V. CLAIMS

What is claimed is:

1. A composition comprising a therapeutically effective amount of mesenchymal stem cell (MSC) secretome and one or more biomolecules that selectively bind to one or more microbial immunogens; inhibit the ability of a microbe to inhabit a host; or inhibit, decrease, reduce, ameliorate, and/or prevent one or more secondary conditions caused by a microbial infection.

2. The composition of claim 1, wherein the one or more biomolecules comprise a peptide, polypeptide, protein, siRNA, shRNA, or microRNA (miRNA) which act concurrently and synergistically to directly affect viral infection and/or replication.

3. The composition of claim 1 or 2, wherein the biomolecule comprises a peptide, polypeptide, protein, siRNA, shRNA, or microRNA (miRNA) which act concurrently and synergistically to regulate downstream inflammation and vascular cell related pathologies in response to microbial infection.

4. The composition of claims 2 or 3, wherein the one or more biomolecules comprise a ferritin protein, PAI-1, and/or thrombomodulin.

5. The composition of claims 2 or 3, wherein the miRNA is selected from the group of miRNA comprising hsa-let-7a-5p, hsa-let-7b-5p, hsa-let-7c-5p, hsa-let-7d-3p, hsa-let-7e-5p, hsa-let-7g-5p, hsa-let-7i, hsa-let-7i-5p, hsa-miR-100-5p, hsa-miR-103a-3p, hsa-miR-106a-5p, hsa-miR-106b-5p, hsa-mir-10b, hsa-miR-10b-5p, hsa-mir-1246, hsa-miR-1246, hsa-miR-125a-5p, hsa-miR-125b-5p, hsa-miR-130a-3p, hsa-mir-130b, hsa-miR-130b-3p, hsa-miR-132-3p, hsa-miR-136-5p, hsa-miR-138-5p, hsa-miR-139-5p, hsa-mir-140, hsa-miR-140-3p, hsa-miR-145-5p, hsa-mir-146a, hsa-miR-146a-5p, hsa-miR-148a-3p, hsa-miR-152-3p, hsa-miR-15a-5p, hsa-miR-15b-5p, hsa-mir-16-1, hsa-mir-16-2, hsa-miR-16-5p, hsa-miR-17-5p, hsa-miR-181a-5p, hsa-miR-191-5p, hsa-miR-193a-5p, hsa-miR-193b-3p, hsa-miR-197-3p, hsa-miR-199a-3p, hsa-miR-199a-5p, hsa-miR-199b-5p, hsa-miR-19a-3p, hsa-miR-19b-3p, hsa-miR-20a-5p, hsa-mir-203a, hsa-miR-203a-3p, hsa-miR-214-3p, hsa-mir-21, hsa-miR-21-3p, hsa-miR-21-5p, hsa-mir-221, hsa-miR-221-3p, hsa-mir-222, hsa-miR-222-3p, hsa-miR-22-3p, hsa-miR-23a-3p, hsa-miR-23b-3p, hsa-mir-24-1, hsa-mir-24-2, hsa-miR-24-3p, hsa-mir-25, hsa-miR-25-3p, hsa-miR-26a-5p, hsa-miR-27a-3p, hsa-mir-27b, hsa-miR-27b-3p, hsa-miR-29a-3p, hsa-miR-29c-3p, hsa-miR-30a-5p, hsa-miR-30a-5p, hsa-miR-30b-5p, hsa-miR-30c-5p, hsa-mir-30d, hsa-miR-30d-5p, hsa-

mir-30e, hsa-miR-30e-5p, hsa-miR-31-3p, hsa-miR-31-5p, hsa-miR-320a, hsa-miR-342-3p, hsa-miR-345-5p, hsa-miR-34a-5p, hsa-miR-361-5p, hsa-miR-376a-3p, hsa-miR-376c-3p, hsa-miR-423-3p, hsa-miR-423-5p, hsa-miR-424-5p, hsa-miR-484, hsa-mir-486-1, hsa-mir-486-2, hsa-miR-486-5p, hsa-miR-570-3p, hsa-miR-574-3p, hsa-miR-663a, hsa-miR-874-3p, hsa-mir-92a-1, hsa-mir-92a-2, hsa-miR-92a-3p, hsa-miR-92b-3p, hsa-mir-93, hsa-miR-93-5p, hsa-miR-940, hsa-miR-99a-5p, and hsa-miR-99b-5p.

6. The composition of claim 5, wherein the miRNA inhibits the bradykinin pathway and is selected from the group consisting of let-7a-5p, hsa-let-7b-5p, hsa-let-7c-5p, hsa-let-7g-5p, hsa-let-7i-5p, hsa-let-7i, hsa-miR-106a-5p, hsa-miR-106b-5p, hsa-miR-15a-5p, hsa-miR-15b-5p, hsa-miR-16-5p, hsa-miR-17-5p, hsa-miR-20a-5p, hsa-miR-23a-3p, hsa-miR-23b-3p, hsa-mir-24-1, hsa-mir-24-2, hsa-miR-25-3p, hsa-miR-92a-3p, hsa-miR-92b-3p, and hsa-miR-93-5p.

