

## SUPPLEMENTARY MATERIAL

Figure S1: Distribution of age (A), BMI (B), sex (C) and smoking (D) in CVD and control group.

Figure S2: Control plots for miRNA sequencing data.

Figure S3: Control plots for transcriptome sequencing data.

Figure S4: Plots for UVE-PLS analysis of miRNA expression in CVD group in comparison to control group.

Figure S5: Receiver Operating Characteristics (ROC) curves for 34 miRNA transcripts selected as signatures of CVD.

Figure S6: Plots for UVE-PLS analysis of genes expression in CVD group compared to control group.

Figure S7: Receiver Operating Characteristics (ROC) curves for 62 genes selected as signatures of CVD.

Figure S8: Results of gene expression deconvolution procedure for seven CVD patients and seven control subjects performed using “quanTIseq” method implemented to immunedeconv 2.0.0 package.

Figure S9: Results of deconvolution procedure performed on gene expression datasets of 7 CVD patients (CVD) and 7 control subjects (Control) using “MCPcounter” method implemented to immunedeconv 2.0.0 package.

Table S1: Measurements of small RNA samples and small RNA libraries as well as results of small RNA sequencing data analysis received from Ion Torrent small RNA Plugin v5.0.5r3.

Table S2: Measurements of transcriptome libraries and results of transcriptome sequencing data analysis received from Ion Torrent RNASeqAnalysis plugin v.5.0.3.0.

Table S3: The set of 96 differentially expressed microRNA transcripts resulted from DESeq2 analysis with  $p < 0.05$  in 34 patients with CVD compared to 19 controls.

Table S4: The set of 48 differentially expressed microRNA transcripts resulted from UVE-PLS analysis in 34 patients with CVD group compared to 19 controls.

Table S5: Results of ROC analysis for 34 miRNA transcripts selected as indicative for CVD. Table S6: Correlation analysis between age and expression of 34 selected miRNA transcripts in CVD group.

Table S7: 183 differentially expressed genes resulted from DESeq2 analysis with  $p < 0.00001$  in seven patients with CVD, compared to seven controls.

Table S8: The set of 74 differentially expressed genes resulted from UVE-PLS analysis in seven patients with CVD compared to seven controls.

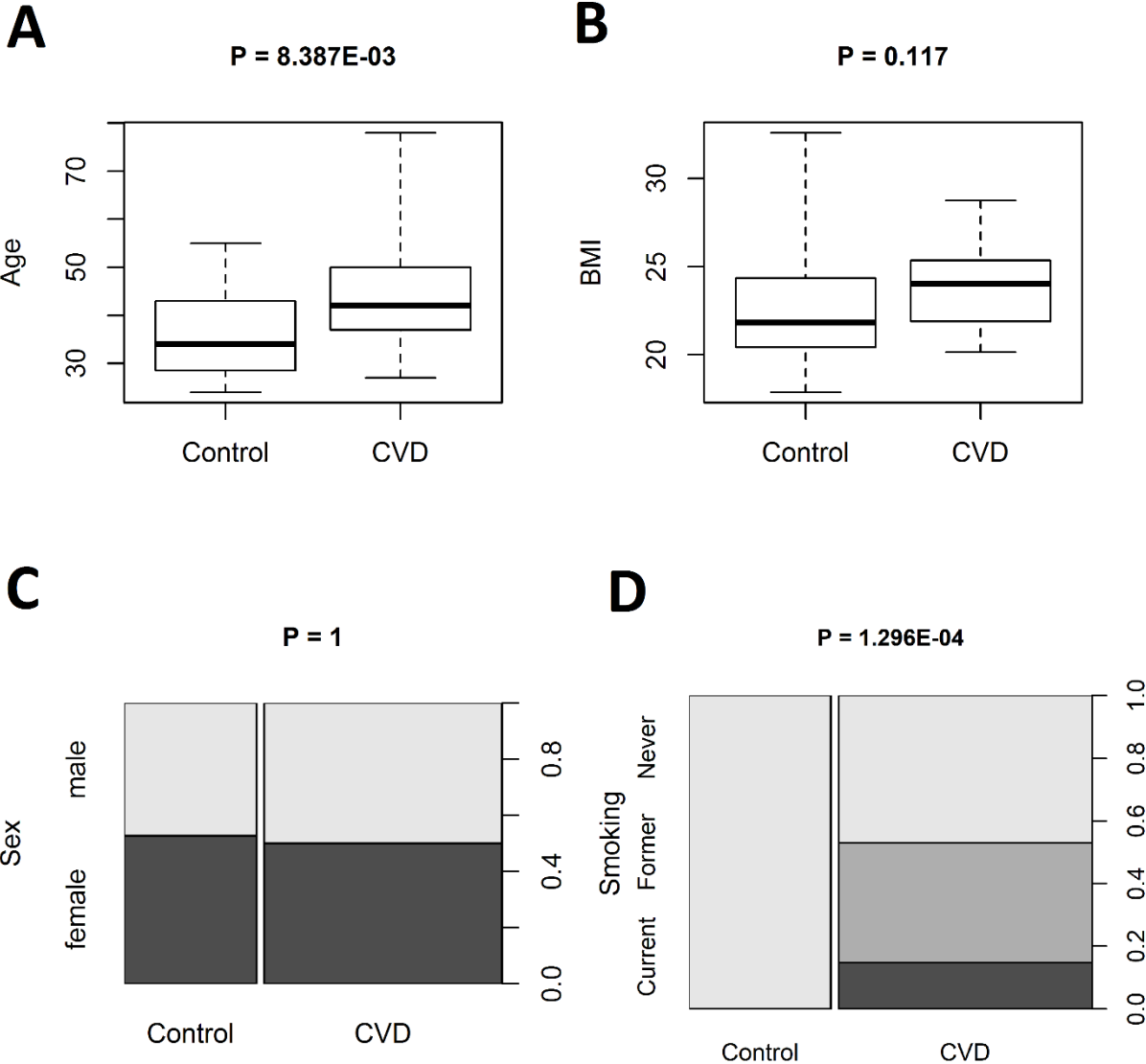
Table S9: Results of ROC analysis for 62 genes selected as indicative for CVD.

Table S10: Correlation analysis between age and expression of 62 selected genes in CVD group.

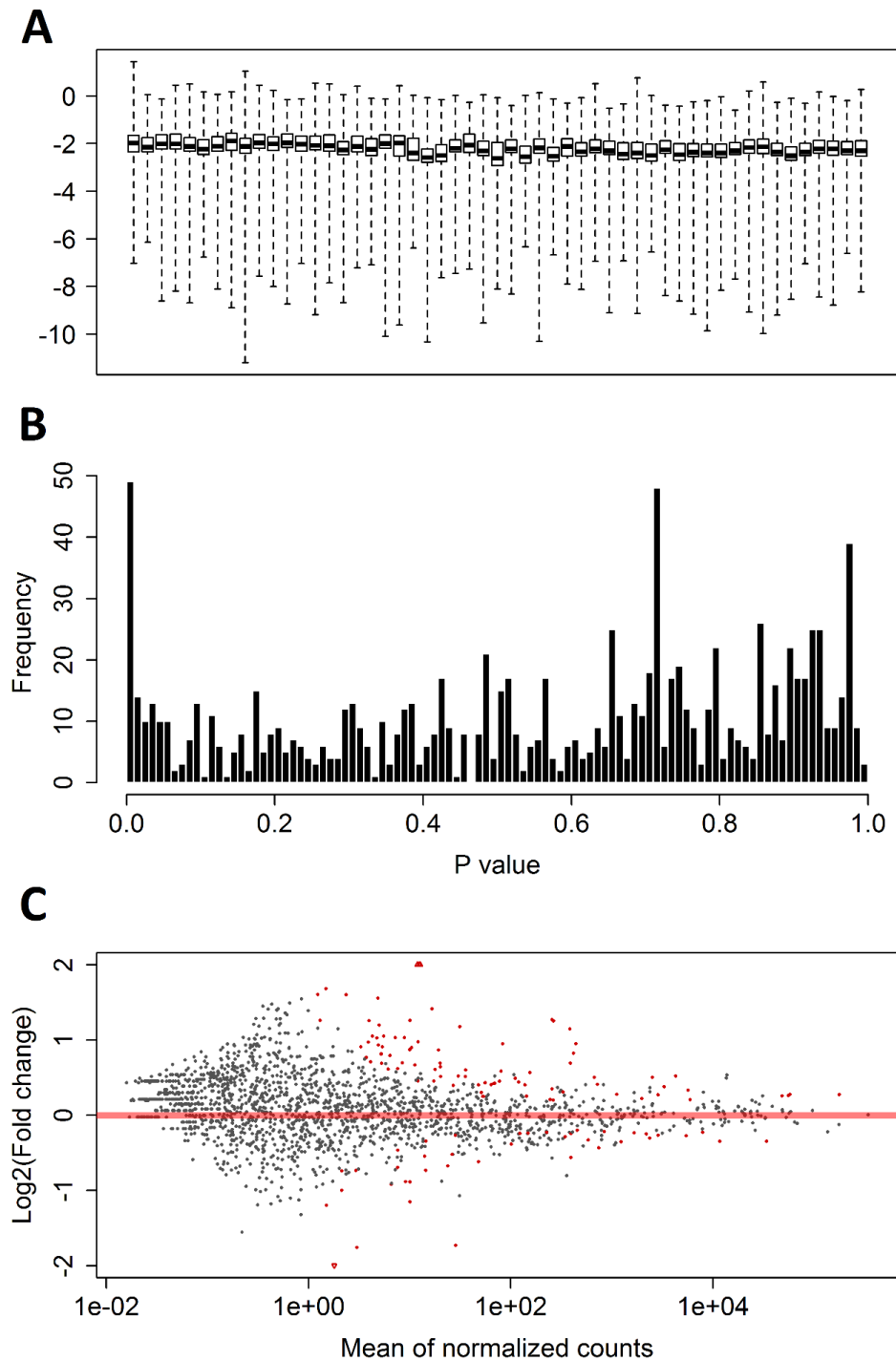
Table S11: Twelve experimentally validated miRNA:gene pairs found among 31 miRNAs and 62 genes indicative for CVD using multiMiR package.

Table S12: Top 10%-predicted miRNA:gene pairs found among 31 miRNAs and 62 genes indicative for CVD using multiMiR package.

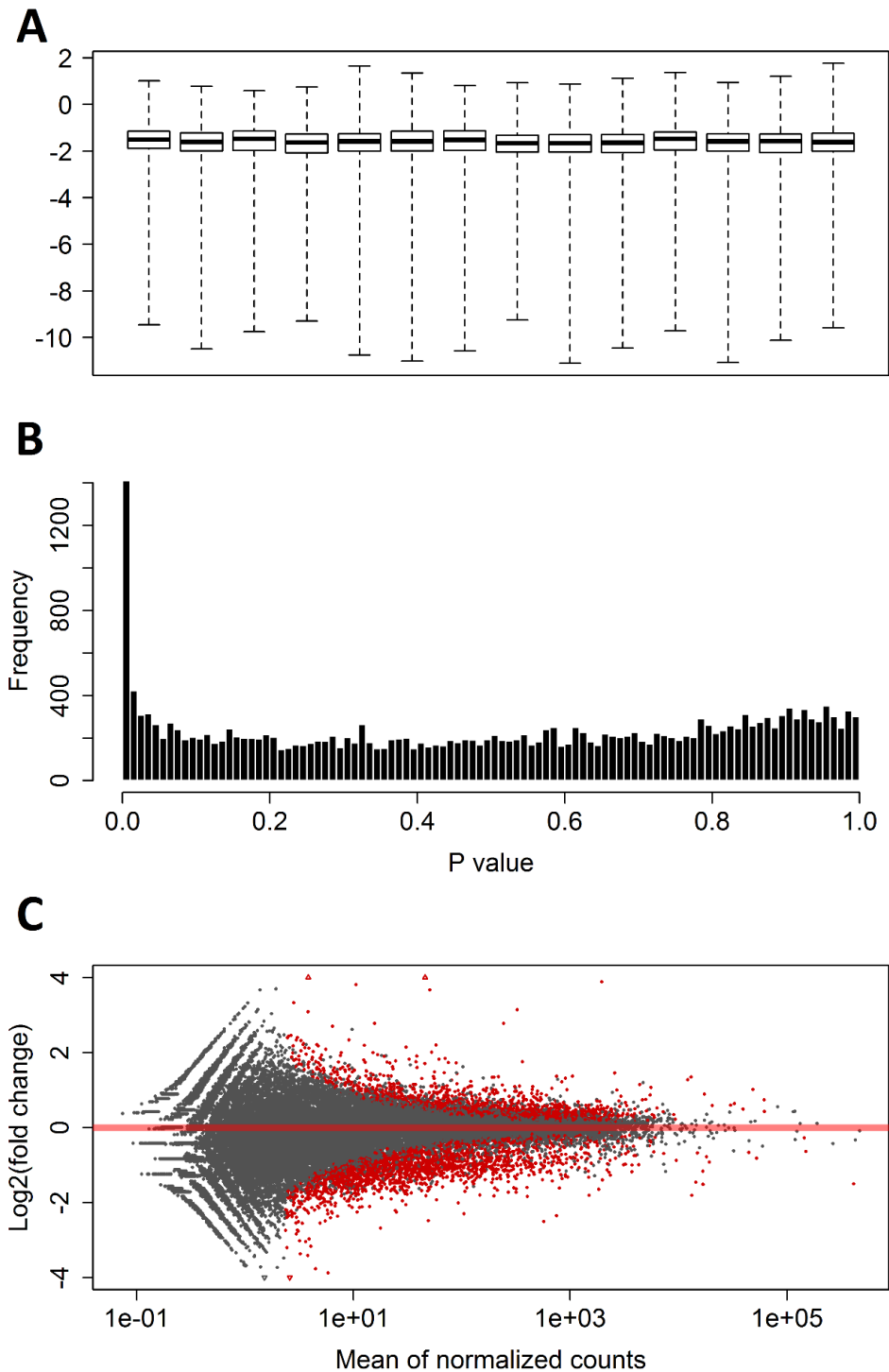
Supplementary Figures



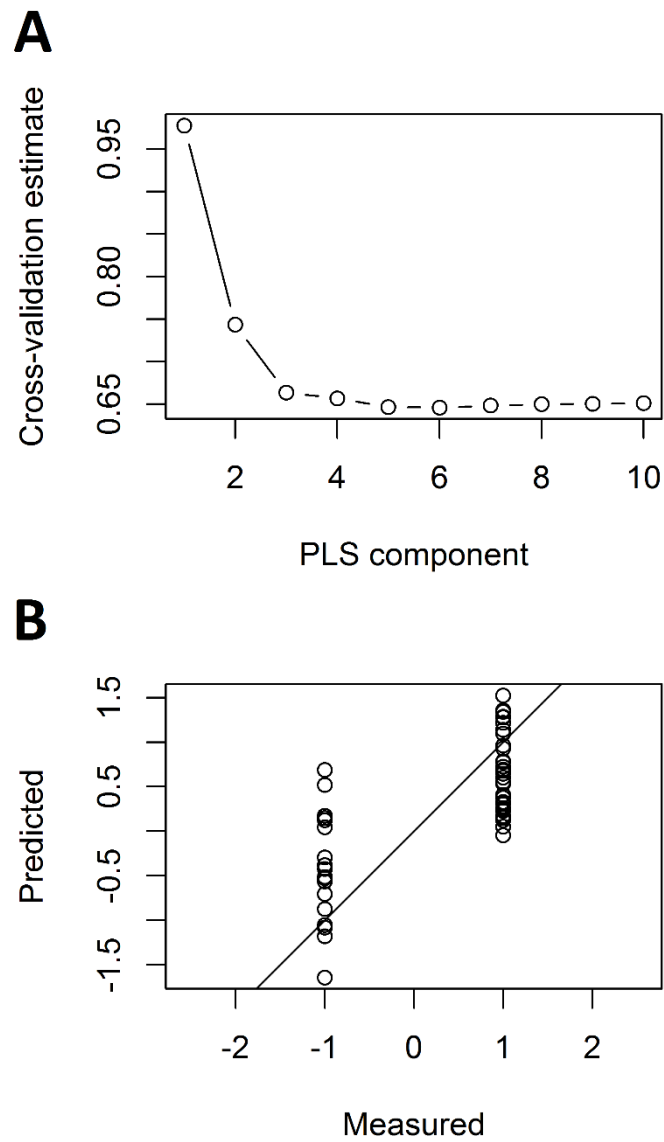
**Figure S1.** Distribution of age (A), BMI (B), sex (C) and smoking (D) in CVD and control group. Statistical significance ( $P$  values) was evaluated using two-sided Mann-Whitney U test (for age and BMI) and two-sided Fisher exact test (for sex and smoking). In the boxplots, whiskers define region between minimum and maximum values, boxes cover values between 25% and 75% quantile and horizontal lines inside boxes mark median value. Spine plot (C) presents percentage distribution of sex (black – female, gray – male) and spine plot (D) presents percentage distribution of smoking (black – current smokers, medium grey – former smokers, light grey – non-smokers).



