

Supplementary Figure 1: (A) PCA score plot using ESI positive mode UPLC-IMS-HRMS inner arm skin surface data, over 14 000 markers, revealing partial separation between TB positive $n=10$, $m=30$, (yellow) and control, $n=18$, $m=54$, (red) groups. (B) OPLS-DA score plot using ESI positive mode UPLC-IMS-HRMS showing clear separation between TB positive (green) and control groups (red). Plots were generated in MetaboAnalyst V6.0.

Supplementary Table 1: Top 50 features identified by fold change analysis

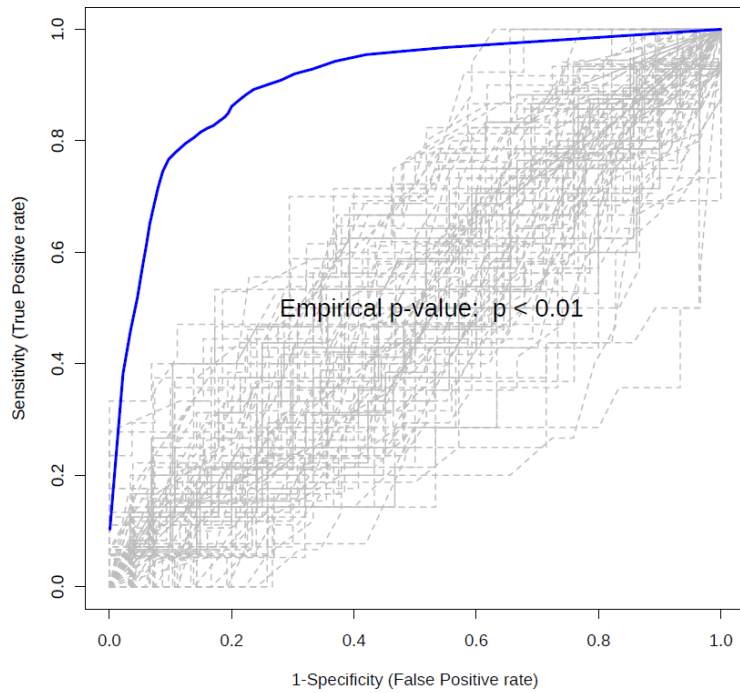
| Peaks(mz/rt) | Fold | Change | log ₂ (FC) |
|--------------|-----------------------|----------|-----------------------|
| 1 | 444.31222_13.653_3.30 | 0.009522 | -6.7145 |
| 2 | 288.23464_15.260_2.50 | 0.010096 | -6.63 |
| 3 | 150.12878_4.345_1.48 | 0.01029 | -6.6025 |
| 4 | 232.17070_12.985_2.07 | 0.016152 | -5.9522 |
| 5 | 367.22734_15.086_2.98 | 0.016575 | -5.9148 |
| 6 | 274.21794_14.777_2.40 | 0.025161 | -5.3127 |
| 7 | 479.34862_14.371_3.41 | 0.027755 | -5.1711 |
| 8 | 420.34511_14.184_3.27 | 0.028144 | -5.151 |
| 9 | 615.44403_16.094_4.31 | 34.034 | 5.0889 |
| 10 | 420.21520_13.986_3.20 | 31.959 | 4.9982 |
| 11 | 398.23365_13.985_3.10 | 29.384 | 4.8769 |
| 12 | 327.22973_13.344_2.58 | 0.037689 | -4.7297 |
| 13 | 246.18538_13.287_2.18 | 0.038385 | -4.7033 |
| 14 | 485.28772_14.209_3.43 | 0.041208 | -4.6009 |
| 15 | 389.20875_15.087_3.37 | 0.042103 | -4.5699 |
| 16 | 428.31520_15.019_3.32 | 0.045164 | -4.4687 |
| 17 | 571.41795_16.140_4.11 | 19.514 | 4.2864 |
| 18 | 413.23468_13.562_3.20 | 0.053315 | -4.2293 |
| 19 | 659.47017_16.177_4.53 | 18.65 | 4.2211 |
| 20 | 325.19822_10.989_2.37 | 0.0556 | -4.1688 |
| 21 | 359.21956_10.667_2.55 | 0.056681 | -4.141 |
| 22 | 703.49606_16.154_4.73 | 16.984 | 4.0861 |
| 23 | 543.36931_14.622_3.70 | 0.059204 | -4.0782 |

