CLAIMS

1. A biocompatible composition comprising silk fibroin or silk fibroin fragments, hyaluronic acid (HA), and polyethylene glycol (PEG) and/or polypropylene glycol (PPG),

wherein a portion of the HA is modified or crosslinked by one or more linker moieties comprising one or more of polyethylene glycol (PEG), polypropylene glycol (PPG), and a secondary alcohol, and

wherein a portion of the silk fibroin or silk fibroin fragments are free and/or uncrosslinked.

2. The composition of claim 1, wherein a portion of the silk fibroin or silk fibroin fragments are modified or crosslinked.

3. The composition of any one of claims 1 or 2, wherein a portion of the silk fibroin or silk fibroin fragments are crosslinked to HA, and/or~~.~~

~~4. The composition of any one of claims 1 to 3,~~ wherein a portion of the silk fibroin or silk fibroin fragments are crosslinked to silk fibroin or silk fibroin fragments.

~~5~~4. The ~~tissue filler~~composition of any one of claims 1 to ~~4~~3, wherein the silk fibroin or silk fibroin fragments are substantially devoid of sericin.

~~6~~5. The composition of any one of claims 1 to ~~5~~4, wherein a portion of silk fibroin or silk fibroin fragments have an average weight average molecular weight selected from between 5 kDa to 38 kDa, from between 14 kDa to 30 kDa, from between 6 kDa to 17 kDa, from between 39 kDa to 54 kDa, ~~low molecular weight~~ from between 31 kDa to 55 kDa, from between 39 kDa to 54 kDa, or~~, medium molecular weight,~~ from between 55 kDa to 150 kDa~~and high molecular weight~~.

~~7~~6. The composition of any one of claims 1 to ~~6~~5, wherein the silk fibroin or silk fibroin fragments have a polydispersity of between 1 and about 5.0.

~~8. The composition of any one of claims 1 to 6, wherein the silk fibroin or silk fibroin fragments have a polydispersity of between about 1.5 and about 3.0.~~

~~9. The composition of any one of claims 1 to 8, wherein the composition has a degree of modification (MoD) of about 5%, about 6%, about 7%, about 8%, about 9%, about 10%, about 11%, about 12%, about 13%, about 14%, or about 15%.~~

~~10~~7. The composition of any one of claims 1 to ~~9~~6, wherein modification or cross-linking is obtained using as cross-linker a monoepoxy- or diepoxy-PEG, a monoglycidyl-, diglycidyl-, or polyglycidyl-PEG, a monoglycidyl- or diglycidyl-PEG, a monoepoxy- or diepoxy-PPG, a monoglycidyl-, diglycidyl-, or polyglycidyl-PPG, a monoglycidyl- or diglycidyl-PPG, or any combinations thereof.

~~11~~8. The composition of any one of claims 1 to ~~10~~7, further comprising lidocaine.

~~12. The composition of any one of claims 1 to 11, wherein the composition is a gel or a hydrogel.~~

~~13~~9. The composition of any one of claims 1 to ~~12~~8, wherein the total concentration of HA and silk fibroin or silk fibroin fragments in the composition is about 15 mg/mL, about 16 mg/mL, about 17 mg/mL, about 18 mg/mL, about 19 mg/mL, about 20 mg/mL, about 21 mg/mL, about 22 mg/mL, about 23 mg/mL, about 24 mg/mL, about 25 mg/mL, about 26 mg/mL, about 27 mg/mL, about 28 mg/mL, about 29 mg/mL, about 30 mg/mL, about 31 mg/mL, about 32 mg/mL, about 33 mg/mL, about 34 mg/mL, about 35 mg/mL, about 36 mg/mL, about 37 mg/mL, about 38 mg/mL, about 39 mg/mL, or about 40 mg/mL.