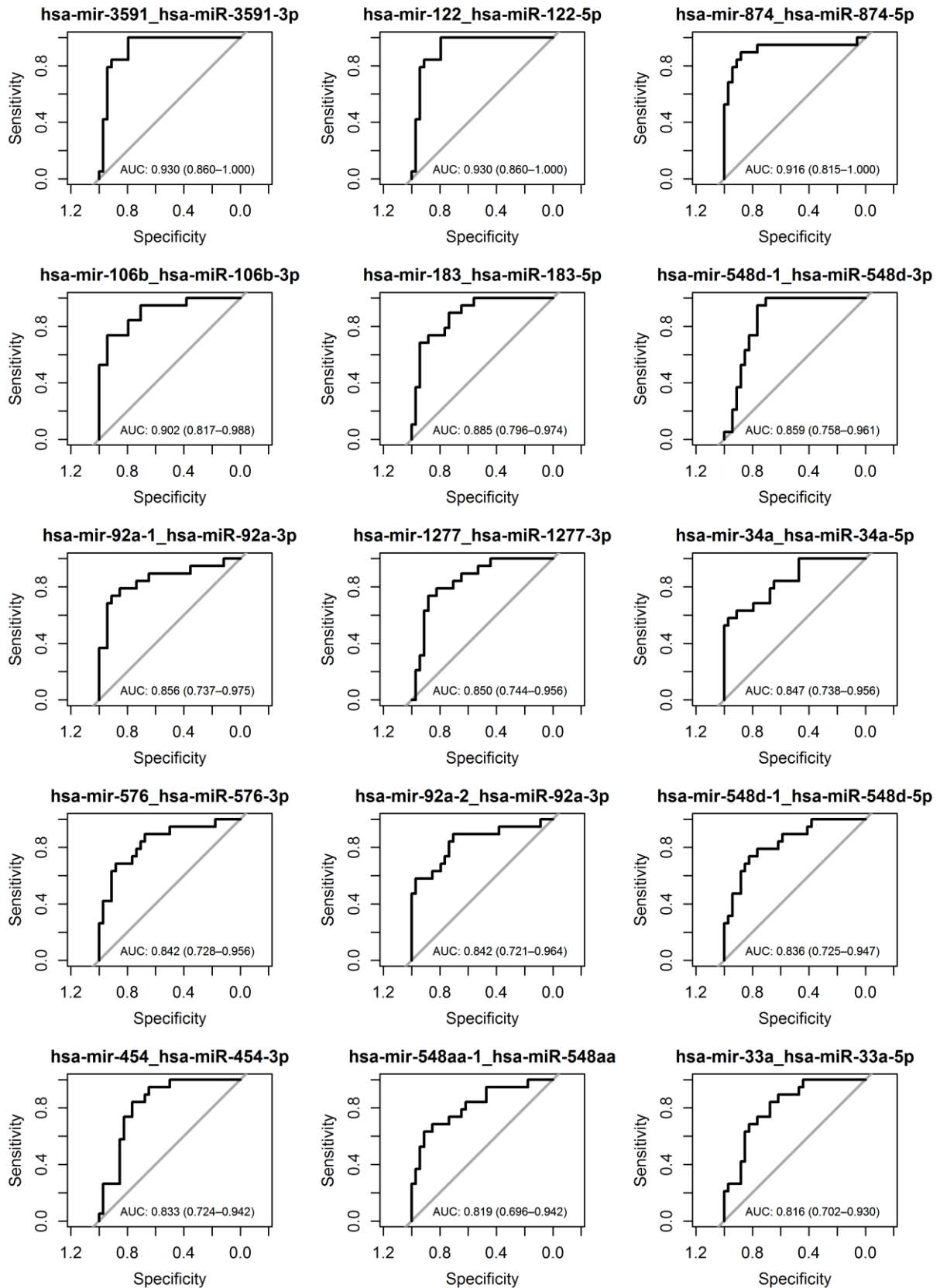
**Figure S2.** Control plots for miRNA sequencing data. **(A)** Boxplot of Cook's distances of miRNAs across samples. Whiskers cover the region between minimum and maximum values of Cook's distance, boxes include the region between 25% and 75% quartile, horizontal lines inside boxes mark median value. **(B)** Histogram of  $P$  values received from DESeq2 analysis. **(C)** MA plot of DESeq2 results ( $\log_2$  fold changes of differentially expressed miRNAs over the average of normalized counts). Red points on MA plot indicate differentially expressed miRNAs with  $P$  values  $< 0.1$ .



**Figure S3.** Control plots for transcriptome sequencing data. **(A)** Boxplot of Cook's distances of samples. Whiskers cover the region between minimum and maximum value of Cook's distance, boxes include the region between 25% and 75% quartile, horizontal lines inside boxes mark median value. **(B)** Histogram of  $P$  values received from DESeq2 analysis. **(C)** MA plot of DESeq2 results (log<sub>2</sub> fold changes of differentially expressed genes over the average of normalized counts). Red points on MA plot indicate differentially expressed genes with  $P$  values < 0.1.



**Figure S4.** Plots for UVE-PLS analysis of miRNA expression in CVD group in comparison to control group. **(A)** The arrangement of prediction error and PLS components. **(B)** Plot of cross-validated predictions versus measured values.



**Figure S5.** Receiver Operating Characteristics (ROC) curves for 34 miRNA transcripts selected as signatures of CVD. Plots include values of AUC (areas under curves) with 95% confidence interval in brackets.

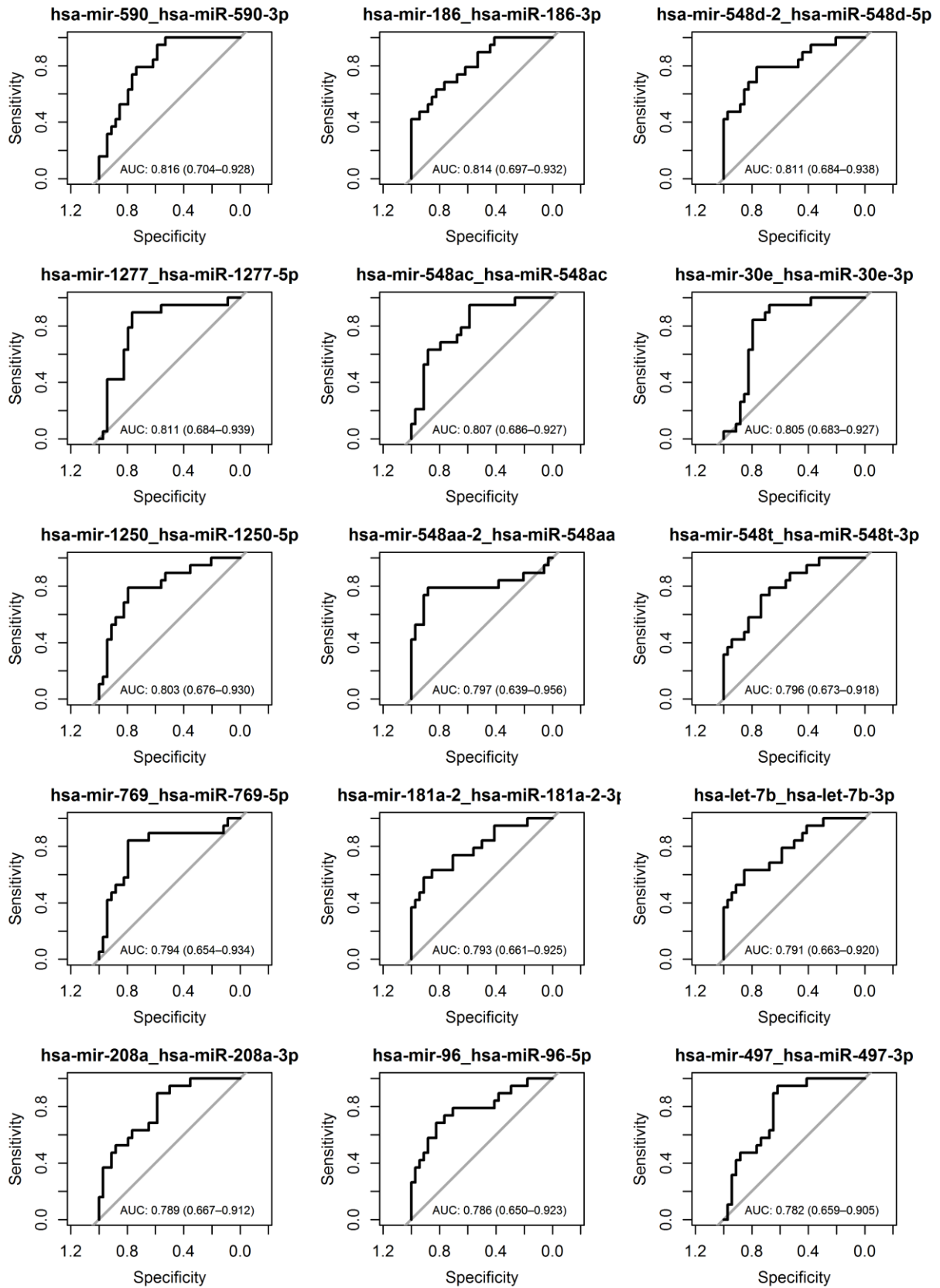


Figure S5. (continued).



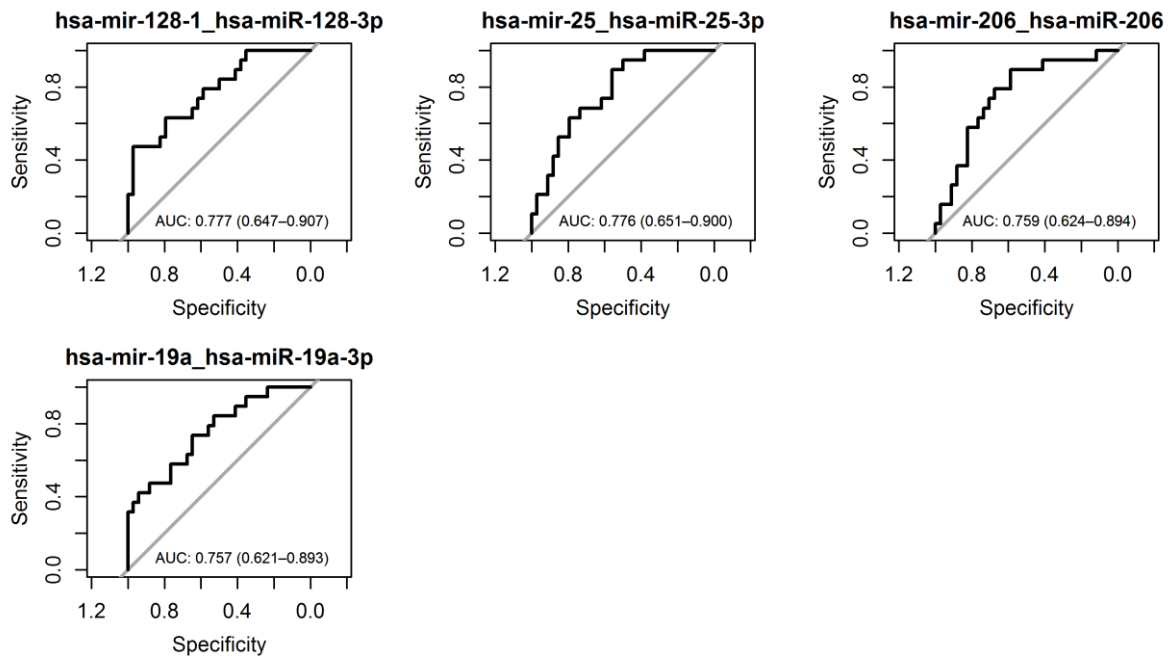
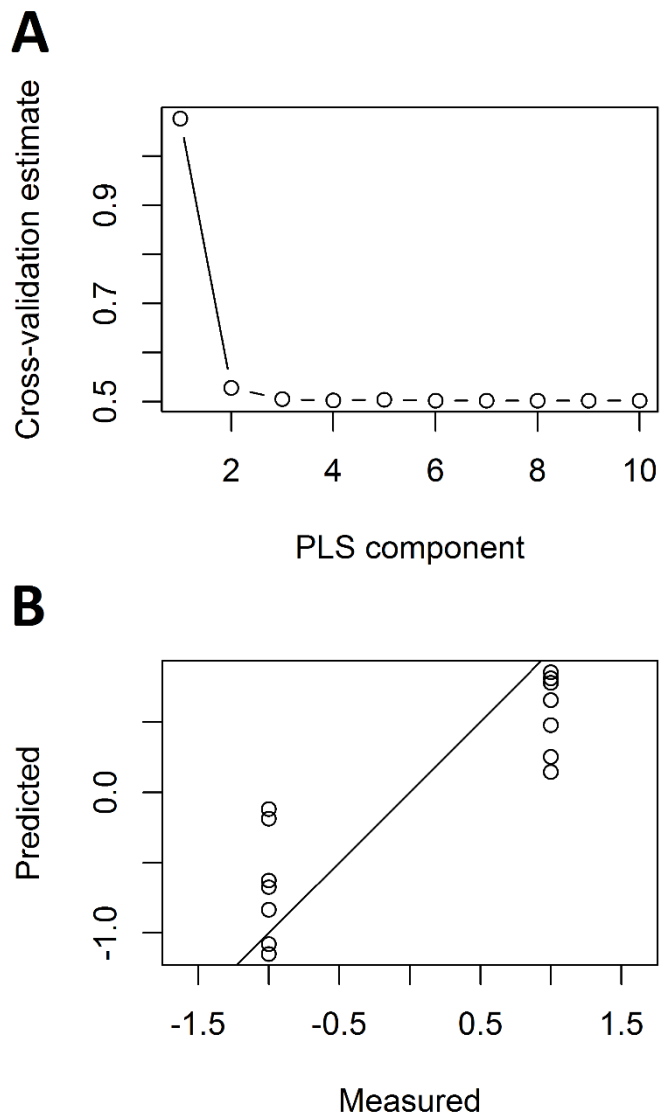
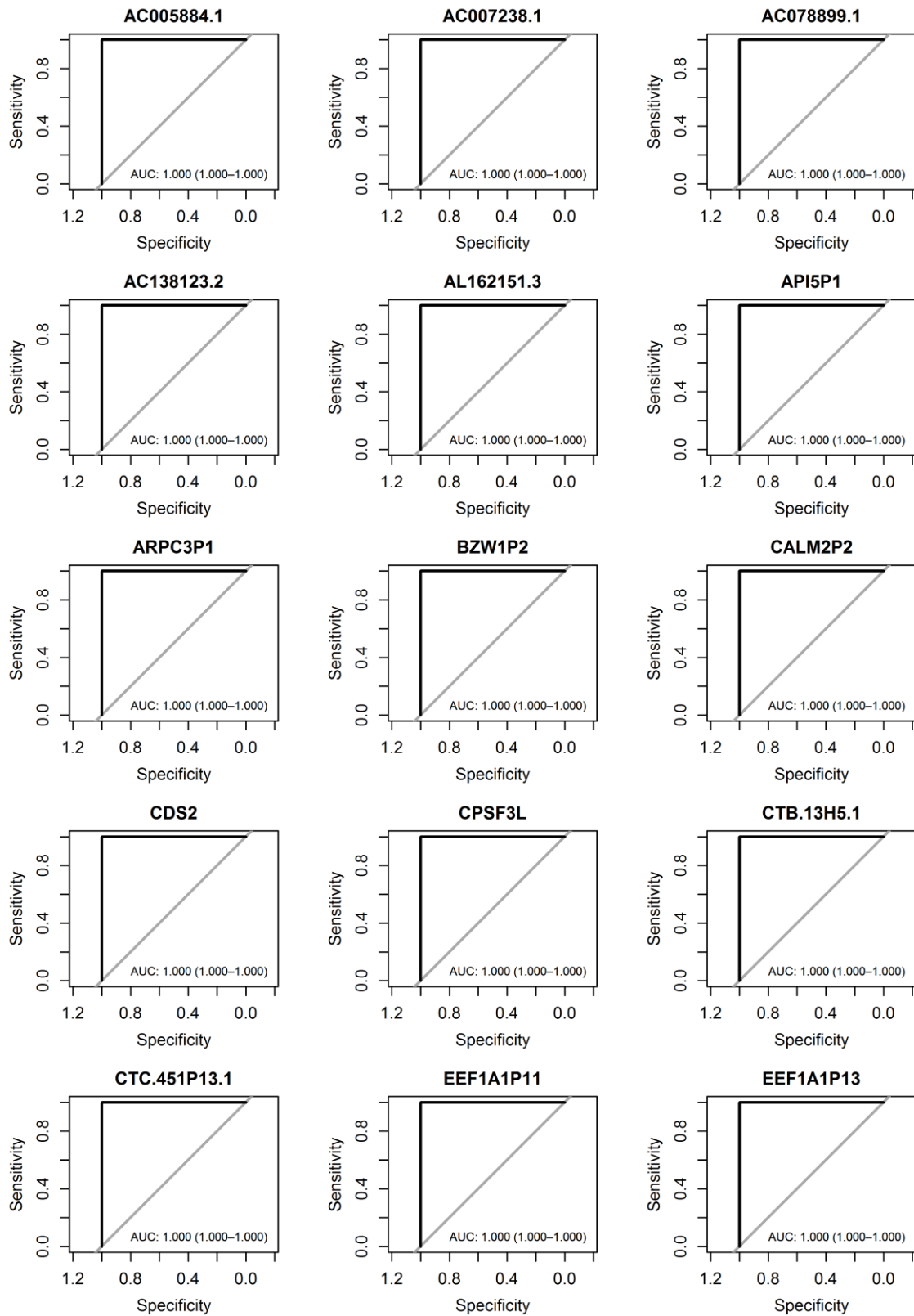


Figure S5. (continued).



