Claims

1. An engineered thermostable ferritin assembly comprising a modified ferritin subunit derived from a wildtype *Archaeoglobus fulgidus* ferritin assembly subunit, wherein the modified ferritin subunit comprises the amino acid sequence set forth in SEQ ID NO: 1, except that the modified ferritin subunit lacks residues 165-173 of SEQ ID NO: 1, and comprises 0 or more amino acid substitutions at one or more positions selected from the group consisting of E65, F116, E128, E131, and D138 of SEQ ID NO: 1, and wherein the engineered thermostable ferritin assembly comprises pores communicating the interior with the exterior of the assembly, exhibits enhanced thermostability relative to said wildtype ferritin assembly and is stable at lower salt concentrations than said wildtype ferritin assembly.
2. The engineered ferritin assembly of claim 1, wherein the assembly possesses a net positive interior charge, or a net neutral interior charge.
3. The engineered ferritin assembly of claim 2, wherein the modified ferritin subunit comprises an amino acid substitution at any one or more positions selected from E65, E128, E131, and D138.
4. The engineered ferritin assembly of any one of claims 1 to 3, wherein the modified ferritin subunit further comprises
   a) a substitution at position F116 of SEQ ID NO: 1 which renders the engineered assembly capable of assembly and/or disassembly dependent on pH; and/or
   b) an amino acid sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5 and SEQ ID NO: 8.
5. The engineered ferritin assembly of any one of claims 1 to 4, wherein a polypeptide, nucleic acid or small molecule is encapsulated within the ferritin assembly.
6. The engineered ferritin assembly of any one of claims 1 to 5, wherein the modified ferritin subunit is fused to a polypeptide or nucleic acid and said polypeptide or nucleic acid is encapsulated within the ferritin assembly.
7. The engineered ferritin assembly of claim 6, wherein the polypeptide is fused to the modified ferritin subunit through a joining sequence.
8. The engineered ferritin assembly of any one of claims 1 to 7 wherein the said stability in low salt concentrations is provided by chemical crosslinking of subunits.
9. An in vitro method of forming an engineered thermostable ferritin assembly comprising at least one modified ferritin subunit, the method comprising adjusting the pH from an acidic pH to basic pH of a sample comprising at least one modified ferritin subunit of claim 4.

10. The method of claim 9, further comprising a polypeptide or a nucleic acid in the sample whereby said polypeptide or nucleic acid is encapsulated by the engineered ferritin assembly at basic pH of the sample.

11. The method of claim 9 or 10, wherein the acidic pH in the sample is at least about 4.0 and/or the basic pH in the sample is about 8.0.

12. The method of claim 10 or 11, wherein the polypeptide or nucleic acid is fused to at least one modified ferritin subunit.

13. A method of encapsulating a polypeptide in an engineered thermostable ferritin assembly, comprising:
1) introducing into a cell a nucleic acid comprising:
a) a first sequence that encodes a first modified ferritin subunit lacking an unstructured carboxy-terminal sequence that a wildtype ferritin subunit possesses; and
b) a second sequence that encodes a second modified ferritin subunit lacking an unstructured carboxy-terminal sequence that a wildtype ferritin subunit possesses fused to a polypeptide;
2) expressing the first and second sequences; and
3) forming a ferritin assembly that encapsulates the polypeptide,
wherein at least one of the first or second modified ferritin subunit is as defined in claim 1.

14. The method of claim 13, wherein the first and second sequences are introduced into the cell on separate plasmids.

15. A method of delivering an engineered thermostable ferritin assembly into a cell, comprising contacting the cell with a ferritin assembly of any one of claims 1 to 8.

16. The method of claim 15, wherein the ferritin assembly comprises a cell targeting moiety.

17. An isolated plasmid or vector nucleic acid comprising

a) a sequence that encodes a modified thermostable ferritin subunit; and/or
b) a sequence that encodes a modified ferritin subunit fused to a polypeptide,

wherein the modified ferritin subunit is as defined in any one of claims 1 to 8.

18. A composition or combination comprising at least one engineered thermostable ferritin assembly of any one of claims 1 to 8 for use in the prophylaxis or treatment of disease in a subject.

19. The composition or combination of claim 18, wherein the at least one engineered thermostable ferritin assembly comprises:

i) an enzyme; and/or

ii) one or more additional therapeutic agents.

20. The composition or combination of claim 18, which is a vaccine.

21. Use of at least one engineered thermostable ferritin assembly of any one of claims 1 to 14 in the manufacture of a medicament for the prophylaxis or treatment of a disease in a subject.

22. A kit, to encapsulate a polypeptide or nucleic acid within an engineered thermostable ferritin assembly, the kit comprising:

a) at least one modified ferritin subunit according to any one of claims 1 to 8, or

b) a plasmid or vector nucleic acid of claim 17.

23. The engineered ferritin assembly of claim 3, wherein the amino acid substitution comprises;

i) substitutions E65K, E128K, E131K and D138A, which cause the assembly to have a net positive interior charge; or

ii) substitutions E65Q and D138A, which cause the assembly to have a net neutral interior charge.

24. The engineered ferritin assembly of claim 4, wherein the substitution is F116H.