**Supplementary Files**

**Supplementary Figure 1. Validation of differentially expressed exo-miRNAs between neuropsychological lower- and higher-performing groups in the PHI study alone.**

**Supplementary Table 1. All differentially expressed exo-miRNAs between neuropsychological higher- and lower-performing groups.**

**Supplementary Table 2. All differentially expressed exo-miRNAs between neuropsychological higher- and lower-performing groups within the PHI study alone.**

**Supplementary Table 3. KEGG Pathway enrichment analysis for differentially expressed exo-miRNAs in the PHI study alone.**

**Supplementary Table 4. All differentially expressed exo-miRNAs between participants with and without HIV infection.**

**Supplementary Figure 1.**

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**Validation of differentially expressed exo-miRNAs between neuropsychological lower- and higher-performing groups in the PHI study alone.** Validation of differentially expressed exo-miRNAs between neuropsychological lower- and higher-performing groups in the PHI study alone. The red points indicate exo-miRNAs with differential expression p < 0.05, and the grey points represent no significant difference between the neuropsychological (NP) groups. X-axis represents log2(fold-change) of exosomal microRNAs (lower vs. higher NP performance), and y-axis represents the –log10(p-value) of differences exo-miRNA expression (lower vs. higher NP performance).

**Supplementary Table 1. All differentially expressed exo-miRNAs between neuropsychological higher- and lower-performing groups.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **exo-miRNA** | **baseMean** | **log2FoldChange** | **lfcSE** | **stat** | **pvalue** | **padj** |
| hsa-miR-206 | 189.763 | 3.322 | 0.631 | 5.261 | 1.43E-07 | 1.41E-04 |
| hsa-miR-193b-5p | 77.846 | 2.380 | 0.607 | 3.920 | 8.84E-05 | 0.031 |
| hsa-miR-193a-5p | 461.686 | 1.719 | 0.440 | 3.904 | 9.48E-05 | 0.031 |
| hsa-miR-30a-5p | 2504.437 | 1.102 | 0.301 | 3.658 | 2.25E-04 | 0.050 |
| hsa-miR-216b-3p | 10.211 | 4.408 | 1.242 | 3.549 | 3.86E-04 | 0.063 |
| hsa-miR-708-3p | 10.327 | 3.719 | 1.089 | 3.415 | 6.37E-04 | 0.070 |
| hsa-miR-499a-5p | 173.867 | 1.376 | 0.403 | 3.418 | 6.30E-04 | 0.070 |
| hsa-miR-499b-3p | 173.867 | 1.376 | 0.403 | 3.418 | 6.30E-04 | 0.070 |
| hsa-miR-1183 | 30.907 | 2.678 | 0.824 | 3.250 | 0.001 | 0.098 |
| hsa-miR-375 | 1740.890 | 1.493 | 0.461 | 3.241 | 0.001 | 0.098 |
| hsa-miR-483-5p | 287.039 | 1.844 | 0.573 | 3.219 | 0.001 | 0.098 |
| hsa-miR-1246 | 16.214 | 1.679 | 0.568 | 2.954 | 0.003 | 0.220 |
| hsa-miR-122-5p | 145632.167 | 2.036 | 0.743 | 2.740 | 0.006 | 0.310 |
| hsa-miR-3591-3p | 145632.167 | 2.036 | 0.743 | 2.740 | 0.006 | 0.310 |
| hsa-miR-511-5p | 180.524 | 1.275 | 0.464 | 2.748 | 0.006 | 0.310 |
| hsa-miR-150-5p | 887.336 | 1.273 | 0.459 | 2.777 | 0.005 | 0.310 |
| hsa-miR-99a-5p | 16714.625 | 1.066 | 0.390 | 2.732 | 0.006 | 0.310 |
| hsa-miR-141-3p | 40.084 | 1.416 | 0.530 | 2.674 | 0.007 | 0.352 |
| hsa-miR-200a-5p | 10.352 | 2.197 | 0.844 | 2.603 | 0.009 | 0.395 |
| hsa-miR-873-5p | 20.541 | 1.678 | 0.689 | 2.438 | 0.015 | 0.419 |
| hsa-miR-10b-3p | 52.309 | 1.269 | 0.504 | 2.520 | 0.012 | 0.419 |
| hsa-miR-125b-5p | 913.687 | 1.121 | 0.455 | 2.463 | 0.014 | 0.419 |
| hsa-miR-150-3p | 90.220 | 1.119 | 0.443 | 2.524 | 0.012 | 0.419 |
| hsa-miR-10b-5p | 5029.362 | 1.115 | 0.466 | 2.392 | 0.017 | 0.419 |
| hsa-miR-4443 | 26.887 | 1.093 | 0.449 | 2.432 | 0.015 | 0.419 |
| hsa-miR-379-5p | 622.843 | -0.992 | 0.418 | -2.374 | 0.018 | 0.419 |
| hsa-miR-433-3p | 346.304 | -1.088 | 0.459 | -2.372 | 0.018 | 0.419 |
| hsa-miR-379-3p | 13.654 | -1.481 | 0.625 | -2.368 | 0.018 | 0.419 |
| hsa-miR-618 | 20.347 | 1.854 | 0.800 | 2.317 | 0.021 | 0.422 |
| hsa-miR-3150a-5p | 11.213 | 1.223 | 0.530 | 2.310 | 0.021 | 0.422 |
| hsa-miR-3150b-3p | 11.213 | 1.223 | 0.530 | 2.310 | 0.021 | 0.422 |
| hsa-miR-100-5p | 1257.505 | 1.100 | 0.477 | 2.308 | 0.021 | 0.422 |
| hsa-miR-370-3p | 632.191 | -1.033 | 0.461 | -2.240 | 0.025 | 0.454 |
| hsa-miR-656-3p | 10.735 | -2.040 | 0.912 | -2.236 | 0.025 | 0.454 |
| hsa-miR-215-5p | 775.602 | 1.058 | 0.492 | 2.148 | 0.032 | 0.465 |
| hsa-miR-411-5p | 183.030 | -1.060 | 0.494 | -2.143 | 0.032 | 0.465 |
| hsa-miR-205-5p | 14.206 | 1.877 | 0.899 | 2.088 | 0.037 | 0.474 |
| hsa-miR-195-3p | 28.393 | 1.155 | 0.550 | 2.103 | 0.036 | 0.474 |
| hsa-miR-1185-1-3p | 76.341 | -1.151 | 0.552 | -2.084 | 0.037 | 0.474 |
| hsa-miR-382-3p | 31.238 | -1.410 | 0.673 | -2.094 | 0.036 | 0.474 |
| hsa-miR-516b-5p | 13.337 | 1.626 | 0.814 | 1.998 | 0.046 | 0.506 |
| hsa-miR-615-3p | 28.062 | 1.126 | 0.568 | 1.983 | 0.047 | 0.506 |