**Figure S6.** Plots for UVE-PLS analysis of genes expression in CVD group compared to control group. **(A)** The arrangement of prediction error and PLS components. **(B)** Plot of cross-validated predictions versus measured values.



**Figure S7.** Receiver Operating Characteristics (ROC) curves for 62 genes selected as signatures of CVD. Plots include values of AUC (areas under curves) with 95% confidence interval in brackets.

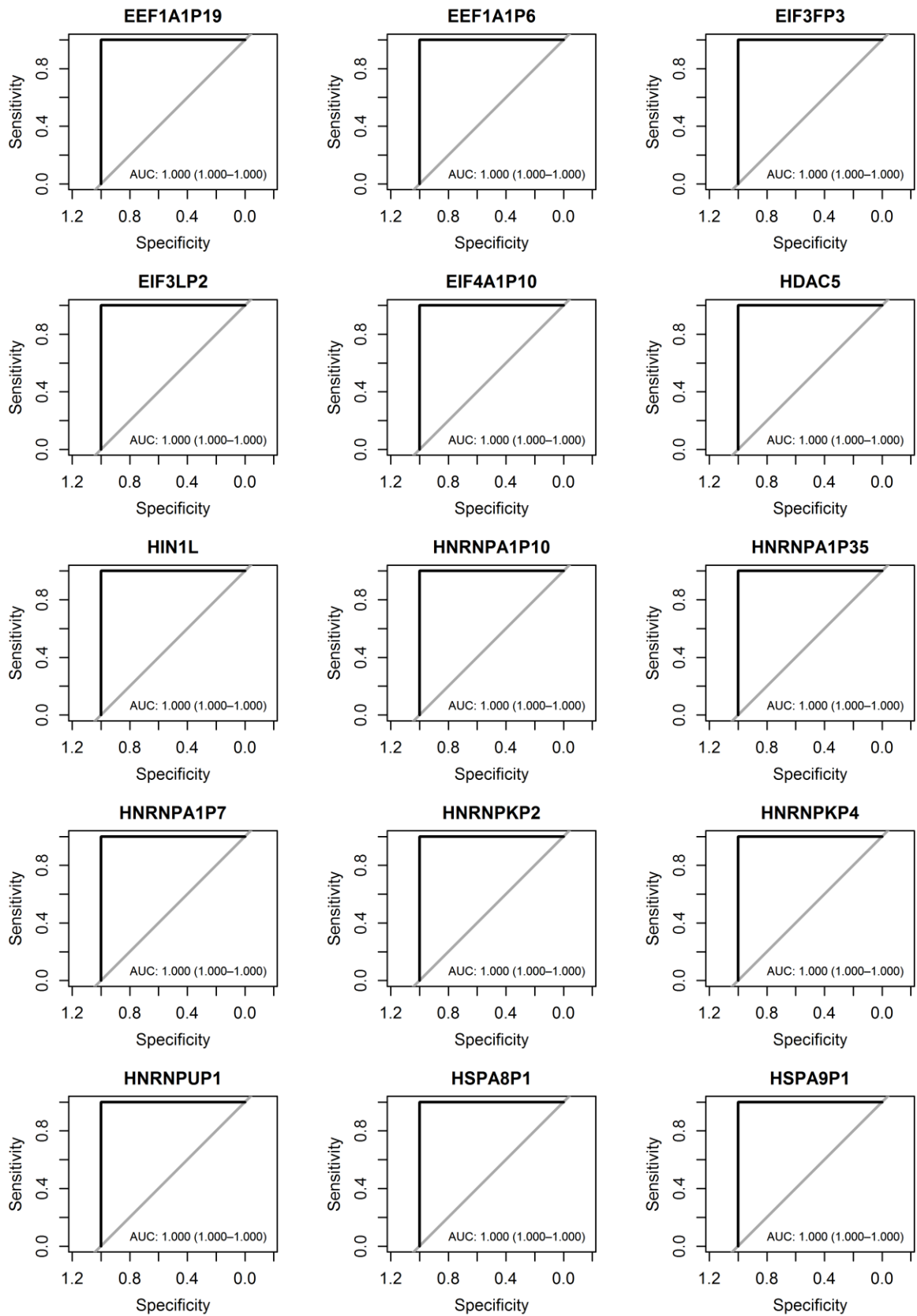


Figure S7. (continued).

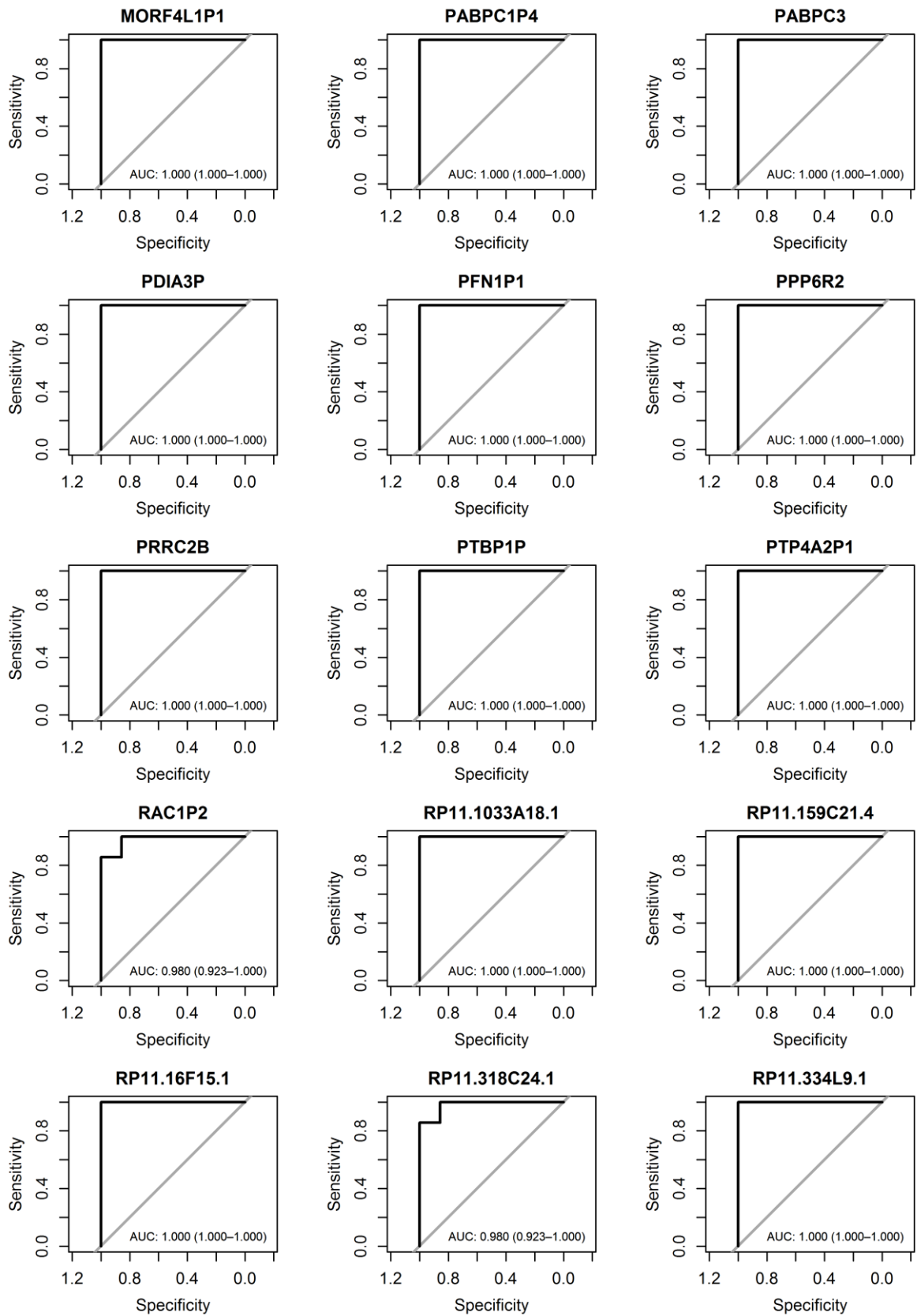


Figure S7. (continued).

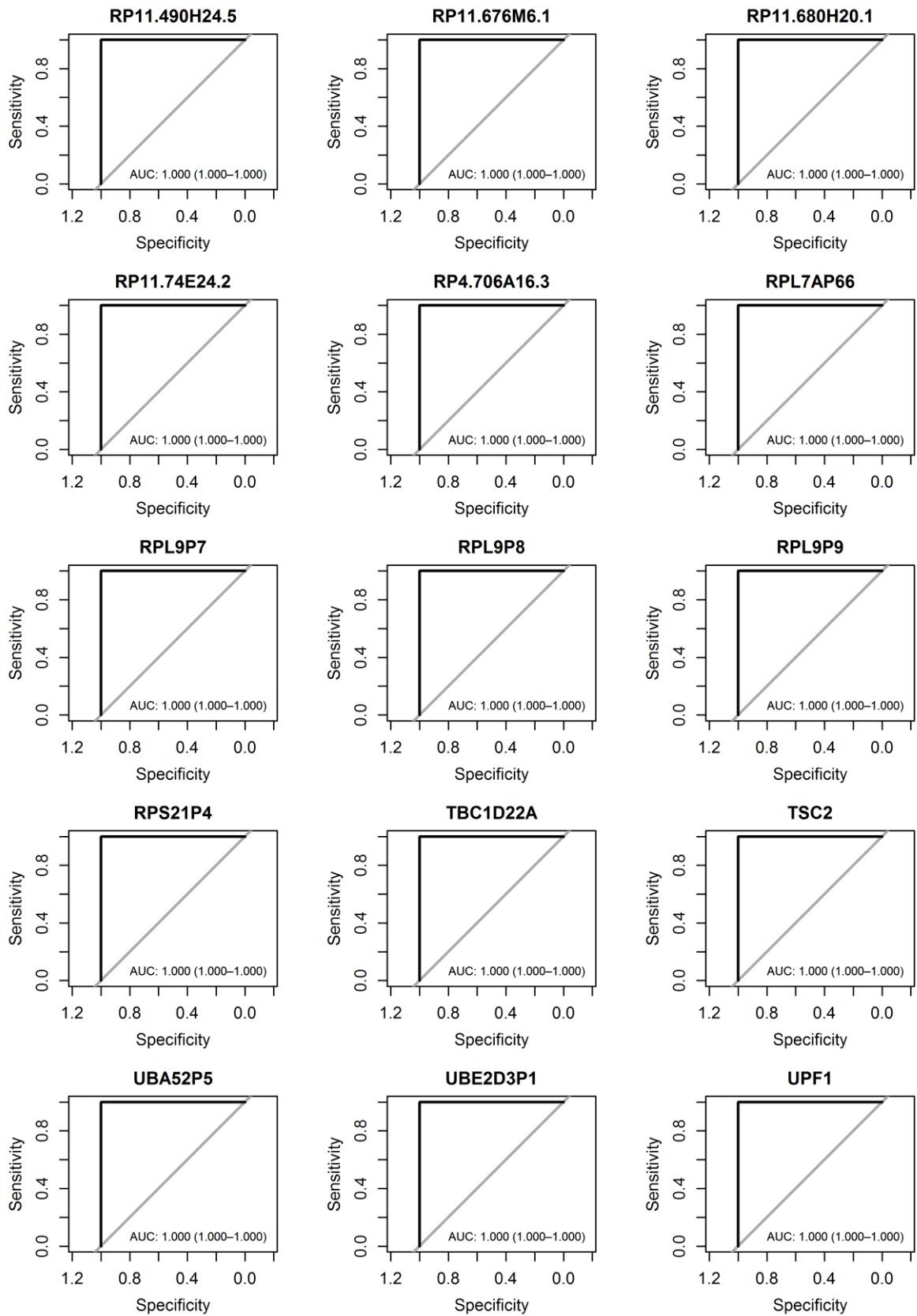
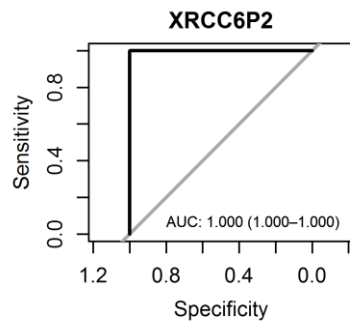
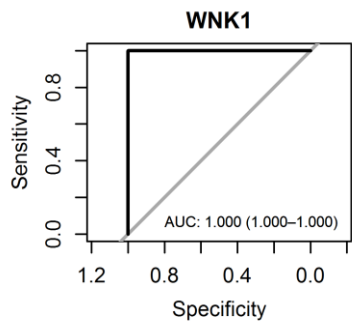
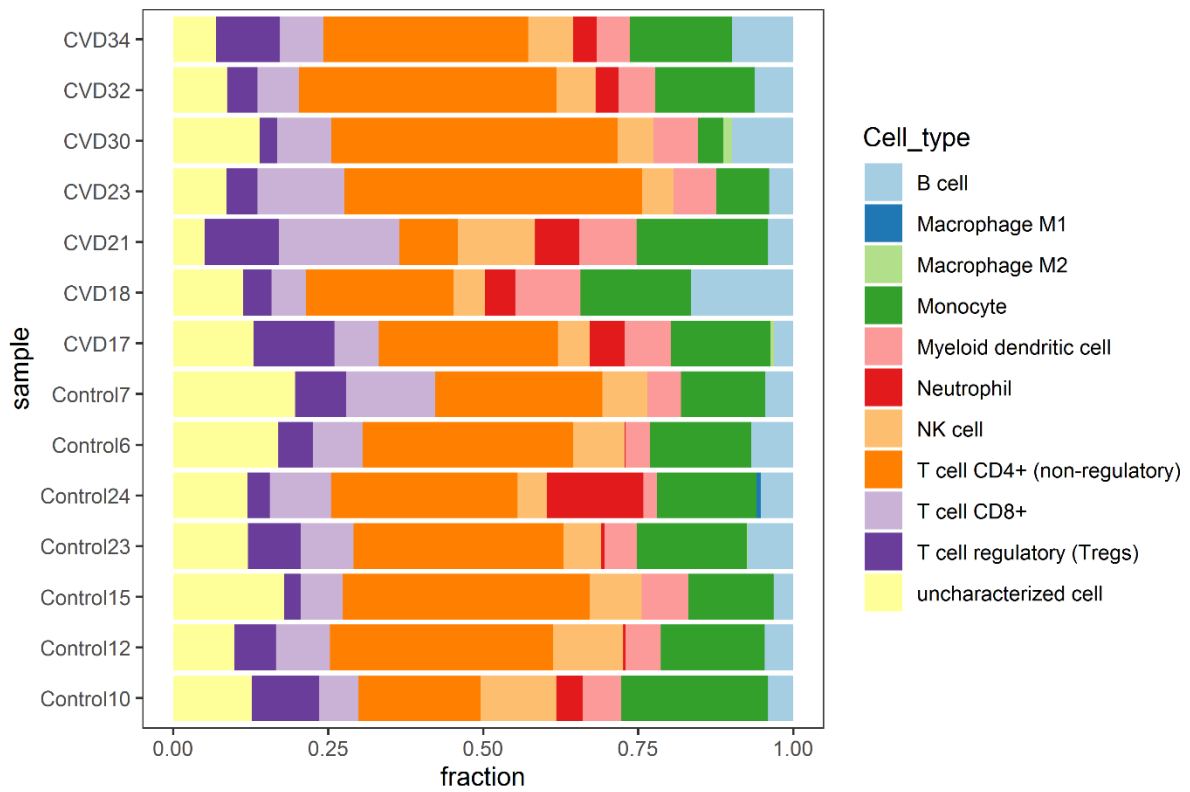


Figure S7. (continued).

