WHAT IS CLAIMED IS:

1. Use of a polynucleotide comprising nucleic acid sequences encoding therapeutic genes in the manufacture of a medicament for the treatment of a brain disease, disorder, or injury in a subject, wherein the medicament is to be administered intracellularly into skin cells of the subject to produce skin-derived exosomes containing the therapeutic gene or gene expression product thereof.

2. The use of claim 1, wherein the brain disease is a neurodegenerative disease.

3. The use of claim 2, wherein the neurodegenerative disease comprises Alzheimer's Disease (AD), Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS), and Huntington's disease (HD).

4. The use of claim 1, wherein the brain disease is a brain cancer.

5. The use of claim 1, wherein the brain disease is a stroke or ischemia.

6. The use of claim 1, wherein the brain injury is a traumatic brain injury.

7. The use of claim 1, wherein the therapeutic gene is a vasculogenic factor.

8. The use of claim 7, wherein the vasculogenic factor comprises Etv2, Fli1, VEGFA, VEGFB, VEGFC, VEGFD, bFGF, Sox17, Oct4, Klf4, or any combination thereof.

9. The use of claim 1, wherein the therapeutic gene is a neurogenic factor.

10. The use of claim 7, wherein the neurogenic factor is selected from the group consisting of Ascl1, Ascl2, Ascl3, Ascl5, Neurog1, Neurog2, Neurog3, Neurod1, Neurod2, Neurod4, Neurod6, Atoh1, Atoh7, Atoh8, Myf5, Ptf1a, Brn3c, Brn3a, Brn3b, Brn1, Brn2, Brn4 , Oct4, Oct6, Pit1, Brn5, Myt1l, and Nurr1, or any combination thereof.

11. The use of claim 1, wherein the therapeutic gene is an siRNA or miRNA that inhibits APP.

12. The use of claim 11, wherein the miRNA is selected from the group consisting of hsa-miR-106b-5p, hsa-miR-101-3p, hsa-miR-520c-3p, hsa-miR-106a-5p, hsa-miR-20a-5p, hsa-miR-17-5p, hsa-miR-15a-5p, hsa-miR-130a-3p, hsa-let-7d-5p, hsa-let-7a-5p, hsa-miR-16-5p, hsa-miR-144-3p, hsa-miR-4422, hsa-let-7f-1-3p, hsa-let-7a-3p, hsa-let-7b-3p, hsa-miR-98-3p, hsa-miR-380-3p, hsa-miR-6835-3p, hsa-miR-4772-5p, hsa-miR-101-3p, hsa-miR-4719, hsa-miR-520f-3p, hsa-miR-3908, hsa-miR-4269, hsa-miR-323a-3p, hsa-miR-6715b-5p, hsa-miR-153-3p, hsa-miR-4495, hsa-miR-4786-5p, hsa-miR-3911, hsa-miR-6085, and hsa-miR-6813-5p, or any combination thereof.

13. The use of claim 1, wherein the therapeutic gene is an siRNA or miRNA that inhibits MAPT.

14. The use of claim 13, wherein the miRNA is selected from the group consisting of hsa-miR-34c-5p, hsa-miR-657, hsa-miR-4728-5p, and hsa-miR-3978, or any combination thereof.

15. The use of claim 1, wherein the therapeutic gene is an anti-Inflammatory gene.

16. The use of claim 15, wherein the anti-Inflammatory gene is selected from the group consisting of PPARγ, Il-10, Il-27, Trem2, and IkBα, and Sirt1, or any combination thereof.

17. The use of claim 1, wherein the therapeutic gene is an siRNA or miRNA that targets a pro-inflammatory gene.

18. The use of claim 17, wherein the pro-inflammatory gene is P2X4R, TLR4, CX3CR1, or IL-1β.

19. Use of an agent that inhibits exosomal release from the skin to reducing trafficking to the brain in the manufacture of a medicament for the treatment of a neurological disease in a subject, wherein the medicament is to be administered to the skin of the subject.

20. The use of claim 19, wherein the agent is a neutral sphingomyelinase inhibitor.