

CLAIMS

We claim:

1. A composition comprising:
 - (a) a modified human amniotic fluid (HAF); and
 - (b) HAF-derived nanoparticles;wherein the nanoparticles have a diameter of greater than 30 nm, and the concentration of the particles in the composition is at least 1×10^8 particles/ml.
2. The composition of claim 1, wherein the concentration of the particles in the composition is at least 1×10^9 particles/ml, or at least 1×10^{10} particles/ml.
3. The composition of claim 2, wherein the concentration of the particles in the composition is at least 1×10^{11} particles/ml.
4. The composition of claim 3, wherein the concentration of the particles in the composition is in a range of about 2×10^{11} particles/ml to about 1.1×10^{12} particles/ml.
5. The composition of claim 1, wherein the nanoparticles have a diameter in a range of 50 nm to 250 nm.
6. The composition of claim 5, wherein the nanoparticles have an average or mean diameter in a range of 100 to 200 nm.
7. The composition of claim 1, wherein the nanoparticles comprise membrane encapsulated extracellular vesicles.
8. The composition of claim 1, wherein the nanoparticles comprise exosomes.
9. The composition of claim 1, wherein the nanoparticles comprise surface-bound protein CD63.
10. The composition of claim 9, wherein the composition comprises CD63 at a concentration of at least 10 pg/ml, at least 300 pg/ml or at least 400 pg/ml.

11. The composition of claim 1, wherein the nanoparticles comprise three or more surface-bound proteins selected from the group consisting of CD9, CD63, CD81, CD326 and CD133.
12. The composition of claim 11, wherein the nanoparticles further comprise two or more surface-bound proteins selected from CD14, CD24, CD42a, CD44, CD29, CD14 and CD146.
13. The composition of claim 12, wherein the nanoparticles further comprise surface bound proteins HLA-DR, HLA-DP and HLA-DQ.
14. The composition of claim 1, wherein the nanoparticles comprise one, two, three, four, five, ten, twenty, twenty-five or thirty or more miRNAs selected from Table 1.
15. The composition of claim 14, wherein the nanoparticles comprise five or more miRNAs selected from hsa-let-7b, hsa-mir-200c, hsa-mir-30d, hsa-mir-125a, hsa-mir-483, hsa-mir-34c, hsa-mir-200a, hsa-mir-148a, hsa-mir-191, hsa-mir-21, hsa-mir-146a, hsa-mir-26b, hsa-mir-92b, hsa-mir-342, hsa-mir-34b, hsa-mir-423, hsa-mir-205, hsa-mir-203a, hsa-mir-99b, hsa-mir-375, hsa-mir-10b, hsa-mir-449c, hsa-mir-320a and hsa-let-7f-2.
16. The composition of claim 14, wherein the nanoparticles comprise ten or more miRNAs selected from hsa-let-7b, hsa-mir-200c, hsa-mir-30d, hsa-mir-125a, hsa-mir-483, hsa-mir-34c, hsa-mir-200a, hsa-mir-148a, hsa-mir-191, hsa-mir-21, hsa-mir-146a, hsa-mir-26b, hsa-mir-92b, hsa-mir-342, hsa-mir-34b, hsa-mir-423, hsa-mir-205, hsa-mir-203a, hsa-mir-99b, hsa-mir-375, hsa-mir-10b, hsa-mir-449c, hsa-mir-320a, hsa-let-7f-2, hsa-mir-23a, hsa-mir-27b, hsa-mir-93, hsa-mir-221, hsa-mir-425, hsa-mir-151a, hsa-mir-190b, hsa-mir-223, hsa-mir-1180, hsa-mir-184, hsa-mir-361, hsa-mir-182, hsa-mir-92a-1, hsa-mir-29a, hsa-mir-183, hsa-mir-204, hsa-mir-574, hsa-mir-532, hsa-mir-28, hsa-mir-744, hsa-mir-2110, hsa-mir-140, hsa-mir-1307, hsa-mir-193b, hsa-mir-660, hsa-mir-224, hsa-mir-196b, hsa-mir-339, hsa-mir-186, hsa-mir-3065, hsa-mir-378a, hsa-mir-16-1, hsa-mir-338, hsa-mir-126, hsa-mir-95, hsa-mir-142, hsa-mir-328, hsa-mir-335, hsa-mir-125b-2, hsa-mir-149 and hsa-mir-150.

17. The composition of claim 1, wherein the nanoparticles comprise hsa-mir-30d, hsa-mir-191, hsa-mir-21 and hsa-mir-146a.
18. The composition of claim 1, wherein the nanoparticles comprise two or more miRNAs selected from hsa-mir-30d, hsa-mir-191, hsa-mir-21 and hsa-mir-146a.
19. The composition of claim 1, wherein the nanoparticles comprise DNA polymerase beta, DNA polymerase lambda, telomerase reverse transcriptase and RAD50.
20. The composition of claim 1, wherein the composition comprises hyaluronic acid at a concentration of at least 200 ng/ml or at least 600 ng/ml.
21. The composition of claim 20, wherein the composition comprises hyaluronic acid at a concentration in a range of 200-2000 ng/ml or 600-2000 ng/ml.
22. The composition of claim 1, wherein the composition is substantially free of cells.
23. The composition of claim 1, wherein the composition is substantially free of bacteria, fungus and yeast.
24. The composition of claim 1, wherein the composition is substantially free of lanugo and vernix.
25. The composition of claim 1, wherein the composition comprises one or more, two or more, five or more, or ten or more cytokines or growth factors selected from the group consisting of angiogenin (ANG), BLC, EGF, FGF-6, GCP-2, IGFBP-1, IGF-BP2, IGF-BP4, IL-1RA, IL-6, LEPTIN, MCP-1, MIG, MIP-1DELTA, NAP-2, adiponectin (ACRP30), GRO-A, HCC-4, HGF, ICAM-1, IGFBP-6, IL-1R4, IL-6R, IL-8, OPG, sTNFRII, sTNFRI, TIMP-1, TIMP-2, and UPAR.
26. The composition of claim 25, wherein the composition comprises ANG, IL-1RA, MCP-1, IL-6, UPAR, FGF-6, EGF, HGF, LEPTIN and ACRP30.