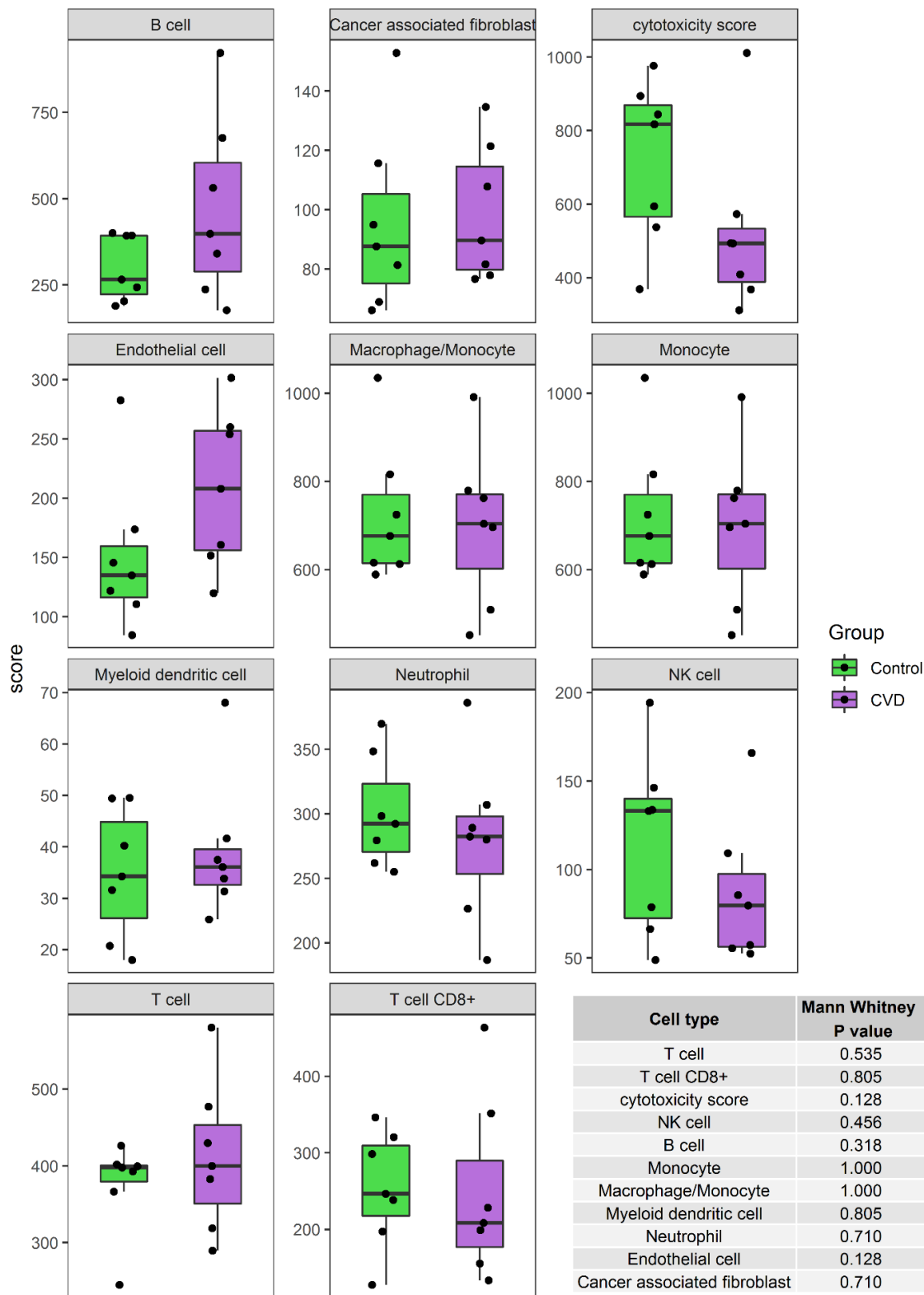


**Figure S7.** (continued).



**Figure S8.** Results of gene expression deconvolution procedure for seven CVD patients and seven control subjects performed using “quanTIseq” method implemented to immunedeconv 2.0.0 package.





**Figure S9.** Results of deconvolution procedure performed on gene expression datasets of 7 CVD patients (CVD) and 7 control subjects (Control) using “MCPcounter” method implemented to immunedeconv 2.0.0 package. Statistical significance of differences in score values between CVD and control groups were calculated using two-sided Mann Whitney test (wilcox.test function in R).

## Supplementary Tables

**Table S1.** Measurements of small RNA samples and small RNA libraries as well as results of small RNA sequencing data analysis received from Ion Torrent small RNA Plugin v5.0.5r3.

| Parameter  | Mean $\pm$ Standard Deviation   | Median    |
|--|---------------------------------|-----------|
| Percentage of microRNA in small RNA samples            | 17.98 $\pm$ 8.14                | 18        |
| Percentage of 94-114 bp* region in small RNA libraries | 48.84 $\pm$ 6.27                | 49        |
| Molar concentration of small RNA libraries (pM)        | 135,715.8 $\pm$ 42,658.12       | 137,815   |
| Ion Sphere Particles enrichment quality control        | 31.02% $\pm$ 4.581%             | 30%       |
| Total number of reads                                  | 8,779,221.98 $\pm$ 4,331,384.11 | 8,108,177 |
| Reads passing filter                                   | 7,903,734.32 $\pm$ 4,055,551.56 | 7,525,029 |
| Number of aligned reads                                | 7,355,398.49 $\pm$ 3,814,853.06 | 6,990,778 |
| Percentage of aligned reads                            | 92.67% $\pm$ 2.19%              | 93.06%    |
| Number of reads aligned to mirBase v21                 | 2,800,864.9 $\pm$ 1,603,122.07  | 2,487,376 |
| Percentage of reads aligned to mirBase v21             | 36.93% $\pm$ 8.06%              | 36.86%    |
| Number of reads aligned to precursors                  | 114,344.79 $\pm$ 62,594.61      | 104,094   |
| microRNAs with 1+ reads                                | 1,106.93 $\pm$ 301.57           | 1,173     |
| microRNAs with 10+ reads                               | 597.26 $\pm$ 87.07              | 599       |
| microRNAs with 100+ reads                              | 304.60 $\pm$ 53.05              | 306       |
| microRNAs with 1,000+ reads                            | 139.95 $\pm$ 26.13              | 139       |
| microRNAs with 10,000+ reads                           | 57.58 $\pm$ 17.97               | 61        |
| Non-uniquely mapped reads                              | 0                               | 0         |
| No feature mappings                                    | 495.46 $\pm$ 304.01             | 404       |
| Ambiguous mappings                                     | 0                               | 0         |
| Percentage of coding reads                             | 18.38% $\pm$ 3.22%              | 18.19%    |
| Percentage of rRNA reads                               | 0.81% $\pm$ 0.91%               | 0.55%     |
| Percentage of tRNA reads                               | 7.52% $\pm$ 6.63%               | 4.16%     |
| Percentage of snoRNA reads                             | 8.79% $\pm$ 3.68%               | 8.62%     |
| Percentage of snRNA reads                              | 0.93% $\pm$ 0.44%               | 0.9%      |
| Percentage of lincRNA reads                            | 1.19% $\pm$ 0.31%               | 1.21%     |
| Percentage of pseudogene reads                         | 0.28% $\pm$ 0.06%               | 0.27%     |

\*base pair

**Table S2.** Measurements of transcriptome libraries and results of transcriptome sequencing data analysis received from Ion Torrent RNASeqAnalysis plugin v.5.0.3.0.

| <b>Parameter</b>                                | <b>Mean ± Standard Deviation</b> | <b>Median</b> |
|---|----------------------------------|---------------|
| Molar concentration of libraries (pM)           | 82,000 ± 22,577.69               | 76,950        |
| Percentage of 50-160 bp* fragments in libraries | 13.93 ± 6.75                     | 13            |
| Ion Sphere Particles enrichment quality control | 23.429% ± 4.033%                 | 21%           |
| Total reads                                     | 35,630,503.93 ± 6,171,010.6      | 35,028,745    |
| Aligned reads                                   | 34,137,367.79 ± 5,698,815.7      | 33,333,896    |
| Percent aligned reads                           | 95.92% ± 1.59%                   | 96.31%        |
| Mean read length                                | 106.11 ± 15.461                  | 104.05        |
| Genes Detected                                  | 15,595.5 ± 4,062.45              | 16,405.5      |
| Isoforms Detected                               | 48,435.71 ± 5,951.03             | 47,947        |
| Reads mapped to genes                           | 10,798,201.43 ± 2,996,793.34     | 10,362,428    |
| Genes with 1+ reads                             | 30,568 ± 1,153.19                | 30,599        |
| Genes with 10+ reads                            | 15,595.5 ± 4,062.45              | 16,405.5      |
| Genes with 100+ reads                           | 8,387.4 ± 2,354.73               | 8,896.5       |
| Genes with 1000+ reads                          | 1,654.57 ± 587.45                | 1,545         |
| Genes with 10000+ reads                         | 77.5 ± 22.66                     | 73.5          |
| Total base reads                                | 3,769,611,717 ± 732,961,248.3    | 3,787,703,121 |
| Total aligned bases                             | 3,090,546,914 ± 607,390,161      | 2,972,554,880 |
| Percent aligned bases                           | 82.21% ± 4.42%                   | 83.37%        |
| Percent coding bases                            | 13.25% ± 5.06%                   | 11.55%        |
| Percent UTR <sup>†</sup> bases                  | 25.63% ± 7.44%                   | 22.88%        |
| Percent ribosomal bases                         | 5.37% ± 1.51%                    | 5.23%         |
| Percent intronic bases                          | 40.22% ± 5.51%                   | 41.22%        |
| Percent intergenic bases                        | 16.33% ± 6.47%                   | 18.76%        |
| Strand balance                                  | 50.24% ± 1.12%                   | 50.32%        |

\*base pair; <sup>†</sup>Untranslated Region

**Table S3.** The set of 96 differentially expressed microRNA transcripts resulted from DESeq2 analysis with  $P < 0.05$  in 34 patients with CVD compared to 19 controls. Presented microRNA transcripts were ordered according to increasing  $P$  value.

| No. | microRNA transcript              | $P$ value | Fold change |
|-----|----------------------------------|-----------|-------------|
| 1.  | hsa-mir-122_hsa-miR-122-5p       | 1.061E-09 | 2.213       |
| 2.  | hsa-mir-3591_hsa-miR-3591-3p     | 1.061E-09 | 2.213       |
| 3.  | hsa-mir-124-2_hsa-miR-124-3p     | 5.001E-07 | 16.991      |
| 4.  | hsa-mir-183_hsa-miR-183-5p       | 2.052E-06 | 1.932       |
| 5.  | hsa-mir-124-1_hsa-miR-124-3p     | 2.127E-05 | 10.053      |
| 6.  | hsa-mir-548d-1_hsa-miR-548d-3p   | 2.127E-05 | 1.617       |
| 7.  | hsa-mir-1277_hsa-miR-1277-3p     | 2.127E-05 | 1.773       |
| 8.  | hsa-mir-34a_hsa-miR-34a-5p       | 3.809E-05 | 1.931       |
| 9.  | hsa-mir-92a-1_hsa-miR-92a-3p     | 7.893E-05 | 0.832       |
| 10. | hsa-mir-874_hsa-miR-874-5p       | 1.286E-04 | 0.543       |
| 11. | hsa-mir-486_hsa-miR-486-5p       | 1.720E-04 | 2.411       |
| 12. | hsa-mir-486-2_hsa-miR-486-3p     | 1.720E-04 | 2.413       |
| 13. | hsa-mir-486_hsa-miR-486-3p       | 2.110E-04 | 2.384       |
| 14. | hsa-mir-486-2_hsa-miR-486-5p     | 2.110E-04 | 2.384       |
| 15. | hsa-mir-106b_hsa-miR-106b-3p     | 2.468E-04 | 0.796       |
| 16. | hsa-mir-454_hsa-miR-454-3p       | 3.039E-04 | 1.213       |
| 17. | hsa-mir-576_hsa-miR-576-3p       | 3.039E-04 | 2.043       |
| 18. | hsa-mir-92a-2_hsa-miR-92a-3p     | 3.039E-04 | 0.841       |
| 19. | hsa-mir-124-3_hsa-miR-124-3p     | 3.441E-04 | 8.268       |
| 20. | hsa-mir-548d-1_hsa-miR-548d-5p   | 3.441E-04 | 1.349       |
| 21. | hsa-mir-186_hsa-miR-186-3p       | 3.608E-04 | 1.357       |
| 22. | hsa-mir-548d-2_hsa-miR-548d-5p   | 3.608E-04 | 1.350       |
| 23. | hsa-mir-548aa-1_hsa-miR-548aa    | 5.130E-04 | 1.325       |
| 24. | hsa-mir-548aa-2_hsa-miR-548aa    | 1.020E-03 | 1.338       |
| 25. | hsa-mir-33a_hsa-miR-33a-5p       | 1.020E-03 | 1.207       |
| 26. | hsa-mir-590_hsa-miR-590-3p       | 1.020E-03 | 1.166       |
| 27. | hsa-mir-181a-2_hsa-miR-181a-2-3p | 1.020E-03 | 0.677       |
| 28. | hsa-mir-548t_hsa-miR-548t-3p     | 1.808E-03 | 1.323       |
| 29. | hsa-mir-1277_hsa-miR-1277-5p     | 1.837E-03 | 1.329       |
| 30. | hsa-let-7b_hsa-let-7b-3p         | 2.056E-03 | 1.322       |
| 31. | hsa-mir-548e_hsa-miR-548e-3p     | 2.502E-03 | 1.429       |
| 32. | hsa-mir-3960_hsa-miR-3960        | 2.533E-03 | 0.451       |
| 33. | hsa-mir-128-1_hsa-miR-128-3p     | 2.667E-03 | 0.850       |
| 34. | hsa-mir-4284_hsa-miR-4284        | 2.709E-03 | 0.302       |
| 35. | hsa-mir-96_hsa-miR-96-5p         | 3.726E-03 | 2.291       |
| 36. | hsa-mir-22_hsa-miR-22-3p         | 4.626E-03 | 1.259       |
| 37. | hsa-mir-30e_hsa-miR-30e-3p       | 5.532E-03 | 0.740       |
| 38. | hsa-mir-548ac_hsa-miR-548ac      | 5.532E-03 | 1.761       |
| 39. | hsa-mir-664a_hsa-miR-664a-5p     | 5.532E-03 | 1.315       |
| 40. | hsa-mir-769_hsa-miR-769-5p       | 5.532E-03 | 0.871       |
| 41. | hsa-mir-19a_hsa-miR-19a-3p       | 5.824E-03 | 1.194       |
| 42. | hsa-mir-506_hsa-miR-506-5p       | 6.776E-03 | 2.388       |
| 43. | hsa-mir-206_hsa-miR-206          | 7.995E-03 | 2.036       |
| 44. | hsa-mir-1250_hsa-miR-1250-5p     | 8.559E-03 | 0.619       |
| 45. | hsa-mir-196a-2_hsa-miR-196a-5p   | 8.922E-03 | 2.663       |

|     |                                |           |       |
|-----|--------------------------------|-----------|-------|
| 46. | hsa-mir-7641-1_hsa-miR-7641    | 8.944E-03 | 2.263 |
| 47. | hsa-mir-25_hsa-miR-25-3p       | 8.944E-03 | 0.860 |
| 48. | hsa-mir-497_hsa-miR-497-3p     | 9.309E-03 | 1.437 |
| 49. | hsa-mir-208a_hsa-miR-208a-3p   | 9.808E-03 | 3.208 |
| 50. | hsa-mir-497_hsa-miR-497-5p     | 1.165E-02 | 1.480 |
| 51. | hsa-mir-548d-2_hsa-miR-548d-3p | 1.165E-02 | 1.429 |
| 52. | hsa-mir-548f-2_hsa-miR-548f-3p | 1.165E-02 | 1.755 |
| 53. | hsa-mir-424_hsa-miR-424-3p     | 1.210E-02 | 1.500 |
| 54. | hsa-mir-424_hsa-miR-424-5p     | 1.541E-02 | 1.418 |
| 55. | hsa-mir-454_hsa-miR-454-5p     | 1.566E-02 | 1.232 |
| 56. | hsa-mir-330_hsa-miR-330-3p     | 1.666E-02 | 0.849 |
| 57. | hsa-mir-339_hsa-miR-339-3p     | 1.677E-02 | 0.846 |
| 58. | hsa-mir-196a-1_hsa-miR-196a-5p | 1.697E-02 | 2.393 |
| 59. | hsa-mir-7847_hsa-miR-7847-3p   | 1.711E-02 | 1.909 |
| 60. | hsa-mir-6836_hsa-miR-6836-3p   | 1.711E-02 | 0.296 |
| 61. | hsa-mir-450b_hsa-miR-450b-5p   | 1.711E-02 | 1.520 |
| 62. | hsa-mir-5582_hsa-miR-5582-3p   | 1.921E-02 | 1.878 |
| 63. | hsa-mir-503_hsa-miR-503-5p     | 1.921E-02 | 1.419 |
| 64. | hsa-mir-4433b_hsa-miR-4433b-3p | 2.015E-02 | 1.617 |
| 65. | hsa-mir-4433_hsa-miR-4433-5p   | 2.015E-02 | 1.617 |
| 66. | hsa-mir-598_hsa-miR-598-3p     | 2.081E-02 | 1.154 |
| 67. | hsa-mir-542_hsa-miR-542-3p     | 2.228E-02 | 1.405 |
| 68. | hsa-let-7f-1_hsa-let-7f-1-3p   | 2.343E-02 | 1.193 |
| 69. | hsa-mir-19b-1_hsa-miR-19b-3p   | 2.563E-02 | 1.212 |
| 70. | hsa-mir-1246_hsa-miR-1246      | 2.563E-02 | 3.038 |
| 71. | hsa-mir-34a_hsa-miR-34a-3p     | 2.707E-02 | 1.863 |
| 72. | hsa-mir-4423_hsa-miR-4423-3p   | 2.788E-02 | 2.942 |
| 73. | hsa-mir-335_hsa-miR-335-5p     | 2.788E-02 | 1.436 |
| 74. | hsa-mir-19b-2_hsa-miR-19b-3p   | 3.123E-02 | 1.199 |
| 75. | hsa-mir-490_hsa-miR-490-3p     | 3.227E-02 | 2.041 |
| 76. | hsa-mir-146b_hsa-miR-146b-5p   | 3.228E-02 | 0.786 |
| 77. | hsa-mir-340_hsa-miR-340-5p     | 3.372E-02 | 1.156 |
| 78. | hsa-mir-135a-1_hsa-miR-135a-5p | 3.377E-02 | 1.561 |
| 79. | hsa-mir-3198-2_hsa-miR-3198    | 3.456E-02 | 1.959 |
| 80. | hsa-mir-34b_hsa-miR-34b-5p     | 3.462E-02 | 1.734 |
| 81. | hsa-mir-138-2_hsa-miR-138-5p   | 3.468E-02 | 0.601 |
| 82. | hsa-mir-195_hsa-miR-195-5p     | 3.468E-02 | 1.238 |
| 83. | hsa-mir-599_hsa-miR-599        | 3.511E-02 | 0.436 |
| 84. | hsa-mir-193b_hsa-miR-193b-3p   | 3.547E-02 | 0.651 |
| 85. | hsa-mir-4664_hsa-miR-4664-5p   | 3.559E-02 | 0.601 |
| 86. | hsa-mir-181a-2_hsa-miR-181a-5p | 3.683E-02 | 0.854 |
| 87. | hsa-mir-222_hsa-miR-222-3p     | 4.029E-02 | 0.828 |
| 88. | hsa-mir-619_hsa-miR-619-5p     | 4.324E-02 | 0.541 |
| 89. | hsa-mir-138-1_hsa-miR-138-5p   | 4.615E-02 | 0.627 |
| 90. | hsa-mir-885_hsa-miR-885-5p     | 4.812E-02 | 2.074 |
| 91. | hsa-mir-200b_hsa-miR-200b-5p   | 4.819E-02 | 1.830 |
| 92. | hsa-mir-186_hsa-miR-186-5p     | 4.819E-02 | 1.299 |
| 93. | hsa-mir-342_hsa-miR-342-3p     | 4.819E-02 | 0.786 |
| 94. | hsa-mir-583_hsa-miR-583        | 4.819E-02 | 2.072 |
| 95. | hsa-mir-1268b_hsa-miR-1268b    | 4.913E-02 | 1.590 |
| 96. | hsa-mir-21_hsa-miR-21-5p       | 4.982E-02 | 1.209 |

