 1-3, wherein R^8 and R^9 are each -$CH_2CH_2CH_2CH_3$.

5. The micelle of claim 1, wherein R^8 and R^8 are taken together with the corresponding nitrogen to which they are attached to form an optionally substituted 5 to 7-membered ring.

6. The micelle of claim 1 or 5, wherein R^8 and R^9 taken together are -$CH_2(CH_2)_2CH_2$-, -$CH_2(CH_2)_3CH_2$-, or -$CH_2(CH_2)_4CH_2$-.

7. The micelle of any one of claims 1-6, wherein x_3 is an integer from 50-200, 60-160, or 90-140.

8. The micelle of claim 7, wherein x_3 is 90-140.

9. The micelle of any one of claims 1-8, wherein y_3 is an integer from 1-6, 1-5, 1-4, or 1-3.

10. The micelle of any one of claims 1-8, wherein y_3 is 0.

11. The micelle of any one of claims 1-10, wherein z_3 is an integer from 1-9, 1-8, 1-7, 1-6, 1-5, 1-4, or 1-3.

12. The micelle of any one of claims 1-10, wherein z_3 is 0.

13. The micelle of any one of claims 1-12, wherein n_3 is an integer from 60-150 or 100-140.

14. The micelle of claim 13, wherein n_3 is 100-140.

15. The micelle of any one of claims 1-14, wherein X^3 is a halogen.

16. The micelle of claim 15, wherein X^3 is -Br.

17. The micelle of any one of claims 1-16, wherein the protein is a protein of about 5 to about 20 KDa optionally a cytokine or fragment thereof, or is an antibody optionally an engineered antibody, or a fragment thereof.

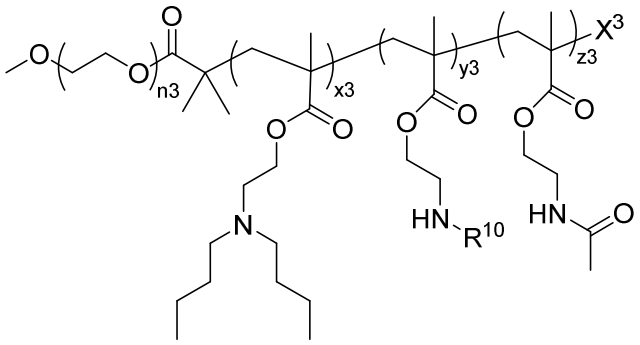
18. The micelle of claim 17, wherein the cytokine is an interleukin (IL), chemokine, interferon, lymphokine, monokine, colony stimulating factor, or tumor necrosis factor, optionally an IL-2, IL-1, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-15, IL-17, or IL-18 protein, or a fragment thereof.

~~19. The micelle of claim 17, wherein the antibody or fragment thereof is a bispecific antibody or a fragment thereof or a fusion protein, optionally a bi-specific T-cell engager (BiTE).~~

~~20. The micelle of any one of claims 1-19, wherein the fluorescent dye has an excitation spectrum from about 400 nm to about 900 nm, or about: 400, 450, 500, 550, 600, 650, 700, 750, 800, or 850 nm, optionally coumarin, rhodamine, cyanine, xanthene, fluorescein, or a sulfonated or negatively charged form thereof, or a compound from **FIG. 22**.~~

~~2~~19. A micelle comprising:

(i) a block copolymer of Formula (IV), or a pharmaceutically acceptable salt, solvate, or hydrate thereof:



Formula (IV),

wherein:

n_3 is an integer from 10-200;

x_3 is an integer from 40-300;

y_3 is an integer from 0-6;

z_3 is an integer from 0-10;

each R^{10} is independently hydrogen or ICG; and

X^3 is a halogen, -OH, or -C(O)OH; and

(ii) a therapeutic agents encapsulated by the block copolymer,

wherein the therapeutic agent is a protein conjugated to a fluorescent dye.

