

**CLAIMS**

1. An *in-vitro* tissue engineering system comprising the polypeptide and at least one layer and/or fiber of cellulose, wherein the polypeptide comprises a cellulose binding domain (CBD), a cell effector protein (CEP); and a linker linking the CBD to the CEP.
2. The tissue engineering system of claim 1, wherein the CBD has at least 70% homology to the amino acid sequence set forth in SEQ ID NO: 1.
3. The tissue engineering system of claim 1 or 2, wherein the linker has a length of 10-25 amino acids.
4. The tissue engineering system of any one of claims 1-3, wherein the CEP is selected from: a growth factor, a hormone, a cytokine, a pro-apoptotic factor, an anti-apoptotic factor, a vascular growth factor, a cell differentiation factor, a bone growth factor, other protein required for cell viability like transferrin, or a combination thereof.
5. The tissue engineering system of claim 4, wherein the CEP is a cell differentiation factor, a growth factor, a cytokine or a growth hormone.
6. The tissue engineering system of claim 4, wherein the CEP is selected from: FGF2, IGF1, TGF $\beta$ 1, EGF, LIF, Activin A, NRG1, PDGF, IL6, IL13 or any combination thereof.
7. The tissue engineering system of any one of claims 1-6, wherein the linker comprises a cleavage site characterized by enabling cleavage by a site-specific protease at a predetermined cleavage efficiency, such that when the polypeptide is exposed to the protease, a sustained release of the CEP from the CBD is obtained
8. The tissue engineering system of claim 7, wherein the cleavage site is positioned 5 amino acids or less upstream of the N' terminus of the CEP or 5 amino acids or less downstream of the C' terminus of the CEP.
9. The tissue engineering system of claim 7 or 8, wherein the cleavage cite is a TEV-proteas cleavage site.

10. The tissue engineering system of any one of claims 7-9, wherein the cleavage site is modified to provide a lower cleavage efficiency, as compared to an unmodified version of the cleavage site.
11. The tissue engineering system of claim 10, wherein the modification comprises a deletion of one or more amino acids, an addition of one or more an amino acid, or a substitution of one or more amino acids.
12. The tissue engineering system of claim 11, wherein the modification comprises a chemical modification of one or more amino acids.
13. The tissue engineering system of any one of claims 7-12, wherein the cleavage site is a cleavage site of a protease having a catalytic efficiency ( $k_{cat}/K_M$ ) of below  $1.5 \cdot 10^3 \text{ m}^{-1} \text{ s}^{-1}$  at normal mammalian cell growth conditions.
14. The tissue engineering system of any one of claims 1-13, wherein the half-life of the CEP is higher when bound to CBD and/or to the linker as compared to in its free form.
15. The tissue engineering system of any one of claims 1-14, wherein the linker increases the half-life of the CBD.
16. The tissue engineering system of any one of claims 1-15, comprising at least two layers and/or fibers of cellulose.
17. The tissue engineering system of claim 16, wherein each of the at least two layers and/or fibers is associated with chimeric peptides including different CEPs.
18. The tissue engineering system of any one of claims 16-17, wherein the at least one layer comprises at least two types of chimeric polypeptides, each comprising different CEPs.
19. The tissue engineering system of claim 18, wherein a first of the two types of chimeric polypeptides comprises a differentiation factor and a second of the two types of chimeric polypeptides comprises a growth factor associated with differentiation.

20. The tissue engineering system of claim 19, wherein the linker of the first of the two types of chimeric polypeptides comprises a linker comprising a first cleavage site characterized by enabling cleavage by a site-specific protease at a first predetermined cleavage efficiency and the second of the two types of chimeric polypeptides comprises a linker comprising a second cleavage site characterized by enabling cleavage by a site-specific protease at a second predetermined cleavage efficiency, the second cleavage efficiency being lower than the first cleavage efficiency.
21. A chimeric polypeptide for use in *in-vitro* tissue engineering, the polypeptide comprising:
- a. a cellulose binding domain (CBD);
  - b. a cell effector protein (CEP); and
  - c. a linker linking the CBD to the CEP.
22. The chimeric polypeptide of claim 21, wherein the CBD has at least 70% homology to the amino acid sequence set forth in SEQ ID NO. 1.
23. The chimeric polypeptide of claim 21 or 22, wherein the linker has a length of 10-25 amino acids.
24. The chimeric polypeptide of any one of claims 21-23, wherein the CEP is selected from: a growth factor, a hormone, a cytokine, a pro-apoptotic factor, an anti-apoptotic factor, a vascular growth factor, a cell differentiation factor, a bone growth factor, other protein required for cell viability like transferrin, or a combination thereof.
25. The chimeric polypeptide of claim 24, wherein the CEP is a cell differentiation factor, a growth factor, a cytokine or a growth hormone.
26. The chimeric polypeptide of claim 24, wherein the CEP is selected from: FGF2, IGF1, TGF $\beta$ 1, EGF, LIF, Activin A, NRG1, PDGF, IL6, IL13 or any combination thereof.
27. The chimeric polypeptide of any one of claims 21-26, wherein the linker comprises a cleavage site characterized by enabling cleavage by a site-specific protease at a