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**Table S4.** The set of 48 differentially expressed microRNA transcripts resulted from UVE-PLS analysis in in 34 patients with CVD group compared to 19 controls. Presented microRNA transcripts were ordered according to decreasing PLS coefficients.

| No  | microRNA transcript            | PLS coefficient |
|-----|--------------------------------|-----------------|
| 1.  | hsa-mir-122_hsa-miR-122-5p     | 4.713E-02       |
| 2.  | hsa-mir-3591_hsa-miR-3591-3p   | 4.706E-02       |
| 3.  | hsa-mir-1277_hsa-miR-1277-3p   | 4.037E-02       |
| 4.  | hsa-mir-296_hsa-miR-296-5p     | 4.009E-02       |
| 5.  | hsa-mir-183_hsa-miR-183-5p     | 3.828E-02       |
| 6.  | hsa-mir-34a_hsa-miR-34a-5p     | 3.447E-02       |
| 7.  | hsa-mir-576_hsa-miR-576-3p     | 3.210E-02       |
| 8.  | hsa-mir-548ac_hsa-miR-548ac    | 2.868E-02       |
| 9.  | hsa-mir-208a_hsa-miR-208a-3p   | 2.770E-02       |
| 10. | hsa-mir-206_hsa-miR-206        | 2.760E-02       |
| 11. | hsa-mir-96_hsa-miR-96-5p       | 2.644E-02       |
| 12. | hsa-mir-1277_hsa-miR-1277-5p   | 2.130E-02       |
| 13. | hsa-mir-548d-1_hsa-miR-548d-3p | 2.093E-02       |
| 14. | hsa-mir-335_hsa-miR-335-5p     | 1.940E-02       |
| 15. | hsa-mir-186_hsa-miR-186-3p     | 1.651E-02       |
| 16. | hsa-mir-497_hsa-miR-497-3p     | 1.629E-02       |
| 17. | hsa-mir-548d-1_hsa-miR-548d-5p | 1.470E-02       |
| 18. | hsa-mir-548d-2_hsa-miR-548d-5p | 1.465E-02       |
| 19. | hsa-mir-548aa-1_hsa-miR-548aa  | 1.459E-02       |
| 20. | hsa-mir-548aa-2_hsa-miR-548aa  | 1.456E-02       |
| 21. | hsa-mir-454_hsa-miR-454-5p     | 1.453E-02       |
| 22. | hsa-mir-19b-1_hsa-miR-19b-3p   | 1.217E-02       |
| 23. | hsa-mir-33a_hsa-miR-33a-5p     | 1.130E-02       |
| 24. | hsa-let-7b_hsa-let-7b-3p       | 1.091E-02       |
| 25. | hsa-mir-454_hsa-miR-454-3p     | 1.050E-02       |
| 26. | hsa-mir-19a_hsa-miR-19a-3p     | 8.377E-03       |
| 27. | hsa-mir-548t_hsa-miR-548t-3p   | 8.103E-03       |
| 28. | hsa-mir-590_hsa-miR-590-3p     | 6.737E-03       |
| 29. | hsa-mir-128-1_hsa-miR-128-3p   | -7.843E-03      |
| 30. | hsa-mir-25_hsa-miR-25-3p       | -8.997E-03      |
| 31. | hsa-mir-342_hsa-miR-342-3p     | -1.069E-02      |
| 32. | hsa-mir-769_hsa-miR-769-5p     | -1.146E-02      |
| 33. | hsa-mir-106b_hsa-miR-106b-3p   | -1.146E-02      |
| 34. | hsa-let-7g_hsa-let-7g-3p       | -1.155E-02      |
| 35. | hsa-mir-330_hsa-miR-330-3p     | -1.217E-02      |
| 36. | hsa-mir-378a_hsa-miR-378a-5p   | -1.269E-02      |
| 37. | hsa-mir-92a-1_hsa-miR-92a-3p   | -1.403E-02      |
| 38. | hsa-mir-378c_hsa-miR-378c      | -1.412E-02      |
| 39. | hsa-mir-92a-2_hsa-miR-92a-3p   | -1.433E-02      |
| 40. | hsa-mir-30e_hsa-miR-30e-3p     | -1.507E-02      |
| 41. | hsa-mir-1301_hsa-miR-1301-3p   | -1.530E-02      |
| 42. | hsa-mir-181b-1_hsa-miR-181b-5p | -1.719E-02      |
| 43. | hsa-mir-485_hsa-miR-485-3p     | -1.937E-02      |
| 44. | hsa-mir-181b-2_hsa-miR-181b-5p | -2.242E-02      |

|     |                                  |            |
|-----|----------------------------------|------------|
| 45. | hsa-mir-193b_hsa-miR-193b-3p     | -2.251E-02 |
| 46. | hsa-mir-181a-2_hsa-miR-181a-2-3p | -3.243E-02 |
| 47. | hsa-mir-1250_hsa-miR-1250-5p     | -3.325E-02 |
| 48. | hsa-mir-874_hsa-miR-874-5p       | -3.432E-02 |

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**Table S5.** Results of ROC analysis for 34 miRNA transcripts selected as indicative for CVD.

| miRNA transcript                 | ROC-AUC <sup>1</sup> | Threshold | Specificity | Sensitivity | Accuracy | Positive Predictive Value | Negative Predictive Value |
|----------------------------------|----------------------|-----------|-------------|-------------|----------|---------------------------|---------------------------|
| hsa-mir-122_hsa-miR-122-5p       | 0.930                | 8.370     | 1.000       | 0.794       | 0.868    | 1.000                     | 0.731                     |
| hsa-mir-3591_hsa-miR-3591-3p     | 0.930                | 8.370     | 1.000       | 0.794       | 0.868    | 1.000                     | 0.731                     |
| hsa-mir-874_hsa-miR-874-5p       | 0.916                | 3.231     | 0.895       | 0.882       | 0.887    | 0.938                     | 0.810                     |
| hsa-mir-106b_hsa-miR-106b-3p     | 0.902                | 9.288     | 0.737       | 0.941       | 0.868    | 0.865                     | 0.875                     |
| hsa-mir-183_hsa-miR-183-5p       | 0.885                | 6.209     | 0.895       | 0.735       | 0.792    | 0.926                     | 0.654                     |
| hsa-mir-548d-1_hsa-miR-548d-3p   | 0.859                | 4.268     | 0.947       | 0.765       | 0.830    | 0.963                     | 0.692                     |
| hsa-mir-92a-1_hsa-miR-92a-3p     | 0.856                | 11.531    | 0.737       | 0.912       | 0.849    | 0.861                     | 0.824                     |
| hsa-mir-1277_hsa-miR-1277-3p     | 0.850                | 8.298     | 0.737       | 0.882       | 0.830    | 0.857                     | 0.778                     |
| hsa-mir-34a_hsa-miR-34a-5p       | 0.847                | 8.177     | 0.579       | 0.971       | 0.830    | 0.805                     | 0.917                     |
| hsa-mir-576_hsa-miR-576-3p       | 0.842                | 3.131     | 0.895       | 0.676       | 0.755    | 0.920                     | 0.607                     |
| hsa-mir-92a-2_hsa-miR-92a-3p     | 0.842                | 11.078    | 0.895       | 0.706       | 0.774    | 0.923                     | 0.630                     |
| hsa-mir-548d-1_hsa-miR-548d-5p   | 0.836                | 5.703     | 0.737       | 0.824       | 0.792    | 0.848                     | 0.700                     |
| hsa-mir-454_hsa-miR-454-3p       | 0.833                | 10.038    | 0.842       | 0.765       | 0.792    | 0.897                     | 0.667                     |
| hsa-mir-548aa-1_hsa-miR-548aa    | 0.819                | 5.833     | 0.632       | 0.912       | 0.811    | 0.816                     | 0.800                     |
| hsa-mir-33a_hsa-miR-33a-5p       | 0.816                | 11.459    | 0.842       | 0.676       | 0.736    | 0.885                     | 0.593                     |
| hsa-mir-590_hsa-miR-590-3p       | 0.816                | 10.945    | 0.947       | 0.588       | 0.717    | 0.952                     | 0.563                     |
| hsa-mir-186_hsa-miR-186-3p       | 0.814                | 6.794     | 0.632       | 0.824       | 0.755    | 0.800                     | 0.667                     |
| hsa-mir-548d-2_hsa-miR-548d-5p   | 0.811                | 5.736     | 0.789       | 0.765       | 0.774    | 0.867                     | 0.652                     |
| hsa-mir-1277_hsa-miR-1277-5p     | 0.811                | 9.430     | 0.895       | 0.765       | 0.811    | 0.929                     | 0.680                     |
| hsa-mir-548ac_hsa-miR-548ac      | 0.807                | 2.365     | 0.947       | 0.588       | 0.717    | 0.952                     | 0.563                     |
| hsa-mir-30e_hsa-miR-30e-3p       | 0.805                | 9.635     | 0.842       | 0.794       | 0.811    | 0.900                     | 0.696                     |
| hsa-mir-1250_hsa-miR-1250-5p     | 0.803                | 3.005     | 0.789       | 0.794       | 0.792    | 0.871                     | 0.682                     |
| hsa-mir-548aa-2_hsa-miR-548aa    | 0.797                | 5.956     | 0.789       | 0.882       | 0.849    | 0.882                     | 0.789                     |
| hsa-mir-548t_hsa-miR-548t-3p     | 0.796                | 5.506     | 0.737       | 0.735       | 0.736    | 0.833                     | 0.609                     |
| hsa-mir-769_hsa-miR-769-5p       | 0.794                | 8.815     | 0.842       | 0.794       | 0.811    | 0.900                     | 0.696                     |
| hsa-mir-181a-2_hsa-miR-181a-2-3p | 0.793                | 8.788     | 0.579       | 0.912       | 0.792    | 0.795                     | 0.786                     |
| hsa-let-7b_hsa-let-7b-3p         | 0.791                | 6.923     | 0.632       | 0.853       | 0.774    | 0.806                     | 0.706                     |
| hsa-mir-208a_hsa-miR-208a-3p     | 0.789                | 0.402     | 0.895       | 0.588       | 0.698    | 0.909                     | 0.548                     |
| hsa-mir-96_hsa-miR-96-5p         | 0.786                | 1.916     | 0.684       | 0.824       | 0.774    | 0.824                     | 0.684                     |
| hsa-mir-497_hsa-miR-497-3p       | 0.782                | 4.930     | 0.947       | 0.618       | 0.736    | 0.955                     | 0.581                     |
| hsa-mir-128-1_hsa-miR-128-3p     | 0.777                | 10.835    | 0.474       | 0.971       | 0.792    | 0.767                     | 0.900                     |
| hsa-mir-25_hsa-miR-25-3p         | 0.776                | 9.665     | 0.895       | 0.559       | 0.679    | 0.905                     | 0.531                     |
| hsa-mir-206_hsa-miR-206          | 0.759                | 2.125     | 0.895       | 0.588       | 0.698    | 0.909                     | 0.548                     |
| hsa-mir-19a_hsa-miR-19a-3p       | 0.757                | 15.562    | 0.737       | 0.647       | 0.679    | 0.815                     | 0.538                     |

<sup>1</sup>Area under ROC curve.



**Table S6:** Correlation analysis between age and expression of 34 selected miRNA transcripts in CVD group. MiRNA transcripts were ordered according to increasing *P* value.

| miRNA transcript                 | Correlation coefficient | <i>P</i> value |
|----------------------------------|-------------------------|----------------|
| hsa-mir-548ac_hsa-miR-548ac      | -0.35                   | 0.039          |
| hsa-mir-1277_hsa-miR-1277-3p     | 0.31                    | 0.077          |
| hsa-mir-208a_hsa-miR-208a-3p     | -0.30                   | 0.084          |
| hsa-mir-128-1_hsa-miR-128-3p     | -0.26                   | 0.133          |
| hsa-mir-548d-1_hsa-miR-548d-3p   | 0.25                    | 0.157          |
| hsa-mir-19a_hsa-miR-19a-3p       | -0.24                   | 0.168          |
| hsa-mir-92a-1_hsa-miR-92a-3p     | -0.22                   | 0.205          |
| hsa-mir-186_hsa-miR-186-3p       | -0.21                   | 0.224          |
| hsa-mir-576_hsa-miR-576-3p       | -0.20                   | 0.247          |
| hsa-mir-874_hsa-miR-874-5p       | 0.20                    | 0.252          |
| hsa-mir-769_hsa-miR-769-5p       | 0.18                    | 0.296          |
| hsa-let-7b_hsa-let-7b-3p         | 0.16                    | 0.364          |
| hsa-mir-183_hsa-miR-183-5p       | -0.15                   | 0.395          |
| hsa-mir-96_hsa-miR-96-5p         | 0.14                    | 0.441          |
| hsa-mir-206_hsa-miR-206          | 0.13                    | 0.456          |
| hsa-mir-92a-2_hsa-miR-92a-3p     | -0.12                   | 0.485          |
| hsa-mir-30e_hsa-miR-30e-3p       | -0.12                   | 0.504          |
| hsa-mir-34a_hsa-miR-34a-5p       | 0.12                    | 0.512          |
| hsa-mir-122_hsa-miR-122-5p       | -0.12                   | 0.514          |
| hsa-mir-3591_hsa-miR-3591-3p     | -0.12                   | 0.515          |
| hsa-mir-548t_hsa-miR-548t-3p     | 0.10                    | 0.565          |
| hsa-mir-497_hsa-miR-497-3p       | 0.10                    | 0.576          |
| hsa-mir-33a_hsa-miR-33a-5p       | 0.09                    | 0.609          |
| hsa-mir-1250_hsa-miR-1250-5p     | -0.09                   | 0.620          |
| hsa-mir-25_hsa-miR-25-3p         | 0.09                    | 0.627          |
| hsa-mir-590_hsa-miR-590-3p       | 0.09                    | 0.629          |
| hsa-mir-548aa-2_hsa-miR-548aa    | 0.07                    | 0.674          |
| hsa-mir-548d-1_hsa-miR-548d-5p   | 0.06                    | 0.721          |
| hsa-mir-1277_hsa-miR-1277-5p     | -0.05                   | 0.757          |
| hsa-mir-454_hsa-miR-454-3p       | 0.05                    | 0.795          |
| hsa-mir-548aa-1_hsa-miR-548aa    | 0.03                    | 0.854          |
| hsa-mir-548d-2_hsa-miR-548d-5p   | 0.03                    | 0.859          |
| hsa-mir-106b_hsa-miR-106b-3p     | -0.02                   | 0.922          |
| hsa-mir-181a-2_hsa-miR-181a-2-3p | 0.00                    | 0.978          |

**Table S7.** 183 differentially expressed genes resulted from DESeq2 analysis with  $P < 0.00001$  in seven patients with CVD, compared to seven controls. Presented genes were ordered according to increasing  $P$  value. Gene names not assigned to gene symbols by HUGO Multi-symbol checker were termed as “Unmatched”. Gene symbols in brackets are synonyms or previous gene symbols.