**Supplementary Table 2. All differentially expressed exo-miRNAs between neuropsychological higher- and lower-performing groups within the PHI study alone.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **exo-miRNA** | **baseMean** | **log2FoldChange** | **lfcSE** | **stat** | **pvalue** | **padj** |
| hsa-miR-708-3p | 11.068 | 5.240 | 1.587 | 3.302 | 0.001 | 0.999 |
| hsa-let-7a-5p | 26161.968 | -1.473 | 0.507 | -2.903 | 0.004 | 0.999 |
| hsa-let-7f-5p | 21971.054 | -1.405 | 0.522 | -2.690 | 0.007 | 0.999 |
| hsa-miR-371a-3p | 6.270 | 4.543 | 1.766 | 2.572 | 0.010 | 0.999 |
| hsa-miR-371b-5p | 6.270 | 4.543 | 1.766 | 2.572 | 0.010 | 0.999 |
| hsa-miR-4745-3p | 3.092 | 4.047 | 1.592 | 2.541 | 0.011 | 0.999 |
| hsa-miR-5100 | 5.286 | 3.033 | 1.241 | 2.444 | 0.015 | 0.999 |
| hsa-miR-141-3p | 28.777 | 1.804 | 0.747 | 2.415 | 0.016 | 0.999 |
| hsa-miR-6754-3p | 6.953 | 3.516 | 1.461 | 2.407 | 0.016 | 0.999 |
| hsa-miR-200a-5p | 8.071 | 3.087 | 1.284 | 2.404 | 0.016 | 0.999 |
| hsa-miR-454-3p | 32.775 | -2.573 | 1.072 | -2.401 | 0.016 | 0.999 |
| hsa-miR-30d-3p | 87.869 | 1.027 | 0.444 | 2.314 | 0.021 | 0.999 |
| hsa-let-7e-5p | 1096.865 | -1.471 | 0.643 | -2.288 | 0.022 | 0.999 |
| hsa-miR-4755-3p | 11.675 | 1.608 | 0.709 | 2.268 | 0.023 | 0.999 |
| hsa-miR-125b-2-3p | 31.149 | 1.939 | 0.855 | 2.267 | 0.023 | 0.999 |
| hsa-miR-205-5p | 13.511 | 2.381 | 1.051 | 2.265 | 0.023 | 0.999 |
| hsa-miR-1299 | 2.834 | -2.583 | 1.147 | -2.253 | 0.024 | 0.999 |
| hsa-miR-181b-2-3p | 1.599 | 3.852 | 1.727 | 2.231 | 0.026 | 0.999 |
| hsa-miR-4742-3p | 17.895 | 1.526 | 0.702 | 2.176 | 0.030 | 0.999 |
| hsa-miR-6808-3p | 4.416 | -2.500 | 1.158 | -2.158 | 0.031 | 0.999 |
| hsa-miR-4449 | 5.169 | 2.619 | 1.218 | 2.149 | 0.032 | 0.999 |
| hsa-miR-125b-5p | 731.853 | 1.383 | 0.655 | 2.113 | 0.035 | 0.999 |
| hsa-miR-193a-5p | 292.088 | 1.407 | 0.668 | 2.107 | 0.035 | 0.999 |
| hsa-miR-1183 | 29.339 | 2.652 | 1.268 | 2.091 | 0.037 | 0.999 |
| hsa-miR-1538 | 8.259 | 1.868 | 0.905 | 2.064 | 0.039 | 0.999 |
| hsa-miR-548k | 19.202 | -1.522 | 0.752 | -2.024 | 0.043 | 0.999 |
| hsa-miR-429 | 8.041 | 1.957 | 0.968 | 2.023 | 0.043 | 0.999 |
| hsa-let-7c-5p | 1461.969 | -0.850 | 0.421 | -2.020 | 0.043 | 0.999 |
| hsa-miR-3678-3p | 2.623 | 3.820 | 1.905 | 2.005 | 0.045 | 0.999 |
| hsa-miR-7110-3p | 6.868 | -2.038 | 1.017 | -2.005 | 0.045 | 0.999 |
| hsa-miR-7155-3p | 6.263 | 2.734 | 1.373 | 1.991 | 0.046 | 0.999 |