~~14. The composition of any one of claims 1 to 13, wherein the ratio of HA to silk fibroin or silk fibroin fragments in the composition is about 91/9, about 92/8, about 93/7, about 94/6, about 95/5, about 96/4, about 97/3, about 18/12, about 27/3,~~

~~about 29.4/0.6, about 99/1, about 92.5/7.5, about 90/10, about 80/20, about 70/30, about 60/40, or about 50/50.~~

~~15. The composition of any one of claims 1 to 13, wherein the ratio of HA to silk fibroin or silk fibroin fragments in the composition is about 50/50, about 51/49, about 52/48, about 53/47, about 54/46, about 55/45, about 56/44, about 57/43, about 58/42, about 59/41, about 60/40, about 61/39, about 62/38, about 63/37, about 64/36, about 65/35, about 66/34, about 67/33, about 68/32, about 69/31, about 70/30, about 71/29, about 72/28, about 73/27, about 74/26, about 75/25, about 76/24, about 77/23, about 78/22, about 79/21, about 80/20, about 81/19, about 82/18, about 83/17, about 84/16, about 85/15, about 86/14, about 87/13, about 88/12, about 89/11, about 90/10, about 91/9, about 92/8, about 93/7, about 94/6, about 95/5, about 96/4, about 97/3, about 98/2, or about 99/1.~~

~~16. The composition of any one of claims 1 to 17, wherein the total concentration of free and/or uncrosslinked silk fibroin or silk fibroin fragments in the composition is about 1 mg/mL, about 2 mg/mL, about 3 mg/mL, about 4 mg/mL, about 5 mg/mL, about 6 mg/mL, about 7 mg/mL, or about 8 mg/mL.~~

~~17~~10. The composition of any one of claims 1 to ~~16~~9, wherein a portion of the free and/or uncrosslinked silk fibroin or silk fibroin fragments comprises silk microparticles having a median particle size ranging from 1.0 μm to 50.0 μm, from 1.0 μm to 25.0 μm, from 1.0 μm to 10.0 μm, from 30.0 μm to 50.0 μm, from 35.0 μm to 45.0 μm, from 35.0 μm to 55.0 μm, or from 25.0 μm to 45.0 μm.

~~18~~11. The composition of any one of claims 1 to ~~17~~10, wherein the composition is injectable through 30G or 27G needles, and having an injection force through a 30G needle between about 10 N and about 80 N.

~~19. The composition of any one of claims 1 to 17, wherein the composition is injectable through a 30G needle with an injection force of about 1 N, about 2 N, about 3 N, about 4 N, about 5 N, about 6 N, about 7 N, about 8 N, about 9 N, about 10 N, about 11 N, about 12 N, about 13 N, about 14 N, about 15 N, about 16 N, about 17 N,~~

~~about 18 N, about 19 N, about 20 N, about 21 N, about 22 N, about 23 N, about 24 N, about 25 N, about 26 N, about 27 N, about 28 N, about 29 N, about 30 N, about 31 N, about 32 N, about 33 N, about 34 N, about 35 N, about 36 N, about 37 N, about 38 N, about 39 N, about 40 N, about 41 N, about 42 N, about 43 N, about 44 N, about 45 N, about 46 N, about 47 N, about 48 N, about 49 N, about 50 N, about 51 N, about 52 N, about 53 N, about 54 N, about 55 N, about 56 N, about 57 N, about 58 N, about 59 N, about 60 N, about 61 N, about 62 N, about 63 N, about 64 N, about 65 N, about 66 N, about 67 N, about 68 N, about 69 N, about 70 N, about 71 N, about 72 N, about 73 N, about 74 N, about 75 N, about 76 N, about 77 N, about 78 N, about 79 N, about 80 N, about 81 N, about 82 N, about 83 N, about 84 N, about 85 N, about 86 N, about 87 N, about 88 N, about 89 N, about 90 N, about 91 N, about 92 N, about 93 N, about 94 N, about 95 N, about 96 N, about 97 N, about 98 N, about 99 N, or about 100 N.~~

~~20~~12. The composition of any one of claims 1 to ~~19~~11, wherein the composition has a storage modulus (*G'*) of from about 5 Pa to about 500 Pa, from about 15 Pa to about 50 Pa, from about 50 Pa to about 100 Pa, from about 100 Pa to about 200 Pa, from about 200 Pa to about 300 Pa, from about 300 Pa to about 350 Pa, from about 350 Pa to about 400 Pa, from about 400 Pa to about 450 Pa, or from about 450 Pa to about 500 Pa.