27. The composition of claim 1, wherein the composition comprises one or more of ACRP30, AGRP, ANGPT2, AREG, AXL, B-NGF, BFGF, BTC, CCL28, CTAK, DTK, EGFR, ENA-78, FAS, FGF-4, FGF-9, G-CSF, GTR, GTR LIGAND, GRO, GRO-ALPHA, HCC-4, HGF, I-TAC, ICAM-1, ICAM-3, IGF-1SR, IGFBP-3, IGFBP-6, IL-11, IL-12 P40, IL-12 P70, IL-17, IL-1R1, IL-2R ALPHA, IL-6R, IL-8, IL1R4, MIF, MIP-1 ALPHA, MIP-2 BETA, MIP-3 BETA, MSP ALPHA, NT-4, OPG, OSM, PLGF, SGP130, STNFR1, STNFR2, TECK, THPO, TIMP-1, TIMP-2, TRAIL R3, TRAIL R4, UPAR, VEGF, VEGF-D, XCL1, ANG, BDNF, BLC, BMP4, BMP6, CCL23, CNTF, EGF, Eotaxin 1, Eotaxin 2, Eotaxin 3, FGF-6, FGF-7, FLT3-LIGAND, FRACTALKINE, GCP-2, GDNF, GM-CSF, I-309, IGF-1, IGFBP1, IGFBP2, IGFBP4, IL-10, IL-13, IL-15, IL-16, IL-1B, IL-1RA, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-1A, INF GAMMA, LEPTIN, LIGHT, M-CSF, MCP-1, MCP-2, MCP-3, MCP4, MDC, MIG, MIP-1A, MIP-3A, NAP-2, NT-3, PARC, PDGFBB, RANTES, SCF, SDF1A, TARC, TGF-B1, TGF-B3, TNFA and TNFB.

28. A pharmaceutical composition comprising
a composition comprising:
(i) a modified human amniotic fluid (HAF); and
(ii) HAF-derived nanoparticles; wherein the nanoparticles have a diameter of greater than 30 nm, and the concentration of the particles in the composition is at least 1×10^8 particles/ml;
and one or more pharmaceutically acceptable excipients or additives.

29. The pharmaceutical composition of claim 28, wherein the pharmaceutical composition is configured for, or formulated for, oral or parenteral administration.

30. A method of treating a lung disease or lung disorder in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a composition comprising (a) a modified human amniotic fluid (HAF); and (b) HAF-derived nanoparticles; wherein the nanoparticles have a diameter of greater than 30 nm, and the concentration of the particles in the composition is at least 1×10^8 particles/ml, wherein the disease or disorder is selected from acute respiratory syndrome, chronic obstructive pulmonary disease (COPD) and bronchopulmonary dysplasia.

31. The method of claim 30, wherein the lung disease or lung disorder comprises chronic obstructive pulmonary disease (COPD).
32. The method of claim 30, wherein the lung disease or lung disorder comprises bronchopulmonary dysplasia (BPD).
33. The method of claim 30, wherein the lung disease or lung disorder comprises acute respiratory syndrome.
34. The method of claim 33, wherein the subject is infected with a coronavirus.
35. The method of claim 34, wherein the subject is infected with a COVID19 or SARS-associated coronavirus (SARS-CoV2).
36. A method of treating acute brain injury in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a composition comprising (a) a modified human amniotic fluid (HAF); and (b) HAF-derived nanoparticles; wherein the nanoparticles have a diameter of greater than 30 nm, and the concentration of the particles in the composition is at least 1×10^8 particles/ml.
37. A method of treating acute organ failure in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a composition comprising (a) a modified human amniotic fluid (HAF); and (b) HAF-derived nanoparticles; wherein the nanoparticles have a diameter of greater than 30 nm, and the concentration of the particles in the composition is at least 1×10^8 particles/ml.
38. A method of treating arthritis in a subject in need thereof, comprising administering to the subject a therapeutically effective amount of a composition comprising (a) a modified human amniotic fluid (HAF); and (b) HAF-derived nanoparticles; wherein the nanoparticles have a diameter of greater than 30 nm, and the concentration of the particles in the composition is at least 1×10^8 particles/ml.
39. The method of claim 38, wherein the arthritis is osteoarthritis or rheumatoid arthritis.

40. The method of claim 38, wherein the composition is administered by intravenous or intraarticular injection.
41. The method of claim 38, wherein the subject is human.