| | | | |
|----|-----------------------|----------|---------|
| 24 | 363.17766_11.856_2.62 | 0.060495 | -4.047 |
| 25 | 628.37351_15.894_5.16 | 16.252 | 4.0225 |
| 26 | 287.23748_14.871_2.30 | 0.061696 | -4.0187 |
| 27 | 227.12516_7.801_1.83 | 0.062056 | -4.0103 |
| 28 | 255.17548_13.026_2.08 | 16.042 | 4.0038 |
| 29 | 329.24490_14.095_2.69 | 0.06236 | -4.0032 |
| 30 | 359.21933_10.484_2.55 | 0.065065 | -3.942 |
| 31 | 367.22668_15.365_2.89 | 0.068429 | -3.8692 |
| 32 | 235.20557_14.024_1.92 | 14.225 | 3.8303 |
| 33 | 425.30560_15.609_3.27 | 0.070349 | -3.8293 |
| 34 | 481.36439_13.925_3.45 | 0.072233 | -3.7912 |
| 35 | 345.20352_13.136_2.70 | 0.072783 | -3.7803 |
| 36 | 287.23690_15.156_2.26 | 0.073962 | -3.7571 |
| 37 | 347.18309_11.100_2.57 | 0.074072 | -3.7549 |
| 38 | 355.22651_15.863_2.91 | 0.074111 | -3.7542 |
| 39 | 760.58475_14.162_5.34 | 13.45 | 3.7496 |
| 40 | 309.16717_9.402_2.31 | 13.034 | 3.7042 |
| 41 | 315.23182_14.726_2.59 | 0.078733 | -3.6669 |
| 42 | 287.23703_15.526_2.28 | 0.079027 | -3.6615 |
| 43 | 261.10984_7.734_2.04 | 0.081061 | -3.6248 |
| 44 | 347.18296_11.281_2.68 | 0.081799 | -3.6118 |
| 45 | 261.18500_10.661_2.06 | 0.081834 | -3.6112 |
| 46 | 661.18237_16.927_3.80 | 12.209 | 3.6098 |
| 47 | 545.34667_14.924_3.56 | 0.082959 | -3.5915 |
| 48 | 583.36100_14.615_3.85 | 0.083297 | -3.5856 |
| 49 | 409.35608_13.724_3.61 | 11.979 | 3.5825 |
| 50 | 322.21783_14.696_2.72 | 0.08439 | -3.5668 |