| No. | Gene symbol           | Gene name   | $P$ value | Fold change |
|-----|-----------------------|---|-----------|-------------|
| 1.  | <i>TSC2</i>           | TSC complex subunit 2   | 4.87E-17  | 1.4369      |
| 2.  | <i>AC078899.1</i>     | unmatched   | 1.18E-13  | 0.3926      |
| 3.  | <i>RP11-16F15.1</i>   | Unmatched   | 1.18E-13  | 0.3271      |
| 4.  | <i>EEF1A1P19</i>      | eukaryotic translation elongation factor 1 alpha 1 pseudogene 19  | 8.40E-13  | 0.4999      |
| 5.  | <i>HSP90B2P</i>       | heat shock protein 90 beta family member 2, pseudogene            | 4.04E-11  | 0.4115      |
| 6.  | <i>PFN1P1</i>         | profilin 1 pseudogene 1   | 4.04E-11  | 0.3673      |
| 7.  | <i>AC005884.1</i>     | Unmatched   | 4.36E-11  | 0.4013      |
| 8.  | <i>CALM2P2</i>        | calmodulin 2 pseudogene 2   | 4.36E-11  | 0.3855      |
| 9.  | <i>HSPA8P1</i>        | heat shock protein family A (Hsp70) member 8 pseudogene 1         | 4.36E-11  | 0.3791      |
| 10. | <i>RP11-490H24.5</i>  | Unmatched   | 4.36E-11  | 0.3124      |
| 11. | <i>RP4-706A16.3</i>   | Unmatched   | 4.36E-11  | 0.4548      |
| 12. | <i>TBC1D22A</i>       | TBC1 domain family member 22A                                     | 4.36E-11  | 1.4314      |
| 13. | <i>EIF4A1P10</i>      | eukaryotic translation initiation factor 4A1 pseudogene 10        | 4.66E-11  | 0.4609      |
| 14. | <i>HSP90AB3P</i>      | heat shock protein 90 alpha family class B member 3, pseudogene   | 4.66E-11  | 0.3618      |
| 15. | <i>RP11-20O24.4</i>   | Unmatched   | 6.43E-11  | 0.4450      |
| 16. | <i>RP11-1033A18.1</i> | Unmatched   | 7.00E-11  | 0.3813      |
| 17. | <i>EIF3FP3</i>        | eukaryotic translation initiation factor 3 subunit F pseudogene 3 | 1.35E-10  | 0.4425      |
| 18. | <i>TRAPPC9</i>        | trafficking protein particle complex 9                            | 1.38E-10  | 1.5147      |
| 19. | <i>PDIA3P</i>         | protein disulfide isomerase family A member 3 pseudogene 1        | 2.38E-10  | 0.4653      |
| 20. | <i>HSPA9P1</i>        | heat shock protein family A (Hsp70) member 9 pseudogene 1         | 2.76E-10  | 0.4196      |
| 21. | <i>AC007238.1</i>     | unmatched   | 3.62E-10  | 0.4215      |
| 22. | <i>HNRNPA1P7</i>      | heterogeneous nuclear ribonucleoprotein A1 pseudogene 7           | 3.72E-10  | 0.4620      |
| 23. | <i>RP11-262D11.2</i>  | Unmatched   | 4.68E-10  | 0.4851      |
| 24. | <i>RP11-159C21.4</i>  | Unmatched   | 4.81E-10  | 0.3902      |
| 25. | <i>PABPC3</i>         | poly(A) binding protein cytoplasmic 3                             | 1.70E-09  | 0.4141      |
| 26. | <i>EEF1A1P6</i>       | eukaryotic translation elongation factor 1 alpha 1 pseudogene 6   | 1.94E-09  | 0.4414      |
| 27. | <i>RP11-74E24.2</i>   | Unmatched   | 1.94E-09  | 0.5369      |
| 28. | <i>GLUD2</i>          | glutamate dehydrogenase 2   | 2.70E-09  | 0.4752      |
| 29. | <i>XRCC6P2</i>        | X-ray repair cross complementing 6 pseudogene 2                   | 2.89E-09  | 0.3728      |
| 30. | <i>HNRNPKP2</i>       | heterogeneous nuclear ribonucleoprotein K pseudogene 2            | 3.13E-09  | 0.4239      |

|     |                                    |   |          |        |
|-----|------------------------------------|---|----------|--------|
| 31. | <i>EEF1A1P11</i>                   | eukaryotic translation elongation factor 1 alpha 1<br>pseudogene 11                             | 8.40E-09 | 0.4479 |
| 32. | <i>UBA52P5</i>                     | ubiquitin A-52 residue ribosomal protein fusion<br>product 1 pseudogene 5                       | 8.40E-09 | 0.3967 |
| 33. | <i>RPL9P7</i>                      | ribosomal protein L9 pseudogene 7   | 9.10E-09 | 0.4136 |
| 34. | <i>PPP6R2</i>                      | protein phosphatase 6 regulatory subunit 2  | 9.52E-09 | 1.3609 |
| 35. | <i>HSP90B3P</i>                    | heat shock protein 90 beta family member 3,<br>pseudogene                                       | 9.75E-09 | 0.3888 |
| 36. | <i>PSME1</i>                       | proteasome activator subunit 1  | 1.07E-08 | 0.5585 |
| 37. | <i>RP11-334L9.1</i>                | Unmatched   | 1.37E-08 | 0.3330 |
| 38. | <i>RPS21P4</i>                     | ribosomal protein S21 pseudogene 4  | 1.37E-08 | 0.3759 |
| 39. | <i>AC138123.2</i>                  | Unmatched   | 1.38E-08 | 0.4073 |
| 40. | <i>CAP1P2</i>                      | CAP1 pseudogene 2   | 1.38E-08 | 0.4685 |
| 41. | <i>HNRNPKP4</i>                    | heterogeneous nuclear ribonucleoprotein K<br>pseudogene 4                                       | 1.38E-08 | 0.4620 |
| 42. | <i>PTGES3P1</i>                    | prostaglandin E synthase 3 pseudogene 1   | 1.38E-08 | 0.5104 |
| 43. | <i>RPL9P8</i><br>( <i>RPL9P9</i> ) | ribosomal protein L9 pseudogene 8   | 1.38E-08 | 0.4179 |
| 44. | <i>HNRNPA1P10</i>                  | heterogeneous nuclear ribonucleoprotein A1<br>pseudogene 10                                     | 1.39E-08 | 0.4748 |
| 45. | <i>UBL5P2</i>                      | ubiquitin like 5 pseudogene 2   | 1.58E-08 | 0.2991 |
| 46. | <i>B3GNTL1</i>                     | UDP-GlcNAc:betaGal beta-1,3-N-<br>acetylglucosaminyltransferase like 1                          | 1.79E-08 | 1.6047 |
| 47. | <i>hsa-mir-6723</i>                | Unmatched   | 2.78E-08 | 0.5456 |
| 48. | <i>TOM1L2</i>                      | target of myb1 like 2 membrane trafficking<br>protein   | 3.63E-08 | 1.3864 |
| 49. | <i>MORF4L1P1</i>                   | mortality factor 4 like 1 pseudogene 1  | 3.98E-08 | 0.5354 |
| 50. | <i>RPL5P4</i>                      | ribosomal protein L5 pseudogene 4   | 4.39E-08 | 0.4647 |
| 51. | <i>EIF4BP3</i>                     | eukaryotic translation initiation factor 4B<br>pseudogene 3                                     | 4.59E-08 | 0.4610 |
| 52. | <i>RPL39P3</i>                     | ribosomal protein L39 pseudogene 3  | 5.13E-08 | 0.3856 |
| 53. | <i>HSPA8P9</i>                     | heat shock protein family A (Hsp70) member 8<br>pseudogene 9                                    | 5.45E-08 | 0.3551 |
| 54. | <i>YWHAZP2</i>                     | tyrosine 3-monooxygenase/tryptophan 5-<br>monooxygenase activation protein zeta<br>pseudogene 2 | 5.45E-08 | 0.4631 |
| 55. | <i>EEF1A1P5</i>                    | eukaryotic translation elongation factor 1 alpha 1<br>pseudogene 5                              | 6.53E-08 | 0.6110 |
| 56. | <i>CDC42P6</i>                     | cell division cycle 42 pseudogene 6   | 6.53E-08 | 0.4530 |
| 57. | <i>RPL3P4</i>                      | ribosomal protein L3 pseudogene 4   | 6.88E-08 | 0.4887 |
| 58. | <i>CTD-2373J19.1</i>               | Unmatched   | 7.15E-08 | 0.4835 |
| 59. | <i>PTMAP5</i>                      | prothymosin alpha pseudogene 5  | 8.19E-08 | 0.5618 |
| 60. | <i>RP11-676M6.1</i>                | Unmatched   | 8.19E-08 | 0.4978 |
| 61. | <i>CALM2P4</i>                     | calmodulin 2 pseudogene 4   | 8.91E-08 | 0.3755 |
| 62. | <i>RP11-627K11.1</i>               | Unmatched   | 8.93E-08 | 0.4480 |
| 63. | <i>RPL7AP66</i>                    | ribosomal protein L7a pseudogene 66   | 9.71E-08 | 0.4847 |
| 64. | <i>MSNP1</i>                       | moesin pseudogene 1   | 9.82E-08 | 0.4805 |
| 65. | <i>RP11-680H20.1</i>               | Unmatched   | 9.99E-08 | 0.4114 |
| 66. | <i>PSME2P2</i>                     | proteasome activator subunit 2 pseudogene 2   | 1.05E-07 | 0.3109 |
| 67. | <i>GAK</i>                         | cyclin G associated kinase  | 1.10E-07 | 1.2912 |

|      |                                       |  |          |        |
|------|---------------------------------------|--|----------|--------|
| 68.  | <i>HNRNPA1P48</i>                     | heterogeneous nuclear ribonucleoprotein A1<br>pseudogene 48          | 1.20E-07 | 0.4560 |
| 69.  | <i>RPL7AP30</i>                       | ribosomal protein L7a pseudogene 30                                  | 1.24E-07 | 0.3563 |
| 70.  | <i>CTB-13H5.1</i>                     | Unmatched  | 1.41E-07 | 0.4177 |
| 71.  | <i>HNRNPA1P35</i>                     | heterogeneous nuclear ribonucleoprotein A1<br>pseudogene 35          | 1.49E-07 | 0.3498 |
| 72.  | <i>PTBP1P</i>                         | polypyrimidine tract binding protein 1<br>pseudogene                 | 1.53E-07 | 0.4425 |
| 73.  | <i>API5P1</i>                         | apoptosis inhibitor 5 pseudogene 1                                   | 1.57E-07 | 0.3469 |
| 74.  | <i>SC22CB-1E7.1</i>                   | Unmatched  | 1.59E-07 | 0.4434 |
| 75.  | <i>UBE2D3P1</i>                       | ubiquitin conjugating enzyme E2 D3 pseudogene<br>1                   | 1.69E-07 | 0.4852 |
| 76.  | <i>DYNC1I2P1</i>                      | dynein cytoplasmic 1 intermediate chain 2<br>pseudogene 1            | 1.83E-07 | 0.3828 |
| 77.  | <i>AL162151.3</i>                     | Unmatched  | 1.94E-07 | 0.4310 |
| 78.  | <i>RP11-286H14.4</i>                  | Unmatched  | 2.06E-07 | 0.4533 |
| 79.  | <i>RPL9P8</i>                         | ribosomal protein L9 pseudogene 8                                    | 2.34E-07 | 0.4464 |
| 80.  | <i>EEF1A1P13</i>                      | eukaryotic translation elongation factor 1 alpha 1<br>pseudogene 13  | 2.51E-07 | 0.5209 |
| 81.  | <i>PABPC1P4</i>                       | poly(A) binding protein cytoplasmic 1<br>pseudogene 4                | 2.60E-07 | 0.4654 |
| 82.  | <i>HNRNPUP1</i>                       | heterogeneous nuclear ribonucleoprotein U<br>pseudogene 1            | 2.73E-07 | 0.4405 |
| 83.  | <i>UPF1</i>                           | UPF1 RNA helicase and ATPase   | 2.82E-07 | 1.2468 |
| 84.  | <i>RP11-416K24.2</i>                  | Unmatched  | 2.92E-07 | 0.2576 |
| 85.  | <i>PTMAP2</i>                         | prothymosin alpha pseudogene 2                                       | 3.18E-07 | 0.4815 |
| 86.  | <i>RPL7AP6</i>                        | ribosomal protein L7a pseudogene 6                                   | 3.20E-07 | 0.4192 |
| 87.  | <i>ARPC3P1</i>                        | actin related protein 2/3 complex subunit 3<br>pseudogene 1          | 3.72E-07 | 0.3313 |
| 88.  | <i>RPL3P2</i>                         | ribosomal protein L3 pseudogene 2                                    | 3.72E-07 | 0.4349 |
| 89.  | <i>CTNNA1P1</i><br>( <i>CTNNAP1</i> ) | catenin alpha 1 pseudogene 1   | 3.84E-07 | 0.3255 |
| 90.  | <i>HECTD4</i>                         | HECT domain E3 ubiquitin protein ligase 4                            | 4.12E-07 | 1.3706 |
| 91.  | <i>PTP4A2P1</i>                       | PTP4A2 pseudogene 1  | 4.59E-07 | 0.5002 |
| 92.  | <i>WNK1</i>                           | WNK lysine deficient protein kinase 1                                | 4.59E-07 | 1.2575 |
| 93.  | <i>RPLP0P6</i>                        | ribosomal protein lateral stalk subunit P0<br>pseudogene 6           | 4.76E-07 | 0.5054 |
| 94.  | <i>CTC-451P13.1</i>                   | Unmatched  | 4.77E-07 | 0.5126 |
| 95.  | <i>MECP2</i>                          | methyl-CpG binding protein 2   | 4.77E-07 | 1.4360 |
| 96.  | <i>CDS2</i>                           | CDP-diacylglycerol synthase 2  | 5.31E-07 | 1.2409 |
| 97.  | <i>RP11-778D9.4</i>                   | Unmatched  | 5.31E-07 | 0.4437 |
| 98.  | <i>EIF3LP1</i>                        | eukaryotic translation initiation factor 3 subunit L<br>pseudogene 1 | 6.33E-07 | 0.4172 |
| 99.  | <i>RP11-345J4.6</i>                   | Unmatched  | 6.99E-07 | 0.5361 |
| 100. | <i>KLRC1</i>                          | killer cell lectin like receptor C1                                  | 7.09E-07 | 0.3331 |
| 101. | <i>HSP90AB2P</i>                      | heat shock protein 90 alpha family class B<br>member 2, pseudogene   | 7.83E-07 | 0.2673 |
| 102. | <i>BZW1P2</i>                         | basic leucine zipper and W2 domains 1<br>pseudogene 2                | 7.97E-07 | 0.4450 |
| 103. | <i>BRF1</i>                           | BRF1 RNA polymerase III transcription initiation<br>factor subunit   | 8.40E-07 | 1.3745 |