**Supplementary Table 3. KEGG Pathway enrichment analysis for differentially expressed exo-miRNAs in the PHI study alone.**

|  |  |  |  |
| --- | --- | --- | --- |
| **KEGG pathway** | **p-value** | **#genes** | **#microRNAs** |
| Glycosphingolipid biosynthesis - lacto and neolacto series | 1.66E-11 | 15 | 12 |
| Hippo signaling pathway | 2.71E-07 | 62 | 14 |
| Prion diseases | 2.71E-07 | 9 | 7 |
| Transcriptional misregulation in cancer | 1.18E-04 | 70 | 15 |
| Endocytosis | 3.25E-04 | 88 | 15 |
| Thyroid hormone signaling pathway | 3.25E-04 | 49 | 15 |
| TGF-beta signaling pathway | 3.25E-04 | 37 | 14 |
| Proteoglycans in cancer | 6.31E-04 | 85 | 15 |
| Renal cell carcinoma | 8.76E-04 | 32 | 15 |
| Adherens junction | 0.002 | 34 | 15 |
| Ubiquitin mediated proteolysis | 0.002 | 62 | 15 |
| Pathways in cancer | 0.002 | 147 | 15 |
| FoxO signaling pathway | 0.002 | 61 | 14 |
| Chronic myeloid leukemia | 0.003 | 33 | 15 |
| MAPK signaling pathway | 0.003 | 101 | 15 |
| ErbB signaling pathway | 0.008 | 36 | 15 |
| Axon guidance | 0.008 | 54 | 14 |
| PI3K-Akt signaling pathway | 0.025 | 126 | 15 |
| Rap1 signaling pathway | 0.025 | 81 | 15 |
| Hypertrophic cardiomyopathy (HCM) | 0.025 | 38 | 13 |
| Lysine degradation | 0.027 | 19 | 15 |