7. The composition of claim 5, wherein the miRNA inhibits the translation of Bradykinin 2 and is a miRNA selected from the group consisting of hsa-miR-19a-3p, hsa-miR-19b-3p

8. The composition of claim 5, wherein the miRNA inhibits the angiotensin-converting enzyme 2 (ACE 2) receptor or inhibits the transmembrane protease, serine 2 (TMPRSS2) enzyme and is a miRNA selected from the group consisting of hsa-let-7a-5p, hsa-let-7b-5p, hsa-let-7c-5p, hsa-let-7g-5p, hsa-let-7i-5p, hsa-miR-214-3p, and hsa-miR-27a-3p.

9. The composition of claim 5, wherein the miRNA inhibits Kallikrein B1.

10. The composition of any of claims 1-9, wherein the one or more biomolecules inhibit IL-1β, IL-6, TNF-α, GM-CSF, or M-CSF and is selected from the group consisting of hsa-let-7a-5p, hsa-let-7b-5p, hsa-let-7c-5p, hsa-let-7g-5p, hsa-let-7i-5p, hsa-miR-547-3p, hsa-miR-130a-3p, and hsa-miR-181a-5p.

11. The composition of any of claims 1-10, wherein the MSC secretome further comprises prostaglandin E2 (PGE2), transforming growth factor β1 (TGF-β1), hepatocyte growth factor (HGF), stromal cell derived factor-1 (SDF-1), nitric oxide, indoleamine 2,3-dioxygenase, interleukin-4 (IL-4), IL-6, interleukin-10 (IL-10), IL-1 receptor antagonist and soluble TNF-α receptor, insulin-like growth factors, fibroblast growth factors (FGF) 1-23 (especially, FGF1 and FGF2), bone morphogenetic proteins (BMPs) 1-15, epidermal growth factor (EGF), transforming growth factor-α (TGF-α) macrophage-stimulating protein (MSP), platelet derived growth factor (PLGF), vascular endothelial growth factor (VEGF), macrophage colony stimulating factor (M-CSF), insulin, granulocyte colony stimulating factor (G-CSF), granulocyte macrophage colony stimulating factor (GM-CSF estrogen, and/or thyroid hormones.

12. ~~A method of treating, decreasing, inhibiting, reducing, ameliorating and/or preventing a microbial infection or symptoms thereof in a subject comprising administering to a subject~~ Use of the composition of any of claims 1-11 in the manufacture of a medicament for treating, decreasing, inhibiting, reducing, ameliorating and/or preventing a microbial infection or symptoms thereof in a subject.

13. The ~~method of treating, decreasing, inhibiting, reducing, ameliorating and/or preventing a microbial infection or symptoms thereof~~use of claim 12, wherein the composition treats, inhibits, reduces, ameliorates, and/or prevents microbial induced cytokine storm and/or microbial initiated bradykinin storm.

14. The ~~method of treating, decreasing, inhibiting, reducing, ameliorating and/or preventing a microbial infection or symptoms thereof~~use of claim 12, wherein the composition treats, inhibits, reduces, ameliorates, and/or prevents acute respiratory distress syndrome.

15. ~~A method of treating, decreasing, inhibiting, reducing, ameliorating and/or preventing a microbial infection or symptoms thereof in a subject comprising administering to a subject~~ Use of a therapeutically effective amount of MSC secretome and one or more biomolecules that selectively bind to one or more microbial immunogens; inhibit the ability of a microbe to inhabit a host; or inhibit, decrease, reduce, ameliorate, and/or prevent one or more secondary conditions caused by a microbial infection, in the manufacture of a medicament for treating, decreasing, inhibiting, reducing, ameliorating and/or preventing a microbial infection or symptoms thereof in a subject.

16. The ~~method of treating, decreasing, inhibiting, reducing, ameliorating and/or preventing a microbial infection or symptoms thereof~~use of any of claims 12-15, wherein the microbial infection comprises an infection from a virus selected from the group of viruses consisting of Herpes Simplex virus- 1, Herpes Simplex virus-2, Varicella-Zoster virus, Epstein-Barr virus, Cytomegalovirus, Human Herpes virus-6, Variola virus, Vesicular stomatitis virus, Hepatitis A virus, Hepatitis B virus, Hepatitis C virus, Hepatitis D virus, Hepatitis E virus, Rhinovirus, Coronavirus (including, but not limited to avian coronavirus (IBV), porcine coronavirus HKU15 (PorCoV HKU15), Porcine epidemic diarrhea virus (PEDV), HCoV-229E, HCoV-OC43, HCoV-HKU1, HCoV-NL63, SARS-CoV, SARS-CoV-2, or MERS-CoV), Influenza virus A, Influenza virus B, Measles virus, Polyomavirus, Human Papillomavirus, Respiratory syncytial virus, Adenovirus, Coxsackie virus, Chikungunya virus, Dengue virus, Mumps virus, Poliovirus, Rabies virus, Rous sarcoma virus, Reovirus, Yellow fever virus, Ebola virus, Marburg virus, Lassa fever virus, Eastern Equine Encephalitis virus, Japanese Encephalitis virus, St. Louis

Encephalitis virus, Murray Valley fever virus, West Nile virus, Rift Valley fever virus, Rotavirus A, Rotavirus B, Rotavirus C, Sindbis virus, Simian Immunodeficiency virus, Human T-cell Leukemia virus type-1, Hantavirus, Rubella virus, Simian Immunodeficiency virus, Human Immunodeficiency virus type-1, and Human Immunodeficiency virus type-2.