|      |                                   |   |          |        |
|------|-----------------------------------|---|----------|--------|
| 104. | <i>BRD7P2</i>                     | bromodomain containing 7 pseudogene 2                             | 8.46E-07 | 0.4541 |
| 105. | <i>TMSB10P1</i>                   | thymosin beta 10 pseudogene 1                                     | 8.76E-07 | 0.4217 |
| 106. | <i>ANXA2P2</i>                    | annexin A2 pseudogene 2   | 9.24E-07 | 0.4814 |
| 107. | <i>CFL1P4</i>                     | cofilin 1 pseudogene 4  | 9.88E-07 | 0.3852 |
| 108. | <i>AC005795.1</i>                 | Unmatched   | 1.01E-06 | 0.5572 |
| 109. | <i>RP11-216N14.7</i>              | Unmatched   | 1.01E-06 | 2.0662 |
| 110. | <i>FTLP3</i>                      | ferritin light chain pseudogene 3                                 | 1.04E-06 | 0.5024 |
| 111. | <i>LPAR2</i>                      | lysophosphatidic acid receptor 2                                  | 1.04E-06 | 1.5448 |
| 112. | <i>RP11-556K13.1</i>              | Unmatched   | 1.04E-06 | 0.4975 |
| 113. | <i>RP11-434O22.1</i>              | Unmatched   | 1.16E-06 | 0.3615 |
| 114. | <i>AC016739.2</i>                 | Unmatched   | 1.27E-06 | 0.3293 |
| 115. | <i>DPP9</i>                       | dipeptidyl peptidase 9  | 1.56E-06 | 1.5269 |
| 116. | <i>PRRC2B</i>                     | proline rich coiled-coil 2B                                       | 1.56E-06 | 1.2727 |
| 117. | <i>NACA3P</i>                     | NACA family member 3, pseudogene                                  | 1.60E-06 | 0.4007 |
| 118. | <i>RPL4P5</i>                     | ribosomal protein L4 pseudogene 5                                 | 1.65E-06 | 0.4571 |
| 119. | <i>DGKD</i>                       | diacylglycerol kinase delta                                       | 1.78E-06 | 1.3415 |
| 120. | <i>RPL5P23</i>                    | ribosomal protein L5 pseudogene 23                                | 1.78E-06 | 0.4059 |
| 121. | <i>RP11-12M9.3</i>                | Unmatched   | 1.83E-06 | 0.4567 |
| 122. | <i>RP11-773H22.2</i>              | Unmatched   | 1.83E-06 | 0.3240 |
| 123. | <i>POLR2A</i>                     | RNA polymerase II subunit A                                       | 1.93E-06 | 1.3440 |
| 124. | <i>RPL13AP25</i>                  | ribosomal protein L13a pseudogene 25                              | 1.93E-06 | 0.5083 |
| 125. | <i>RP11-318C24.1</i>              | Unmatched   | 1.94E-06 | 0.3135 |
| 126. | <i>RP3-417G15.1</i>               | Unmatched   | 1.95E-06 | 0.4995 |
| 127. | <i>(OTUD4P1)</i><br><i>HIN1L</i>  | OTUD4 pseudogene 1  | 2.08E-06 | 0.4799 |
| 128. | <i>RP11-122C9.1</i>               | Unmatched   | 2.10E-06 | 0.5222 |
| 129. | <i>RP1-102E24.1</i>               | Unmatched   | 2.12E-06 | 0.3355 |
| 130. | <i>TCF25</i>                      | transcription factor 25   | 2.19E-06 | 1.3388 |
| 131. | <i>WASHC2A</i><br><i>(FAM21A)</i> | WASH complex subunit 2A   | 2.21E-06 | 0.6062 |
| 132. | <i>CTD-2270N23.1</i>              | Unmatched   | 2.22E-06 | 0.4548 |
| 133. | <i>RP11-265N6.3</i>               | Unmatched   | 2.22E-06 | 0.3834 |
| 134. | <i>MAP4K2</i>                     | mitogen-activated protein kinase kinase kinase 2                  | 2.22E-06 | 1.5399 |
| 135. | <i>AC000089.3</i>                 | Unmatched   | 2.29E-06 | 0.3857 |
| 136. | <i>EIF3LP2</i>                    | eukaryotic translation initiation factor 3 subunit L pseudogene 2 | 2.33E-06 | 0.4574 |
| 137. | <i>RP11-274E7.2</i>               | Unmatched   | 2.36E-06 | 0.3910 |
| 138. | <i>THRAP3P1</i>                   | thyroid hormone receptor associated protein 3 pseudogene 1        | 2.39E-06 | 0.4249 |
| 139. | <i>TYRO3P</i>                     | TYRO3P protein tyrosine kinase pseudogene                         | 2.43E-06 | 2.1670 |
| 140. | <i>CTD-2554C21.1</i>              | Unmatched   | 2.44E-06 | 0.4892 |
| 141. | <i>RPL18P13</i>                   | ribosomal protein L18 pseudogene 13                               | 2.79E-06 | 0.3358 |
| 142. | <i>RP11-516A11.1</i>              | Unmatched   | 2.89E-06 | 0.3476 |
| 143. | <i>SRP9P1</i>                     | signal recognition particle 9 pseudogene 1                        | 2.89E-06 | 0.4477 |
| 144. | <i>SNORD62B</i>                   | small nucleolar RNA, C/D box 62B                                  | 2.93E-06 | 0.4316 |
| 145. | <i>HSPA8P7</i>                    | heat shock protein family A (Hsp70) member 8 pseudogene 7         | 2.98E-06 | 0.3053 |
| 146. | <i>NISCH</i>                      | Nischarin   | 3.18E-06 | 1.2319 |
| 147. | <i>RPL19P12</i>                   | ribosomal protein L19 pseudogene 12                               | 3.18E-06 | 0.4243 |
| 148. | <i>NUP214</i>                     | nucleoporin 214   | 3.24E-06 | 1.2625 |

|      |                                      |   |          |        |
|------|--------------------------------------|---|----------|--------|
| 149. | <i>RAC1P2</i>                        | Rac family small GTPase 1 pseudogene 2                        | 3.29E-06 | 0.4893 |
| 150. | <i>SNORD20</i>                       | small nucleolar RNA, C/D box 20                               | 3.32E-06 | 0.3994 |
| 151. | <i>RPL13AP5</i>                      | ribosomal protein L13a pseudogene 5                           | 3.76E-06 | 0.4760 |
| 152. | <i>AC022431.1</i>                    | Unmatched   | 3.79E-06 | 0.3990 |
| 153. | <i>RNU2-36P</i>                      | RNA, U2 small nuclear 36, pseudogene                          | 3.85E-06 | 0.3880 |
| 154. | <i>EEF1DP1</i>                       | eukaryotic translation elongation factor 1 delta pseudogene 1 | 3.95E-06 | 0.4753 |
| 155. | <i>HK2P1</i>                         | hexokinase 2 pseudogene 1                                     | 4.10E-06 | 0.4017 |
| 156. | <i>RPS3AP5</i>                       | ribosomal protein S3A pseudogene 5                            | 4.23E-06 | 0.4798 |
| 157. | <i>RP6-145B8.3</i>                   | Unmatched   | 4.32E-06 | 0.3607 |
| 158. | <i>HDAC5</i>                         | histone deacetylase 5   | 4.89E-06 | 1.4317 |
| 159. | <i>DNAH1</i>                         | dynein axonemal heavy chain 1                                 | 4.90E-06 | 1.4204 |
| 160. | <i>NATD1</i><br>( <i>C17orf103</i> ) | N-acetyltransferase domain containing 1                       | 5.09E-06 | 1.6826 |
| 161. | <i>FCGR3B</i>                        | Fc fragment of IgG receptor IIIb                              | 5.69E-06 | 0.3067 |
| 162. | <i>RPL13AP7</i>                      | ribosomal protein L13a pseudogene 7                           | 5.88E-06 | 0.4587 |
| 163. | <i>INTS11</i><br>( <i>CPSF3L</i> )   | integrator complex subunit 11                                 | 5.95E-06 | 1.2458 |
| 164. | <i>RPL23AP2</i>                      | ribosomal protein L23a pseudogene 2                           | 5.95E-06 | 0.4061 |
| 165. | <i>RP11-40C6.2</i>                   | Unmatched   | 6.01E-06 | 0.4510 |
| 166. | <i>PPIAP29</i>                       | peptidylprolyl isomerase A pseudogene 29                      | 6.06E-06 | 0.4568 |
| 167. | <i>RP11-181C21.4</i>                 | Unmatched   | 6.06E-06 | 0.4121 |
| 168. | <i>SNORD62A</i>                      | small nucleolar RNA, C/D box 62A                              | 6.12E-06 | 0.4386 |
| 169. | <i>RPL24P4</i>                       | ribosomal protein L24 pseudogene 4                            | 6.24E-06 | 0.4241 |
| 170. | <i>RPL4P3</i>                        | ribosomal protein L4 pseudogene 3                             | 7.69E-06 | 0.4131 |
| 171. | <i>CPT1A</i>                         | carnitine palmitoyltransferase 1A                             | 7.72E-06 | 2.0161 |
| 172. | <i>DGKZP1</i>                        | diacylglycerol kinase zeta pseudogene 1                       | 7.77E-06 | 0.4929 |
| 173. | <i>IQCN</i><br>( <i>KIAA1683</i> )   | IQ motif containing N   | 8.08E-06 | 1.6856 |
| 174. | <i>RP11-592N21.1</i>                 | Unmatched   | 8.08E-06 | 0.4054 |
| 175. | <i>WASF4P</i>                        | WASP family member 4, pseudogene                              | 8.50E-06 | 0.4786 |
| 176. | <i>AC004074.3</i>                    | Unmatched   | 8.76E-06 | 0.3216 |
| 177. | <i>HNRNPCP2</i>                      | heterogeneous nuclear ribonucleoprotein C pseudogene 2        | 9.35E-06 | 0.5607 |
| 178. | <i>RPL14P1</i>                       | ribosomal protein L14 pseudogene 1                            | 9.35E-06 | 0.4505 |
| 179. | <i>MAT2B</i>                         | methionine adenosyltransferase 2B                             | 9.37E-06 | 0.7523 |
| 180. | <i>RNU1-28P</i>                      | RNA, U1 small nuclear 28, pseudogene                          | 9.53E-06 | 0.2861 |
| 181. | <i>AC010468.1</i>                    | Unmatched   | 9.54E-06 | 0.4572 |
| 182. | <i>RP13-104F24.3</i>                 | Unmatched   | 9.70E-06 | 0.4346 |
| 183. | <i>RP4-561L24.3</i>                  | Unmatched   | 9.82E-06 | 2.5831 |

**Table S8.** The set of 74 differentially expressed genes resulted from UVE-PLS analysis in seven patients with CVD compared to seven controls. Presented genes were ordered according to decreasing PLS coefficients. Gene names not assigned to gene symbols by HUGO Multi-symbol checker were termed as “Unmatched”. Gene symbols in brackets are synonyms or previous gene symbols.

| No. | Gene symbol            | Gene name   | PLS coefficient |
|-----|------------------------|---|-----------------|
| 1.  | <i>TSC2</i>            | TSC complex subunit 2   | 8.197E-04       |
| 2.  | <i>TBC1D22A</i>        | TBC1 domain family member 22A                                     | 7.572E-04       |
| 3.  | <i>PPP6R2</i>          | protein phosphatase 6 regulatory subunit 2                        | 6.225E-04       |
| 4.  | <i>HDAC5</i>           | histone deacetylase 5   | 5.694E-04       |
| 5.  | <i>UPF1</i>            | UPF1 RNA helicase and ATPase                                      | 5.077E-04       |
| 6.  | <i>CDS2</i>            | CDP-diacylglycerol synthase 2                                     | 4.756E-04       |
| 7.  | <i>PRRC2B</i>          | proline rich coiled-coil 2B                                       | 4.693E-04       |
| 8.  | <i>INTS11 (CPSF3L)</i> | integrator complex subunit 11                                     | 4.683E-04       |
| 9.  | <i>ZNF236</i>          | zinc finger protein 236   | 4.418E-04       |
| 10. | <i>HTT</i>             | huntingtin  | 4.399E-04       |
| 11. | <i>SBF1</i>            | SET binding factor 1  | 4.398E-04       |
| 12. | <i>WNK1</i>            | WNK lysine deficient protein kinase 1                             | 4.134E-04       |
| 13. | <i>ZZEF1</i>           | zinc finger ZZ-type and EF-hand domain containing 1               | 3.782E-04       |
| 14. | <i>CHFR</i>            | checkpoint with forkhead and ring finger domains                  | 3.380E-04       |
| 15. | <i>SRSF2</i>           | serine and arginine rich splicing factor 2                        | -3.257E-04      |
| 16. | <i>RP11-624D20.1</i>   | Unmatched   | -5.295E-04      |
| 17. | <i>RP11-141P6.1</i>    | Unmatched   | -5.310E-04      |
| 18. | <i>TOPORS</i>          | TOP1 binding arginine/serine rich protein                         | -7.202E-04      |
| 19. | <i>RAC1P2</i>          | Rac family small GTPase 1 pseudogene 2                            | -8.192E-04      |
| 20. | <i>UBE2D3P1</i>        | ubiquitin conjugating enzyme E2 D3 pseudogene 1                   | -8.801E-04      |
| 21. | <i>PTP4A2P1</i>        | PTP4A2 pseudogene 1   | -9.014E-04      |
| 22. | <i>RNU4-6P</i>         | RNA, U4 small nuclear 6, pseudogene                               | -9.029E-04      |
| 23. | <i>CTC-451P13.1</i>    | Unmatched   | -9.263E-04      |
| 24. | <i>AC083873.4</i>      | Unmatched   | -9.439E-04      |
| 25. | <i>BZW1P2</i>          | basic leucine zipper and W2 domains 1 pseudogene 2                | -9.598E-04      |
| 26. | <i>OTUD4P1 (HIN1L)</i> | OTUD4 pseudogene 1  | -9.962E-04      |
| 27. | <i>EIF3LP2</i>         | eukaryotic translation initiation factor 3 subunit L pseudogene 2 | -9.995E-04      |
| 28. | <i>TPMTP1</i>          | thiopurine S-methyltransferase pseudogene 1                       | -9.996E-04      |
| 29. | <i>PABPC1P4</i>        | poly(A) binding protein cytoplasmic 1 pseudogene 4                | -1.031E-03      |
| 30. | <i>MORF4L1P1</i>       | mortality factor 4 like 1 pseudogene 1                            | -1.045E-03      |
| 31. | <i>RP11-318C24.1</i>   | Unmatched   | -1.062E-03      |
| 32. | <i>RP11-74E24.2</i>    | Unmatched   | -1.067E-03      |
| 33. | <i>RPL7AP66</i>        | ribosomal protein L7a pseudogene 66                               | -1.089E-03      |
| 34. | <i>PTBP1P</i>          | polypyrimidine tract binding protein 1 pseudogene                 | -1.095E-03      |
| 35. | <i>HNRNPUP1</i>        | heterogeneous nuclear ribonucleoprotein U pseudogene 1            | -1.106E-03      |
| 36. | <i>HNRNPKP4</i>        | heterogeneous nuclear ribonucleoprotein K pseudogene 4            | -1.120E-03      |
| 37. | <i>RP11-680H20.1</i>   | Unmatched   | -1.155E-03      |
| 38. | <i>HNRNPKP2</i>        | heterogeneous nuclear ribonucleoprotein K pseudogene 2            | -1.163E-03      |

|     |                         |  |            |
|-----|-------------------------|--|------------|
| 39. | <i>CTB-13H5.1</i>       | Unmatched  | -1.175E-03 |
| 40. | <i>API5P1</i>           | apoptosis inhibitor 5 pseudogene 1                                     | -1.204E-03 |
| 41. | <i>RP11-334L9.1</i>     | Unmatched  | -1.206E-03 |
| 42. | <i>RP11-676M6.1</i>     | Unmatched  | -1.208E-03 |
| 43. | <i>EEF1A1P13</i>        | eukaryotic translation elongation factor 1 alpha 1 pseudogene 13       | -1.211E-03 |
| 44. | <i>HNRNPA1P35</i>       | heterogeneous nuclear ribonucleoprotein A1 pseudogene 35               | -1.223E-03 |
| 45. | <i>HNRNPA1P10</i>       | heterogeneous nuclear ribonucleoprotein A1 pseudogene 10               | -1.227E-03 |
| 46. | <i>HNRNPA1P7</i>        | heterogeneous nuclear ribonucleoprotein A1 pseudogene 7                | -1.232E-03 |
| 47. | <i>PDIA3P1 (PDIA3P)</i> | protein disulfide isomerase family A member 3 pseudogene 1             | -1.240E-03 |
| 48. | <i>RPL9P8</i>           | ribosomal protein L9 pseudogene 8                                      | -1.253E-03 |
| 49. | <i>AL162151.3</i>       | Unmatched  | -1.258E-03 |
| 50. | <i>ARPC3P1</i>          | actin related protein 2/3 complex subunit 3 pseudogene 1               | -1.272E-03 |
| 51. | <i>EIF4A1P10</i>        | eukaryotic translation initiation factor 4A1 pseudogene 10             | -1.286E-03 |
| 52. | <i>RPL9P8 (RPL9P9)</i>  | ribosomal protein L9 pseudogene 8                                      | -1.302E-03 |
| 53. | <i>EEF1A1P19</i>        | eukaryotic translation elongation factor 1 alpha 1 pseudogene 19       | -1.305E-03 |
| 54. | <i>UBA52P5</i>          | ubiquitin A-52 residue ribosomal protein fusion product 1 pseudogene 5 | -1.306E-03 |
| 55. | <i>EEF1A1P11</i>        | eukaryotic translation elongation factor 1 alpha 1 pseudogene 11       | -1.369E-03 |
| 56. | <i>EEF1A1P6</i>         | eukaryotic translation elongation factor 1 alpha 1 pseudogene 6        | -1.375E-03 |
| 57. | <i>RP4-706A16.3</i>     | Unmatched  | -1.394E-03 |
| 58. | <i>AC007238.1</i>       | Unmatched  | -1.398E-03 |
| 59. | <i>HSPA9P1</i>          | heat shock protein family A (Hsp70) member 9 pseudogene 1              | -1.414E-03 |
| 60. | <i>RPL9P7</i>           | ribosomal protein L9 pseudogene 7                                      | -1.417E-03 |
| 61. | <i>AC138123.2</i>       | Unmatched  | -1.422E-03 |
| 62. | <i>EIF3FP3</i>          | eukaryotic translation initiation factor 3 subunit F pseudogene 3      | -1.423E-03 |
| 63. | <i>PFN1P1</i>           | profilin 1 pseudogene 1  | -1.457E-03 |
| 64. | <i>PABPC3</i>           | poly(A) binding protein cytoplasmic 3                                  | -1.468E-03 |
| 65. | <i>AC005884.1</i>       | Unmatched  | -1.488E-03 |
| 66. | <i>RP11-1033A18.1</i>   | Unmatched  | -1.495E-03 |
| 67. | <i>CALM2P2</i>          | calmodulin 2 pseudogene 2  | -1.498E-03 |
| 68. | <i>RP11-490H24.5</i>    | Unmatched  | -1.508E-03 |
| 69. | <i>RPS21P4</i>          | ribosomal protein S21 pseudogene 4                                     | -1.531E-03 |
| 70. | <i>XRCC6P2</i>          | X-ray repair cross complementing 6 pseudogene 2                        | -1.535E-03 |
| 71. | <i>RP11-159C21.4</i>    | Unmatched  | -1.552E-03 |
| 72. | <i>HSPA8P1</i>          | heat shock protein family A (Hsp70) member 8 pseudogene 1              | -1.575E-03 |
| 73. | <i>AC078899.1</i>       | Unmatched  | -1.586E-03 |
| 74. | <i>RP11-16F15.1</i>     | Unmatched  | -2.068E-03 |