~~21~~13. The composition of any one of claims 1 to ~~19~~11, wherein the composition has a loss modulus (*G"*) of from about 5 Pa to about 500 Pa, from about 15 Pa to about 50 Pa, from about 50 Pa to about 100 Pa, from about 100 Pa to about 200 Pa, from about 200 Pa to about 300 Pa, from about 300 Pa to about 350 Pa, from about 350 Pa to about 400 Pa, from about 400 Pa to about 450 Pa, or from about 450 Pa to about 500 Pa.

~~22. The composition of any one of claims 1 to 19, wherein the composition has Tan(δ) (G"/G') between 0 and about 0.2, between about 0.2 and about 0.4, between about 0.4 and about 0.6, between about 0.6 and about 0.8, between about 0.8 and about 1.0, or between about 1.0 and about 1.2.~~

~~23. The composition of any one of claims 1 to 19, wherein the composition has a complex viscosity (η*) between 0 and about 5 Pa·s, between about 5 Pa·s and about 10 Pa·s, between about 10 Pa·s and about 15 Pa·s, between about 15 Pa·s and about 20 Pa·s, or between about 20 Pa·s and about 25 Pa·s.~~

~~24. The composition of any one of claims 1 to 19, wherein the composition has a storage modulus (*G'*) of from about 50 Pa to about 400 Pa, and an injection force (27G) between about 10 N and about 70 N.~~

~~25. The composition of any one of claims 1 to 19, wherein the composition has a storage modulus (*G'*) of from about 10 Pa to about 350 Pa, and an injection force (30G) between about 5 N and about 70 N.~~

~~26. The composition of any one of claims 1 to 19, wherein the composition has a loss modulus (*G"*) of from about 25 Pa to about 350 Pa, and an injection force (27G) between about 10 N and about 70 N.~~

~~27. The composition of any one of claims 1 to 19, wherein the composition has a loss modulus (*G"*) of from about 10 Pa to about 400 Pa, and an injection force (30G) between about 10 N and about 70 N.~~

~~28. The composition of any one of claims 1 to 19, wherein the composition has a storage modulus (*G'*) of from about 25 Pa to about 400 Pa, and Tan(δ) (G"/G') between 0 and about 1.2.~~

~~29. The composition of any one of claims 1 to 19, wherein the composition has a complex viscosity (η*) between about 2.5 and about 25 Pa·s, and an injection force (27G) between about 10 N and about 70 N.~~

~~30. The composition of any one of claims 1 to 19, wherein the composition has a complex viscosity (η*) between about 1 and about 20 Pa·s, and an injection force (30G) between about 5 N and about 75 N.~~

~~31. The composition of any one of claims 1 to 19, wherein the composition has a loss modulus (*G"*) of from about 5 Pa to about 400 Pa, and a storage modulus (*G'*) of from about 1 Pa to about 400 Pa.~~

~~32. The composition of any one of claims 1 to 19, wherein the total concentration of HA and silk fibroin or silk fibroin fragments in the composition is about 15 mg/mL, wherein the composition has a storage modulus (*G'*) of from about 1 Pa to about 350 Pa.~~

~~33. The composition of any one of claims 1 to 19, wherein the total concentration of HA and silk fibroin or silk fibroin fragments in the composition is about 18 mg/mL, wherein the composition has a storage modulus (*G'*) of from about 50 Pa to about 350 Pa.~~