predetermined cleavage efficiency, such that when the polypeptide is exposed to the protease, a sustained release of the CEP from the CBD is obtained

28. The chimeric polypeptide of claim 27, wherein the cleavage site is positioned 5 amino acids or less upstream of the N' terminus of the CEP or 5 amino acids or less downstream of the C' terminus of the CEP.
29. The chimeric polypeptide of claim 26 or 27, wherein the cleavage site is a TEV-proteas cleavage site.
30. The chimeric polypeptide of any one of claims 26-28, wherein the cleavage site is modified to provide a lower cleavage efficiency, as compared to an unmodified version of the cleavage site.
31. The chimeric polypeptide of claim 29, wherein the modification comprises a deletion of one or more amino acids, an addition of one or more an amino acid, or a substitution of one or more amino acids.
32. The chimeric polypeptide of claim 30, wherein the modification comprises a chemical modification of one or more amino acids.
33. The chimeric polypeptide of any one of claims 26-32, wherein the cleavage site is a cleavage site of a protease having a catalytic efficiency ( $k_{cat}/K_M$ ) of below  $1.5 \cdot 10^3 \text{ m}^{-1} \text{ s}^{-1}$  at normal mammalian cell growth conditions.
34. The chimeric polypeptide of any one of claims 21-33, wherein the half-life of the CEP is higher when bound to CBD and/or to the linker as compared to in its free form.
35. The chimeric polypeptide of any one of claims 21-34, wherein the linker increases the half-life of the CBD.
36. A method for *in-vitro* tissue engineering, the method comprising:
  - a. providing a cell growth medium comprising at least one layer and/or fiber of cellulose; the at least one layer of cellulose comprising a chimeric polypeptide

comprising a cellulose binding domain (CBD), a cell effector protein (CEP);  
and a linker linking the CBD to the CEP,

- b. seeding mammalian cells on the at least one layer of cellulose;
- c. growing the cells until an organized tissue is obtained;
- d. harvesting the tissue.

37. The method of claim 36, wherein the at least one layer and/or fiber comprises a first layer with a first chimeric polypeptide comprising a first CEP and a second layer comprising a second chimeric polypeptide comprising a second CEP.
38. The method of claim 37, wherein seeding the mammalian cells comprises seeding a first cell type on the first layer and a second cell type on the second layer.
39. The method of claim 38, wherein the first cell type comprises muscle cells and the second cell type comprises fat cells and wherein the organized tissue is meat.
40. The method of claim 39, wherein the first CEP is a muscle specific growth factor and the second CEP is an adipose specific growth factor.
41. The method of claim 36, wherein the mammalian cells are multipotent or pluripotent cells and wherein the first and second factors cause differentiation of the cells into different cell types.
42. The method of claim 41, wherein the first CEP causes differentiation of the multipotent or pluripotent cells into muscle cells and the second CEP causes differentiation of the multipotent or pluripotent cells into fat cells.
43. The method of any one of claims 36-42, wherein the linker comprises a cleavage site characterized by enabling cleavage by a site-specific protease and wherein the method further comprises exposing the at least one layer of cellulose to the site-specific protease, such that the CEP is sustainably released into the cell growth medium.