**Supplementary Table 4. All differentially expressed exo-miRNAs between participants with and without HIV infection.**

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| **exo-miRNA** | **baseMean** | **log2FoldChange** | **lfcSE** | **stat** | **pvalue** | **padj** |
| hsa-miR-504-5p | 24.84 | 5.98 | 1.38 | 4.33 | 1.00E-05 | 0.020 |
| hsa-miR-9-5p | 129.32 | 3.18 | 0.83 | 3.81 | 1.00E-04 | 0.093 |
| hsa-miR-758-3p | 40.25 | 2.50 | 0.74 | 3.37 | 0.001 | 0.291 |
| hsa-miR-1229-3p | 20.92 | 1.53 | 0.46 | 3.33 | 0.001 | 0.291 |
| hsa-miR-6818-5p | 5.73 | -3.13 | 0.98 | -3.20 | 0.001 | 0.363 |
| hsa-miR-187-3p | 2.69 | 3.96 | 1.33 | 2.98 | 0.003 | 0.640 |
| hsa-miR-6772-3p | 22.18 | 2.24 | 0.77 | 2.91 | 0.004 | 0.688 |
| hsa-miR-4306 | 11.04 | -1.31 | 0.46 | -2.82 | 0.005 | 0.714 |
| hsa-miR-7848-3p | 5.59 | 3.28 | 1.17 | 2.81 | 0.005 | 0.714 |
| hsa-miR-216b-3p | 20.12 | 5.71 | 2.05 | 2.78 | 0.005 | 0.714 |
| hsa-miR-6855-3p | 2.48 | 3.82 | 1.40 | 2.73 | 0.006 | 0.714 |
| hsa-miR-1185-2-3p | 3.38 | 3.50 | 1.29 | 2.71 | 0.007 | 0.714 |
| hsa-miR-4662a-5p | 7.42 | 2.96 | 1.12 | 2.65 | 0.008 | 0.714 |
| hsa-miR-4662b | 7.42 | 2.96 | 1.12 | 2.65 | 0.008 | 0.714 |
| hsa-miR-424-3p | 392.20 | 0.97 | 0.37 | 2.63 | 0.009 | 0.714 |
| hsa-miR-146b-3p | 23.44 | 1.14 | 0.44 | 2.62 | 0.009 | 0.714 |
| hsa-miR-92a-1-5p | 16.37 | 1.41 | 0.54 | 2.61 | 0.009 | 0.714 |
| hsa-miR-1307-3p | 3602.48 | 0.79 | 0.32 | 2.48 | 0.013 | 0.846 |
| hsa-miR-3186-5p | 2.54 | -4.63 | 1.87 | -2.48 | 0.013 | 0.846 |
| hsa-miR-1294 | 36.02 | 1.28 | 0.52 | 2.47 | 0.013 | 0.846 |
| hsa-miR-6866-5p | 13.56 | 1.93 | 0.79 | 2.45 | 0.014 | 0.846 |
| hsa-miR-30e-3p | 2511.88 | 0.67 | 0.28 | 2.42 | 0.016 | 0.846 |
| hsa-miR-6764-5p | 2.40 | 3.55 | 1.48 | 2.40 | 0.016 | 0.846 |
| hsa-miR-3140-3p | 3.72 | 2.86 | 1.19 | 2.40 | 0.016 | 0.846 |
| hsa-miR-3928-3p | 19.32 | 1.47 | 0.61 | 2.39 | 0.017 | 0.846 |
| hsa-let-7e-5p | 1232.60 | 1.15 | 0.48 | 2.39 | 0.017 | 0.846 |
| hsa-miR-937-3p | 7.15 | 1.79 | 0.75 | 2.39 | 0.017 | 0.846 |
| hsa-miR-4489 | 4.09 | 2.69 | 1.14 | 2.37 | 0.018 | 0.846 |
| hsa-miR-411-5p | 156.00 | 1.54 | 0.65 | 2.36 | 0.018 | 0.846 |
| hsa-miR-1287-5p | 92.72 | 0.91 | 0.39 | 2.31 | 0.021 | 0.854 |
| hsa-miR-3064-5p | 20.63 | 1.22 | 0.53 | 2.30 | 0.021 | 0.854 |