17. The ~~method of treating, decreasing, inhibiting, reducing, ameliorating and/or preventing a microbial infection or symptoms thereof~~use of any of claims 12-15, wherein the microbial infection comprises an infection from a bacteria selected from the group of bacteria consisting of Mycobacterium tuberculosis, Mycobacterium bovis, Mycobacterium bovis strain BCG, BCG substrains, Mycobacterium avium, Mycobacterium intracellular, Mycobacterium africanum, Mycobacterium kansasii, Mycobacterium marinum, Mycobacterium ulcerans, Mycobacterium avium subspecies paratuberculosis, Mycobacterium chimaera, Nocardia asteroides, other Nocardia species, Legionella pneumophila, other Legionella species, Acetinobacter baumanii, Salmonella typhi, Salmonella enterica, other Salmonella species, Shigella boydii, Shigella dysenteriae, Shigella sonnei, Shigella flexneri, other Shigella species, Yersinia pestis, Pasteurella haemolytica, Pasteurella multocida, other Pasteurella species, Actinobacillus pleuropneumoniae, Listeria monocytogenes, Listeria ivanovii, Brucella abortus, other Brucella species, Cowdria ruminantium, Borrelia burgdorferi, Bordetella avium, Bordetella pertussis, Bordetella bronchiseptica, Bordetella trematum, Bordetella hinzii, Bordetella pteri, Bordetella parapertussis, Bordetella ansorpii other Bordetella species, Burkholderia mallei, Burkholderia psuedomallei, Burkholderia cepacian, Chlamydia pneumoniae, Chlamydia trachomatis, Chlamydia psittaci, Coxiella burnetii, Rickettsial species, Ehrlichia species, Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus pneumoniae, Streptococcus pyogenes, Streptococcus agalactiae, Escherichia coli, Vibrio cholerae, Campylobacter species, Neiserria meningitidis, Neiserria gonorrhea, Pseudomonas aeruginosa, other Pseudomonas species, Haemophilus influenzae, Haemophilus ducreyi, other Hemophilus species, Clostridium tetani, other Clostridium species, Yersinia enterolitica, and other Yersinia species, and Mycoplasma species. In one aspect the bacteria is not Bacillus anthracis.

18. The ~~method of treating, decreasing, inhibiting, reducing, ameliorating and/or preventing a microbial infection or symptoms thereof~~use of any of claims 12-15, wherein the microbial infection comprises an infection from a fungus selected from the group of fungi consisting of Candida albicans, Cryptococcus neoformans, Histoplasma capsulatum, Aspergillus fumigatus, Coccidiodes immitis, Paracoccidiodes brasiliensis, Blastomyces dermitidis, Pneumocystis carinii, Penicillium marneffi, and Alternaria alternata.

19. The ~~method of treating, decreasing, inhibiting, reducing, ameliorating and/or preventing a microbial infection or symptoms thereof~~use of any of claims 12-15, wherein the microbial infection comprises a parasitic infection with a parasite selected from the group of parasitic organisms consisting of Toxoplasma gondii, Plasmodium falciparum, Plasmodium vivax, Plasmodium malariae, other Plasmodium species, Entamoeba histolytica, Naegleria fowleri, Rhinosporidium seeberi, Giardia lamblia, Enterobius vermicularis, Enterobius gregorii, Ascaris lumbricoides, Ancylostoma duodenale, Necator americanus, Cryptosporidium spp., Trypanosoma brucei, Trypanosoma cruzi, Leishmania major, other Leishmania species, Diphyllobothrium latum, Hymenolepis nana, Hymenolepis diminuta, Echinococcus granulosus, Echinococcus multilocularis, Echinococcus vogeli, Echinococcus oligarthrus, Diphyllobothrium latum, Clonorchis sinensis; Clonorchis viverrini, Fasciola hepatica, Fasciola gigantica, Dicrocoelium dendriticum, Fasciolopsis buski, Metagonimus yokogawai, Opisthorchis viverrini, Opisthorchis felineus, Clonorchis sinensis, Trichomonas vaginalis, Acanthamoeba species, Schistosoma intercalatum, Schistosoma haematobium, Schistosoma japonicum, Schistosoma mansoni, other Schistosoma species, Trichobilharzia regenti, Trichinella spiralis, Trichinella britovi, Trichinella nelsoni, Trichinella nativa, and Entamoeba histolytica.