20. The micelle according to any one of claims 1-19, for use as a medicament.

~~22. The micelle of claim 21, wherein x_3 is 90-140.~~

~~23. The micelle of claim 21 or 22, wherein y_3 is 0.~~

~~24. The micelle of any one of claims 21-23, wherein z_3 is 0.~~

~~25. The micelle of any one of claims 21-24, wherein n_3 is 100-140.~~

~~26. The micelle of any one of claims 21-25, wherein X^3 is a halogen.~~

~~27. The micelle of any one of claims 21-26, wherein the therapeutic agent is a cytokine or fragment thereof or an engineered antibody or fragment thereof.~~

~~28. The micelle of claim 27, wherein the cytokine is IL-2 or a fragment thereof.~~

~~29. The micelle of any one of claims 21-28, wherein the fluorescent dye has an excitation spectrum from about 400 nm to about 900 nm, or about: 400, 450, 500, 550, 600, 650, 700, 750, 800, or 850 nm, optionally coumarin, rhodamine, cyanine, xanthene, fluorescein, or a sulfonated or negatively charged form thereof, or a compound from **FIG. 22**.~~

~~30. A pH response composition of any one of claim 1-29, wherein the composition has a pH transition point and an emission spectrum.~~

~~31. The pH responsive composition of claim 30 wherein the pH transition point is between 4-8, 6-7.5, or 4.5-5.5.~~

~~32. The pH responsive composition of claim 30 or 31, wherein composition has a pH response of less than 0.25 or 0.15 pH units.~~

~~33. The pH responsive composition of any one of claims 30-32, wherein the emission spectrum is from about 700 to about 900 nm.~~

~~34~~21. Use of a micelle according to any one of claims 1-19 in the preparation of a medicament ~~A method~~ for treating cancer ~~in a patient in need thereof, comprising administering to the patient a therapeutically effective amount of a micelle of any one of claims 1-29~~.

~~35~~22. The ~~method~~use of claim ~~34~~21, wherein the cancer is a solid tumor.

2~~3~~6. The ~~method~~use of claim ~~34~~21 or ~~35~~22, wherein the cancer is breast cancer, head and neck squamous cell carcinoma (NHSCC), peritoneal metastasis, lung cancer, ovarian cancer, prostate cancer, bladder cancer, kidney cancer, urethral cancer, esophageal cancer, colorectal cancer, brain cancer, or skin cancer.

~~37~~24. A method for increasing encapsulation of a therapeutic agent into a micelle, comprising conjugating the therapeutic agent with a fluorescent dye.

~~38. The method of claim 37, further comprising contacting the conjugated therapeutic agent with a block copolymer to form the micelle.~~

~~39. The method of claim 37 or 38, wherein the therapeutic agent is a protein of about 5 to about 20 KDa.~~

~~40. The method of claim 39, wherein the protein is a cytokine or fragment thereof.~~

~~41. The method of claim 40, wherein the cytokine is an interleukin (IL), chemokine, interferon, lymphokine, monokine, colony stimulating factor, or tumor necrosis factor.~~

~~42. The method of claim 41, wherein the cytokine is an IL-2, IL-1, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-15, IL-17, or IL-18 protein or a fragment thereof.~~

~~43. The method of claim 37 or 38, wherein the therapeutic agent is an antibody or a fragment thereof.~~

~~44. The method of claim 43, wherein the antibody or fragment thereof is a bispecific antibody or a fragment thereof.~~

~~45. The method of claim 44, wherein the bispecific antibody or fragment thereof is a fusion protein.~~

~~46. The method of claim 45, wherein the fusion protein is a bi-specific T-cell engager (BiTE).~~

~~47. The method of any one of claims 37-46, wherein the fluorescent dye has an excitation spectrum from about 400 nm to about 900 nm.~~

~~48. The method of claim 47, wherein the fluorescent dye has an excitation spectrum about: 400, 450, 500, 550, 600, 650, 700, 750, 800, or 850 nm.~~

~~49. The method of claim 47 or 48, wherein the fluorescent dye is coumarin, rhodamine, cyanine, xanthene, fluorescein, or a sulfonated or negatively charged form thereof, or a compound from **FIG. 22**.~~