~~34. The composition of any one of claims 1 to 19, wherein the total concentration of HA and silk fibroin or silk fibroin fragments in the composition is about 20 mg/mL, wherein the composition has a storage modulus (*G'*) of from about 20 Pa to about 400 Pa.~~

~~35. The composition of any one of claims 1 to 19, wherein the total concentration of HA and silk fibroin or silk fibroin fragments in the composition is about 22 mg/mL, wherein the composition has a storage modulus (*G'*) of from about 25 Pa to about 200 Pa.~~

~~36. The composition of any one of claims 1 to 19, wherein the total concentration of HA and silk fibroin or silk fibroin fragments in the composition is about 24 mg/mL, wherein the composition has a storage modulus (*G'*) of from about 50 Pa to about 350 Pa.~~

~~37. The composition of any one of claims 1 to 19, wherein the total concentration of HA and silk fibroin or silk fibroin fragments in the composition is about 26 mg/mL, wherein the composition has a storage modulus (*G'*) of from about 50 Pa to about 400 Pa.~~

~~38. The composition of any one of claims 1 to 19, wherein the total concentration of HA and silk fibroin or silk fibroin fragments in the composition is about 28 mg/mL, wherein the composition has a storage modulus (*G'*) of from about 150 Pa to about 300 Pa.~~

~~39~~14. The composition of any one of claims 1 to ~~38~~13, further comprising an imaging agent.

~~40. The composition of claim 39, wherein the imaging agent is selected from iodine, DOPA, and imaging nanoparticles.~~

~~41. The composition of claim 39, wherein the imaging agent is selected from a paramagnetic imaging agent and a superparamagnetic imaging agent.~~

~~42. The composition of claim 39, wherein the imaging agent is selected from NP-based magnetic resonance imaging (MRI) contrast agents, positron emission tomography (PET)/single photon emission computed tomography (SPECT) imaging agents, ultrasonically active particles, and optically active (e.g., luminescent, fluorescent, infrared) particles.~~

~~43. The composition of claim 39, wherein the imaging agent is a SPECT imaging agent, a PET imaging agent, an optical imaging agent, an MRI or MRS imaging agent, an ultrasound imaging agent, a multimodal imaging agent, an X-ray imaging agent, or a CT imaging agent.~~

~~44~~15. A composition according to any one of claims 1 to 14 for use in the~~method of~~ treatment or prevention of a disorder, disease, or condition in a subject in need thereof, ~~the method comprising administering to the subject a composition of any one of claims 1 to 43.~~

~~45. The method of claim 44,~~ wherein the condition is a skin condition selected from skin dehydration, lack of skin elasticity, skin roughness, lack of skin tautness, a skin stretch line, a skin stretch mark, skin paleness, a dermal divot, a sunken cheek, a thin lip, a retro-orbital defect, a facial fold, and a wrinkle, and

~~.~~

~~46. The method of claim 44 or claim 45,~~ wherein the composition is administered into a dermal region of the subject.

~~47~~16. A composition according to any one of claims 1 to 14 for use in the treatment or prevention of a disorder, disease, or condition in a subject in need thereof,

~~The method of any of claims 44 to 46,~~ wherein the ~~method~~use is an augmentation, a reconstruction, treating a disease, treating a disorder, correcting a defect or imperfection of a body part, region or area, ~~.~~

~~48. The method of any one of claims 44 to 47, wherein the method is~~ a facial augmentation, a facial reconstruction, treating a facial disease, treating a facial disorder, treating a facial defect, or treating a facial imperfection, and

~~.~~

~~49. The method of any one of claims 44 to 48,~~ wherein the ~~method comprises~~composition is administered into a deep subcutaneous and/or deep supraperiosteal region of the subject~~administration~~.