## CLAIMS

1. An *in-vitro* tissue engineering system comprising a chimeric polypeptide and at least one layer and/or fiber of cellulose, wherein the chimeric polypeptide comprises a cellulose binding domain (CBD), a cell effector protein (CEP); and a linker linking the CBD to the CEP.
2. The tissue engineering system of claim 1, wherein the linker has a length of 10-25 amino acids.
3. The tissue engineering system of claim 1, wherein the CEP is selected from the group consisting of a growth factor, a hormone, a cytokine, a pro-apoptotic factor, an anti-apoptotic factor, a vascular growth factor, a cell differentiation factor, a bone growth factor, other protein required for cell viability like transferrin, and a combination thereof.
4. The tissue engineering system of claim 3, wherein the CEP is selected from the group consisting of FGF2, IGF1, TGF $\beta$ 1, EGF, LIF, Activin A, NRG1, PDGF, IL6, IL13, and any combination thereof.
5. The tissue engineering system of claims 1, wherein the linker comprises a cleavage site characterized by enabling cleavage by a site-specific protease at a predetermined cleavage efficiency, such that when the chimeric polypeptide is exposed to the protease, a sustained release of the CEP from the CBD is obtained.
6. The tissue engineering system of claim 5, wherein the cleavage site is a cleavage site of a protease having a catalytic efficiency ( $k_{cat}/K_M$ ) of below  $1.5 \cdot 10^3 \text{ m}^{-1}\text{s}^{-1}$  at normal mammalian cell growth conditions.
7. The tissue engineering system of claim 1, comprising at least two layers and/or fibers of cellulose, wherein the at least one layer comprises at least two types of chimeric polypeptides, each comprising different CEPs.
8. The tissue engineering system of claim 7, wherein a first of the two types of chimeric polypeptides comprises a differentiation factor and a second of the two types of chimeric polypeptides comprises a growth factor associated with differentiation.

9. A chimeric polypeptide for use in *in-vitro* tissue engineering, the chimeric polypeptide comprising:
  - a. a cellulose binding domain (CBD);
  - b. a cell effector protein (CEP); and
  - c. a linker linking the CBD to the CEP.
10. The chimeric polypeptide of claim 9, wherein the linker has a length of 10-25 amino acids.
11. The chimeric polypeptide of claim 9, wherein the CEP is selected from the group consisting of a growth factor, a hormone, a cytokine, a pro-apoptotic factor, an anti-apoptotic factor, a vascular growth factor, a cell differentiation factor, a bone growth factor, other protein required for cell viability like transferrin, and a combination thereof.
12. The chimeric polypeptide of claim 9, wherein the CEP is selected from the group consisting of FGF2, IGF1, TGFβ1, EGF, LIF, Activin A, NRG1, PDGF, IL6, IL13, and any combination thereof.
13. The chimeric polypeptide of claim 9, wherein the linker comprises a cleavage site characterized by enabling cleavage by a site-specific protease at a predetermined cleavage efficiency, such that when the chimeric polypeptide is exposed to the protease, a sustained release of the CEP from the CBD is obtained.
14. The chimeric polypeptide of claim 13, wherein the cleavage site is a cleavage site of a protease having a catalytic efficiency ( $k_{cat}/K_M$ ) of below  $1.5 \times 10^3 \text{ m}^{-1}\text{s}^{-1}$  at normal mammalian cell growth conditions.
15. A method for *in-vitro* tissue engineering, the method comprising:
  - a. providing a cell growth medium comprising at least one layer and/or fiber of cellulose, the at least one layer of cellulose comprising a chimeric polypeptide comprising a cellulose binding domain (CBD), a cell effector protein (CEP), and a linker linking the CBD to the CEP;
  - b. seeding mammalian cells on the at least one layer of cellulose;

- c. growing the cells until an organized tissue is obtained; and
  - d. harvesting the tissue.
16. The method of claim 15, wherein the at least one layer and/or fiber comprises a first layer with a first chimeric polypeptide comprising a first CEP and a second layer comprising a second chimeric polypeptide comprising a second CEP.
  17. The method of claim 16, wherein seeding the mammalian cells comprises seeding a first cell type on the first layer and a second cell type on the second layer.
  18. The method of claim 17, wherein the first cell type comprises muscle cells and the second cell type comprises fat cells and wherein the organized tissue is meat and wherein the first CEP is a muscle specific growth factor and the second CEP is an adipose specific growth factor.
  19. The method of claim 15, wherein the mammalian cells are multipotent or pluripotent cells and wherein the first and second factors cause differentiation of the cells into different cell types.
  20. The method of claim 15, wherein the linker comprises a cleavage site characterized by enabling cleavage by a site-specific protease and wherein the method further comprises exposing the at least one layer of cellulose to the site-specific protease, such that the CEP is sustainably released into the cell growth medium.