**Table S9.** Results of ROC analysis for 62 genes selected as indicative for CVD.

| Gene                    | ROC-AUC <sup>1</sup> | Threshold | Specificity | Sensitivity | Accuracy | Positive Predictive Value | Negative Predictive Value |
|-------------------------|----------------------|-----------|-------------|-------------|----------|---------------------------|---------------------------|
| <i>AC005884.1</i>       | 1.000                | 6.294     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>AC007238.1</i>       | 1.000                | 5.737     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>AC078899.1</i>       | 1.000                | 6.988     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>AC138123.2</i>       | 1.000                | 7.109     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>AL162151.3</i>       | 1.000                | 6.514     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>API5P1</i>           | 1.000                | 4.669     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>ARPC3P1</i>          | 1.000                | 4.852     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>BZW1P2</i>           | 1.000                | 6.206     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>CALM2P2</i>          | 1.000                | 5.342     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>CDS2</i>             | 1.000                | 10.036    | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>CTB-13H5.1</i>       | 1.000                | 7.446     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>CTC-451P13.1</i>     | 1.000                | 5.822     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>EEF1A1P11</i>        | 1.000                | 9.226     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>EEF1A1P13</i>        | 1.000                | 9.601     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>EEF1A1P19</i>        | 1.000                | 8.575     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>EEF1A1P6</i>         | 1.000                | 11.713    | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>EIF3FP3</i>          | 1.000                | 7.217     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>EIF3LP2</i>          | 1.000                | 5.309     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>EIF4A1P10</i>        | 1.000                | 7.476     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>HDAC5</i>            | 1.000                | 9.888     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>HNRNPA1P10</i>       | 1.000                | 7.474     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>HNRNPA1P35</i>       | 1.000                | 5.228     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>HNRNPA1P7</i>        | 1.000                | 7.641     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>HNRNPKP2</i>         | 1.000                | 6.274     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>HNRNPKP4</i>         | 1.000                | 7.761     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>HNRNPUP1</i>         | 1.000                | 5.304     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>HSPA8P1</i>          | 1.000                | 6.352     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>HSPA9P1</i>          | 1.000                | 5.744     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>INTS11 (CPSF3L)</i>  | 1.000                | 9.544     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>MORF4L1P1</i>        | 1.000                | 7.438     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>OTUD4P1 (HIN1L)</i>  | 1.000                | 5.204     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>PABPC1P4</i>         | 1.000                | 7.550     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>PABPC3</i>           | 1.000                | 8.575     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>PDIA3P1 (PDIA3P)</i> | 1.000                | 7.152     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>PFN1P1</i>           | 1.000                | 6.578     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>PPP6R2</i>           | 1.000                | 9.867     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>PRRC2B</i>           | 1.000                | 11.692    | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>PTBP1P</i>           | 1.000                | 5.423     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>PTP4A2P1</i>         | 1.000                | 5.670     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>RAC1P2</i>           | 0.980                | 6.007     | 0.857       | 1.000       | 0.929    | 0.875                     | 1.000                     |
| <i>RP11-1033A18.1</i>   | 1.000                | 7.100     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>RP11-159C21.4</i>    | 1.000                | 8.052     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>RP11-16F15.1</i>     | 1.000                | 7.326     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>RP11-318C24.1</i>    | 0.980                | 4.523     | 0.857       | 1.000       | 0.929    | 0.875                     | 1.000                     |
| <i>RP11-334L9.1</i>     | 1.000                | 4.450     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>RP11-490H24.5</i>    | 1.000                | 4.660     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>RP11-676M6.1</i>     | 1.000                | 5.758     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |
| <i>RP11-680H20.1</i>    | 1.000                | 6.427     | 1.000       | 1.000       | 1.000    | 1.000                     | 1.000                     |

|                     |       |        |       |       |       |       |       |
|---------------------|-------|--------|-------|-------|-------|-------|-------|
| <i>RP11-74E24.2</i> | 1.000 | 6.302  | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| <i>RP4-706A16.3</i> | 1.000 | 8.025  | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| <i>RPL7AP66</i>     | 1.000 | 6.241  | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| <i>RPL9P7</i>       | 1.000 | 7.833  | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| <i>RPL9P8</i>       | 1.000 | 7.955  | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| <i>RPL9P9</i>       | 1.000 | 7.906  | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| <i>RPS21P4</i>      | 1.000 | 6.861  | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| <i>TBC1D22A</i>     | 1.000 | 9.526  | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| <i>TSC2</i>         | 1.000 | 9.855  | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| <i>UBA52P5</i>      | 1.000 | 5.889  | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| <i>UBE2D3P1</i>     | 1.000 | 6.522  | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| <i>UPF1</i>         | 1.000 | 10.151 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| <i>WNK1</i>         | 1.000 | 11.834 | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |
| <i>XRCC6P2</i>      | 1.000 | 6.147  | 1.000 | 1.000 | 1.000 | 1.000 | 1.000 |

<sup>1</sup>Area under ROC curve.

**Table S10:** Correlation analysis between age and expression of 62 selected genes in CVD group. Genes were ordered according to increasing *P* value.

| Gene                  | Correlation coefficient | <i>P</i> value |
|-----------------------|-------------------------|----------------|
| <i>HSPA8P1</i>        | -0.82                   | 0.024          |
| <i>PTBP1P</i>         | -0.80                   | 0.031          |
| <i>TSC2</i>           | -0.79                   | 0.033          |
| <i>UBA52P5</i>        | -0.77                   | 0.043          |
| <i>HIN1L</i>          | -0.73                   | 0.061          |
| <i>PRRC2B</i>         | -0.70                   | 0.078          |
| <i>MORF4L1P1</i>      | -0.64                   | 0.124          |
| <i>TBC1D22A</i>       | -0.64                   | 0.124          |
| <i>BZW1P2</i>         | -0.63                   | 0.128          |
| <i>AC007238.1</i>     | -0.63                   | 0.130          |
| <i>RP11-676M6.1</i>   | -0.61                   | 0.145          |
| <i>RAC1P2</i>         | 0.61                    | 0.149          |
| <i>CALM2P2</i>        | -0.60                   | 0.155          |
| <i>RP11-490H24.5</i>  | 0.59                    | 0.164          |
| <i>RPS21P4</i>        | -0.58                   | 0.170          |
| <i>HNRNPA1P10</i>     | -0.58                   | 0.170          |
| <i>RP11-159C21.4</i>  | -0.55                   | 0.205          |
| <i>CTC-451P13.1</i>   | 0.53                    | 0.222          |
| <i>AC005884.1</i>     | 0.49                    | 0.264          |
| <i>EEF1A1P19</i>      | 0.47                    | 0.290          |
| <i>HNRNPKP2</i>       | -0.45                   | 0.312          |
| <i>HDAC5</i>          | 0.43                    | 0.335          |
| <i>RP11-334L9.1</i>   | -0.40                   | 0.368          |
| <i>RP11-318C24.1</i>  | -0.40                   | 0.374          |
| <i>RP11-16F15.1</i>   | -0.38                   | 0.402          |
| <i>PABPC1P4</i>       | -0.36                   | 0.426          |
| <i>EEF1A1P6</i>       | -0.34                   | 0.455          |
| <i>HSPA9P1</i>        | 0.33                    | 0.474          |
| <i>RP11-1033A18.1</i> | -0.32                   | 0.486          |
| <i>RPL7AP66</i>       | -0.30                   | 0.516          |
| <i>HNRNPUP1</i>       | -0.30                   | 0.520          |
| <i>PFN1P1</i>         | 0.29                    | 0.531          |
| <i>HNRNPA1P35</i>     | 0.29                    | 0.533          |
| <i>PABPC3</i>         | -0.28                   | 0.542          |
| <i>EIF4A1P10</i>      | 0.28                    | 0.549          |
| <i>RPL9P8</i>         | -0.28                   | 0.549          |
| <i>AC078899.1</i>     | -0.26                   | 0.570          |
| <i>RP4-706A16.3</i>   | 0.26                    | 0.570          |
| <i>PPP6R2</i>         | -0.25                   | 0.583          |

|                      |       |       |
|----------------------|-------|-------|
| <i>PDIA3P</i>        | 0.23  | 0.626 |
| <i>CPSF3L</i>        | 0.22  | 0.630 |
| <i>AL162151.3</i>    | -0.22 | 0.632 |
| <i>XRCC6P2</i>       | -0.22 | 0.633 |
| <i>UBE2D3P1</i>      | 0.22  | 0.642 |
| <i>UPF1</i>          | -0.21 | 0.647 |
| <i>API5P1</i>        | -0.20 | 0.664 |
| <i>HNRNPKP4</i>      | 0.20  | 0.675 |
| <i>ARPC3P1</i>       | 0.19  | 0.678 |
| <i>RP11-74E24.2</i>  | -0.17 | 0.714 |
| <i>RPL9P7</i>        | -0.16 | 0.724 |
| <i>CDS2</i>          | 0.16  | 0.730 |
| <i>EIF3LP2</i>       | 0.14  | 0.763 |
| <i>WNK1</i>          | 0.14  | 0.771 |
| <i>RPL9P9</i>        | -0.13 | 0.780 |
| <i>CTB-13H5.1</i>    | 0.10  | 0.824 |
| <i>AC138123.2</i>    | 0.09  | 0.847 |
| <i>EEF1A1P11</i>     | 0.07  | 0.879 |
| <i>RP11-680H20.1</i> | -0.04 | 0.925 |
| <i>EEF1A1P13</i>     | -0.01 | 0.976 |
| <i>EIF3FP3</i>       | -0.01 | 0.989 |
| <i>PTP4A2P1</i>      | 0.00  | 0.995 |
| <i>HNRNPA1P7</i>     | 0.00  | 0.998 |

**Table S11:** Twelve experimentally validated miRNA:gene pairs found among 31 miRNAs and 62 genes indicative for CVD using multiMiR package. PAR-CLIP - Photoactivatable Ribonucleoside-Enhanced Crosslinking and Immunoprecipitation, HITS-CLIP - High-Throughput Sequencing of RNA isolated by Cross-Linking Immunoprecipitation, CLASH - Cross-linking, Ligation, and Sequencing of Hybrids.

|     | Database   | miRNA ID          | Gene symbol   | Method                     |
|-----|------------|-------------------|---------------|----------------------------|
| 1.  | mirtarbase | hsa-miR-106b-3p   | <i>WNK1</i>   | CLASH                      |
| 2.  |            | hsa-miR-183-5p    | <i>WNK1</i>   | CLASH                      |
| 3.  |            | hsa-let-7b-3p     | <i>WNK1</i>   | PAR-CLIP                   |
| 4.  |            | hsa-miR-590-3p    | <i>WNK1</i>   | HITS-CLIP                  |
| 5.  |            | hsa-miR-19a-3p    | <i>WNK1</i>   | HITS-CLIP                  |
| 6.  |            | hsa-miR-181a-2-3p | <i>WNK1</i>   | HITS-CLIP                  |
| 7.  |            | hsa-miR-92a-3p    | <i>PPP6R2</i> | CLASH                      |
| 8.  |            | hsa-miR-34a-5p    | <i>PRRC2B</i> | CLASH                      |
| 9.  |            | hsa-miR-92a-3p    | <i>PRRC2B</i> | PAR-CLIP, HITS-CLIP, CLASH |
| 10. |            | hsa-miR-25-3p     | <i>PRRC2B</i> | PAR-CLIP                   |
| 11. |            | hsa-miR-497-3p    | <i>PRRC2B</i> | PAR-CLIP                   |
| 12. |            | hsa-miR-33a-5p    | <i>PABPC3</i> | PAR-CLIP, HITS-CLIP        |

**Table S12:** Top 10% predicted miRNA:gene pairs found among 31 miRNAs and 62 genes indicative for CVD using multiMiR package.

|     | Database     | miRNA ID        | Gene symbol     | Database-specific probability value |
|-----|--------------|-----------------|-----------------|-------------------------------------|
| 1.  | diana_microt | hsa-miR-454-3p  | <i>WNK1</i>     | 0.999                               |
| 2.  |              | hsa-miR-548d-3p | <i>CDS2</i>     | 0.961                               |
| 3.  |              | hsa-miR-548aa   | <i>CDS2</i>     | 0.916                               |
| 4.  |              | hsa-miR-548t-3p | <i>CDS2</i>     | 0.916                               |
| 5.  |              | hsa-miR-1277-5p | <i>CDS2</i>     | 0.916                               |
| 6.  |              | hsa-miR-548ac   | <i>CDS2</i>     | 0.908                               |
| 7.  |              | hsa-miR-548ac   | <i>PRRC2B</i>   | 0.888                               |
| 8.  |              | hsa-miR-19a-3p  | <i>WNK1</i>     | 0.865                               |
| 9.  |              | hsa-miR-548d-3p | <i>PRRC2B</i>   | 0.864                               |
| 10. |              | hsa-miR-590-3p  | <i>PABPC3</i>   | 0.854                               |
| 11. |              | hsa-miR-590-3p  | <i>WNK1</i>     | 0.832                               |
| 12. |              | hsa-miR-92a-3p  | <i>PRRC2B</i>   | 0.828                               |
| 13. |              | hsa-miR-576-3p  | <i>WNK1</i>     | 0.819                               |
| 14. |              | hsa-miR-548ac   | <i>WNK1</i>     | 0.815                               |
| 15. |              | hsa-miR-548t-3p | <i>PRRC2B</i>   | 0.811                               |
| 16. |              | hsa-miR-548aa   | <i>PRRC2B</i>   | 0.811                               |
| 17. |              | hsa-miR-454-3p  | <i>PABPC3</i>   | 0.806                               |
| 18. | elmmo        | hsa-let-7b-3p   | <i>WNK1</i>     | 0.846                               |
| 19. |              | hsa-miR-19a-3p  | <i>WNK1</i>     | 0.82                                |
| 20. |              | hsa-miR-96-5p   | <i>TBC1D22A</i> | 0.806                               |
| 21. |              | hsa-miR-92a-3p  | <i>PRRC2B</i>   | 0.802                               |
| 22. |              | hsa-miR-96-5p   | <i>WNK1</i>     | 0.738                               |
| 23. |              | hsa-miR-19a-3p  | <i>PPP6R2</i>   | 0.735                               |
| 24. |              | hsa-miR-454-3p  | <i>WNK1</i>     | 0.717                               |
| 25. |              | hsa-miR-25-3p   | <i>PRRC2B</i>   | 0.676                               |
| 26. |              | hsa-miR-497-3p  | <i>PRRC2B</i>   | 0.561                               |
| 27. |              | hsa-miR-454-3p  | <i>PPP6R2</i>   | 0.54                                |
| 28. |              | hsa-let-7b-3p   | <i>PRRC2B</i>   | 0.524                               |
| 29. |              | hsa-miR-590-3p  | <i>PABPC3</i>   | 0.492                               |
| 30. |              | hsa-miR-590-3p  | <i>WNK1</i>     | 0.491                               |
| 31. | microcosm    | hsa-miR-590-3p  | <i>PABPC3</i>   | 18.5626                             |
| 32. |              | hsa-miR-590-3p  | <i>PABPC3</i>   | 18.5355                             |
| 33. | miranda      | hsa-miR-576-3p  | <i>CDS2</i>     | -1.0983                             |
| 34. |              | hsa-miR-206     | <i>WNK1</i>     | -1.1794                             |
| 35. |              | hsa-let-7b-3p   | <i>WNK1</i>     | -1.2827                             |
| 36. | mirdb        | hsa-miR-454-3p  | <i>WNK1</i>     | 94.25965                            |
| 37. |              | hsa-miR-454-3p  | <i>WNK1</i>     | 94.2407                             |
| 38. | pita         | hsa-miR-34a-5p  | <i>CDS2</i>     | -10.96                              |
| 39. |              | hsa-miR-34a-5p  | <i>TBC1D22A</i> | -11.21                              |
| 40. |              | hsa-miR-92a-3p  | <i>PRRC2B</i>   | -11.38                              |
| 41. |              | hsa-miR-92a-3p  | <i>TBC1D22A</i> | -11.38                              |
| 42. |              | hsa-miR-769-5p  | <i>HDAC5</i>    | -11.51                              |
| 43. |              | hsa-miR-34a-5p  | <i>PPP6R2</i>   | -12.7                               |

|     |            |                |                 |        |
|-----|------------|----------------|-----------------|--------|
| 44. |            | hsa-miR-25-3p  | <i>TBC1D22A</i> | -12.78 |
| 45. |            | hsa-miR-34a-5p | <i>HDAC5</i>    | -14.78 |
| 46. |            | hsa-miR-206    | <i>PRRC2B</i>   | -14.83 |
| 47. | targetscan | hsa-miR-19a-3p | <i>PPP6R2</i>   | -0.243 |
| 48. |            | hsa-miR-25-3p  | <i>PRRC2B</i>   | -0.266 |
| 49. |            | hsa-miR-454-3p | <i>PPP6R2</i>   | -0.31  |
| 50. |            | hsa-miR-454-3p | <i>PABPC3</i>   | -0.317 |
| 51. |            | hsa-miR-128-3p | <i>WNK1</i>     | -0.362 |