~~50~~17. The ~~method~~ composition for use of any one of claims ~~44~~15 to ~~49~~16, wherein the ~~method~~ use comprises cheek augmentation, lip augmentation, dermal implantation, correction of perioral rhytids, and/or correction of nasolabial fold.

~~51. The method of claim 44, wherein the composition is injected into a tissue.~~

~~52. The method of claim 51, wherein the tissue is associated with the disorder, disease, or condition.~~

~~53. The method of claim 51 or claim 52, wherein the composition is administered into a wall of the tissue.~~

~~54. The method of any one of claims 51 to 53, wherein the tissue comprises a portion of a wall of an internal organ.~~

~~55. The method of any one of claims 51 to 54, wherein administration of the composition causes bulking of the tissue.~~

~~56. The method of claim 55, wherein the disorder, disease, or condition is treated or prevented by the bulking of the tissue.~~

~~57~~18. ~~The~~ A ~~method~~ composition according to~~of~~ any one of claims ~~51~~1 to ~~56~~14 for use in the treatment or prevention of a disorder, disease, or conditions in a subject in need thereof,

wherein the disorder, disease, or condition is selected from urinary incontinence, gastroesophageal reflux disease (GERD), vesicoureteral reflux, fecal incontinence, dental tissue defects, vocal cord tissue defects, larynx defects, and other non-dermal soft tissue defects.

~~58. The method of any one of claims 51 to 56, wherein the disorder, disease, or condition is urinary incontinence.~~

~~59. The method of claim 58, wherein the urinary incontinence is stress incontinence, intrinsic sphincter deficiency (ISD), stress incontinence, intrinsic sphincter deficiency (ISD), urge incontinence, overflow incontinence, or enuresis.~~

~~60. The method of claim 58 or 59, wherein the tissue is a portion of the urethra or the urethral sphincter.~~

~~61. The method of any one of claims 51 to 56, wherein the disorder, disease, or condition is gastroesophageal reflux disease (GERD).~~

~~62. The method of claim 61, wherein the tissue is a portion of the lower esophageal sphincter or the diaphragm.~~

~~63. The method of any one of claims 51 to 56, wherein the disorder, disease, or condition is vesicoureteral reflux.~~

~~64. The method of claim 63, wherein the tissue is a portion of the urethral sphincter.~~

~~65. The method of any one of claims 51 to 56, wherein the disorder, disease, or condition is fecal incontinence.~~

~~66. The method of claim 65, wherein the tissue is a portion of the rectum.~~

~~67. The method of claim 65 or claim 66, wherein the composition is administered into a region of a rectal wall.~~

~~68. The method of claim 67, wherein the region of the rectal wall is in the vicinity of the anal sphincter.~~

~~69. The method of claim 68, wherein the composition is administered into the internal sphincter.~~

~~70. The method of any one of claims 51 to 56, wherein the disorder, disease, or condition is a vocal cord tissue defect or larynx defect.~~

~~71. The method of claim 70, wherein the vocal cord tissue defect or larynx defect is selected from glottic incompetence, unilateral vocal cord paralysis, bilateral vocal cord paralysis, paralytic dysphonia, nonparalytic dysphonia, spasmodic dysphonia, incomplete paralysis of the vocal cord ("paresis"), generally weakened vocal cords, scarring of the vocal cords, and any combination thereof.~~

~~72. The method of claim 70 or claim 71, wherein the tissue is a portion of a vocal cord or larynx.~~

~~73~~19. ~~The method~~A composition according to any one of claims 1 to 14 for use in the treatment or prevention of a disorder, disease, or conditions in a subject in need thereof~~of claim 44~~,

wherein the use further comprises~~ing~~ administration ~~ering~~of an anticancer treatment,

wherein the disorder, disease, or condition is selected from cervical cancer, rectal cancer, pulmonary tumors, mediastinum lymphoma, breast cancer, uterine cancer, pancreatic cancer, head and neck cancers, lung cancer, liver cancer, vaginal cancers, benign prostatic hyperplasia (BPH), menorrhagia, uterine fibroids, prostate adenocarcinomas, pancreatic cancer, head and neck cancer, lung cancer, liver cancer, and vaginal cancer.