| hsa-miR-3173-3p | 2.76 | 3.94 | 1.71 | 2.30 | 0.021 | 0.854 |
| hsa-miR-6826-3p | 2.03 | -4.80 | 2.10 | -2.29 | 0.022 | 0.854 |
| hsa-miR-4470 | 5.47 | 2.64 | 1.17 | 2.26 | 0.024 | 0.854 |
| hsa-miR-548n | 3.55 | -3.36 | 1.50 | -2.24 | 0.025 | 0.854 |
| hsa-miR-6894-3p | 7.51 | 2.25 | 1.00 | 2.24 | 0.025 | 0.854 |
| hsa-miR-3065-5p | 18.38 | 1.29 | 0.58 | 2.24 | 0.025 | 0.854 |
| hsa-miR-338-3p | 18.38 | 1.29 | 0.58 | 2.24 | 0.025 | 0.854 |
| hsa-miR-375 | 1965.68 | -1.36 | 0.61 | -2.22 | 0.026 | 0.854 |
| hsa-miR-659-5p | 6.92 | 2.49 | 1.12 | 2.22 | 0.027 | 0.854 |
| hsa-miR-4444 | 2.67 | -2.80 | 1.26 | -2.21 | 0.027 | 0.854 |
| hsa-miR-5001-3p | 3.43 | 3.02 | 1.37 | 2.21 | 0.027 | 0.854 |
| hsa-miR-30b-3p | 53.92 | 0.84 | 0.38 | 2.21 | 0.027 | 0.854 |
| hsa-miR-3656 | 7.42 | 1.52 | 0.70 | 2.19 | 0.029 | 0.871 |
| hsa-miR-127-3p | 3646.23 | 1.04 | 0.48 | 2.18 | 0.029 | 0.871 |
| hsa-miR-378a-5p | 14.30 | 1.39 | 0.64 | 2.16 | 0.031 | 0.871 |
| hsa-miR-4511 | 3.78 | 2.74 | 1.27 | 2.15 | 0.031 | 0.871 |
| hsa-miR-548o-3p | 70.23 | 1.03 | 0.48 | 2.15 | 0.032 | 0.871 |
| hsa-miR-496 | 6.74 | 2.74 | 1.29 | 2.13 | 0.033 | 0.871 |
| hsa-miR-6808-3p | 4.62 | -2.46 | 1.16 | -2.12 | 0.034 | 0.871 |
| hsa-miR-6511a-3p | 8.88 | 1.51 | 0.71 | 2.12 | 0.034 | 0.871 |
| hsa-miR-589-5p | 114.10 | 0.61 | 0.29 | 2.12 | 0.034 | 0.871 |
| hsa-miR-218-5p | 22.96 | 2.10 | 1.00 | 2.11 | 0.035 | 0.871 |
| hsa-miR-130b-5p | 326.83 | 0.76 | 0.36 | 2.11 | 0.035 | 0.871 |
| hsa-miR-145-3p | 344.48 | -0.63 | 0.30 | -2.09 | 0.036 | 0.887 |
| hsa-miR-4435 | 13.86 | 1.30 | 0.63 | 2.06 | 0.040 | 0.935 |
| hsa-miR-4533 | 5.96 | 2.46 | 1.20 | 2.05 | 0.040 | 0.935 |
| hsa-miR-26a-5p | 151045.73 | 0.80 | 0.39 | 2.04 | 0.041 | 0.935 |
| hsa-miR-1254 | 5.86 | 1.77 | 0.87 | 2.04 | 0.041 | 0.935 |
| hsa-miR-370-3p | 553.06 | 1.20 | 0.59 | 2.03 | 0.043 | 0.952 |
| hsa-miR-6807-5p | 5.46 | -2.39 | 1.18 | -2.02 | 0.043 | 0.952 |
| hsa-miR-503-5p | 230.78 | 0.93 | 0.46 | 2.01 | 0.044 | 0.959 |
| hsa-miR-6770-3p | 6.45 | 2.24 | 1.12 | 2.00 | 0.046 | 0.967 |
| hsa-miR-6837-3p | 15.52 | 1.46 | 0.73 | 1.99 | 0.047 | 0.967 |
| hsa-miR-18b-3p | 5.25 | -1.81 | 0.91 | -1.98 | 0.048 | 0.967 |
| hsa-miR-4638-5p | 6.23 | 2.17 | 1.10 | 1.98 | 0.048 | 0.967 |
| hsa-miR-146b-5p | 5366.05 | 0.56 | 0.29 | 1.96 | 0.049 | 0.967 |