~~.~~

~~74~~20. The composition for ~~method~~use of claim ~~73~~19, wherein the anticancer treatment comprises administering one or more of radiation therapy (RT), cryotherapy, drug treatment, heat and/or thermal ablation, radiofrequency and/or microwave, or cryotherapy.

~~75~~21. The composition for ~~method~~ use of claim ~~74~~20, wherein the radiation therapy comprises one or more of external beam radiotherapy, 3D conformal modulated radiotherapy, intensity modulated radiotherapy, interstitial prostate brachytherapy, interstitial prostate brachytherapy using permanent seeds, interstitial prostate brachytherapy using temporary seeds, interstitial prostate brachytherapy using high dose rate remote after loading, external radiation therapy using gamma irradiation, high energy photon beam therapy, proton beam therapy, neutron beam therapy, heavy particle beam therapy, brachytherapy, thermal radiation, or any combination thereof.

~~76~~22. The ~~method~~ composition for use of any one of claims ~~73~~ 19 to ~~75~~21, wherein the composition is administered between a first tissue and a second tissue, or into a space or virtual space between a first tissue and a second tissue, and

~~.~~

~~77. The method of claim 76,~~ wherein upon administration of the composition the first tissue is displaced relative to the second tissue.

~~78. The method of claim 76 or claim 77, wherein the space or virtual space is Denonvilliers' space or a space or virtual space adjacent to Denonvilliers' fascia.~~

~~79. The method of any one of claims 76 to 78, wherein the first tissue receives the anticancer treatment after administration of the composition.~~

~~80~~23. The ~~method~~ composition for use of claim ~~79~~22, wherein the first tissue receives a substantially similar dose of anticancer treatment compared to the anticancer treatment dose the first tissue would receive in the absence of the composition, and

wherein the second tissue receives a lower anticancer treatment dose compared to the anticancer treatment dose the second tissue would receive in the absence of the composition.

~~81. The method of any one of claims 76 to 80, wherein the second tissue receives the anticancer treatment.~~

~~82. The method of claim 81, wherein the second tissue receives a lower anticancer treatment dose compared to the anticancer treatment dose the second tissue would receive in the absence of the composition.~~

~~83. The method of any one of claims 76 to 82, wherein the second tissue receives substantially no anticancer treatment dose.~~

~~84~~24. The ~~method~~ composition for use of any of claims ~~76~~22 to ~~83~~23, wherein the first tissue and the second tissue each independently comprises a tumor tissue, a group of cells, a group of cells and interstitial matter, an organ, a portion of an organ, or an anatomical portion of a body.

~~85~~25. The ~~method~~ composition for use of any one of claims ~~76~~ 22 to ~~83~~24, wherein the first tissue comprises a tumor tissue, and the second tissue comprises an organ.

~~86~~26. The ~~method~~ composition for use of any one of claims ~~76~~ 22 to ~~83~~24, wherein the first tissue comprises an organ, and the second tissue comprises an organ.

~~86~~27. The ~~method~~ composition for use of claim ~~86~~26, wherein the first tissue comprises a portion of prostate and the second tissue comprises a portion of rectum.

~~87. The method of any one of claims 44 to 86, wherein the method further comprises administering an anesthetic.~~

~~88~~28. The ~~method~~ composition for use of any of claims ~~44~~15 to ~~87~~27, further comprising biodegradation of the composition in the subject~~.~~.

~~89. The method of claim 88, wherein the biodegradation is hydrolysis, proteolysis, enzymatic degradation, the action of cells in the body, or a combination thereof.~~

~~90. The method of claim 88,~~

wherein the ~~composition is~~ biodegradation~~ed~~ occurs by hyaluronidase enzymatic ~~degradation~~activity.