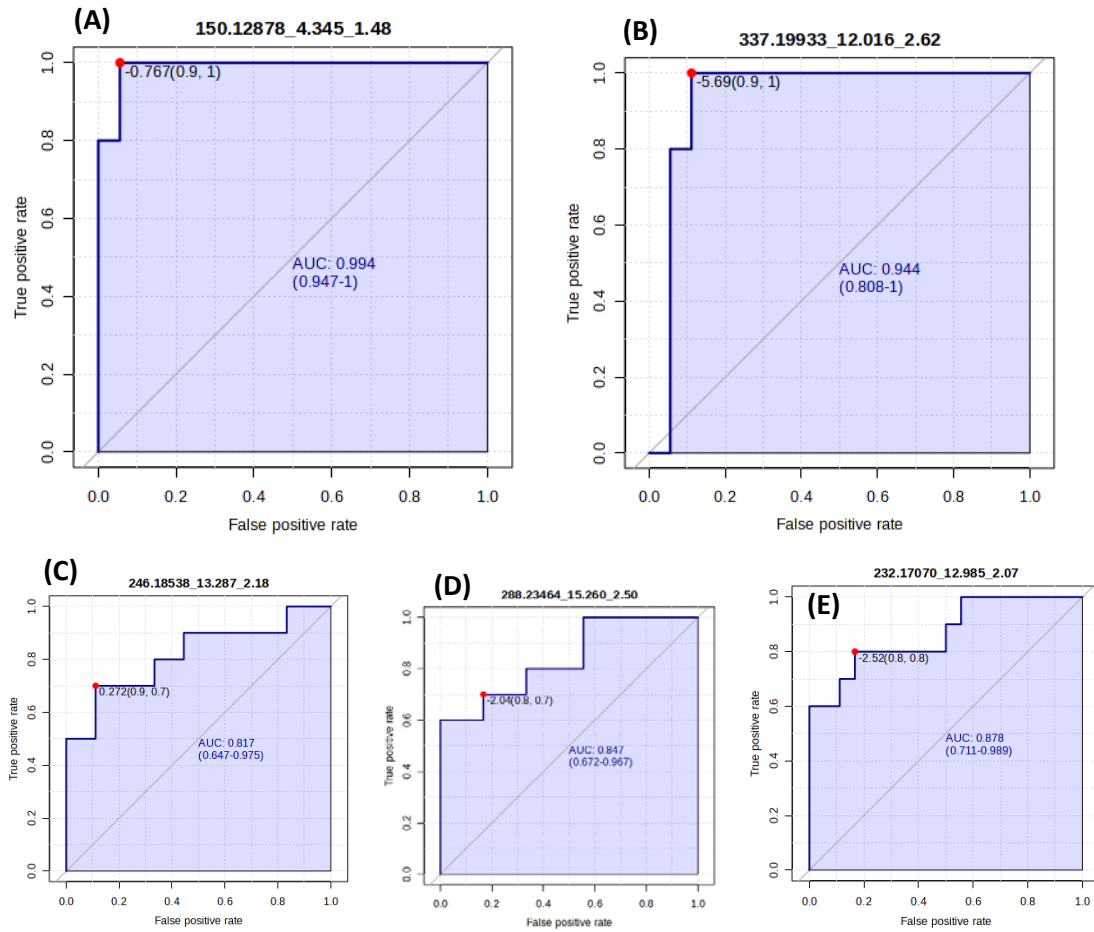
Supplementary Table 2: Top 50 features identified by t-test

| | Peaks(mz/rt) | t.stat | p.value | -log10(p) | FDR |
|----|-----------------------|---------|----------|-----------|----------|
| 1 | 313.17988_16.452_2.54 | -8.1115 | 4.20E-12 | 11.377 | 5.79E-08 |
| 2 | 351.23082_16.453_2.84 | -7.7083 | 2.64E-11 | 10.579 | 1.82E-07 |
| 3 | 345.20354_12.733_2.77 | -7.5005 | 6.76E-11 | 10.17 | 2.82E-07 |
| 4 | 345.20352_13.136_2.70 | -7.3893 | 1.12E-10 | 9.9519 | 2.82E-07 |
| 5 | 337.20052_14.308_2.62 | -7.3707 | 1.21E-10 | 9.9155 | 2.82E-07 |
| 6 | 257.11719_16.452_2.03 | -7.3687 | 1.23E-10 | 9.9115 | 2.82E-07 |
| 7 | 393.22455_13.222_2.78 | -7.1624 | 3.10E-10 | 9.5085 | 5.78E-07 |
| 8 | 363.17766_11.856_2.62 | -7.1446 | 3.36E-10 | 9.4738 | 5.78E-07 |
| 9 | 337.19864_10.464_2.51 | -7.0412 | 5.34E-10 | 9.2728 | 8.17E-07 |
| 10 | 323.22192_14.044_2.58 | -7.0176 | 5.93E-10 | 9.227 | 8.17E-07 |
| 11 | 365.18649_13.169_2.69 | -6.9533 | 7.90E-10 | 9.1023 | 8.89E-07 |
| 12 | 149.02381_12.439_1.23 | -6.9429 | 8.28E-10 | 9.0822 | 8.89E-07 |
| 13 | 281.13825_14.308_2.19 | -6.94 | 8.38E-10 | 9.0766 | 8.89E-07 |
| 14 | 341.21061_14.709_2.72 | -6.7634 | 1.84E-09 | 8.7357 | 1.81E-06 |
| 15 | 352.23947_15.099_2.95 | -6.7064 | 2.37E-09 | 8.626 | 1.95E-06 |
| 16 | 309.20601_14.309_2.46 | -6.7053 | 2.38E-09 | 8.6239 | 1.95E-06 |

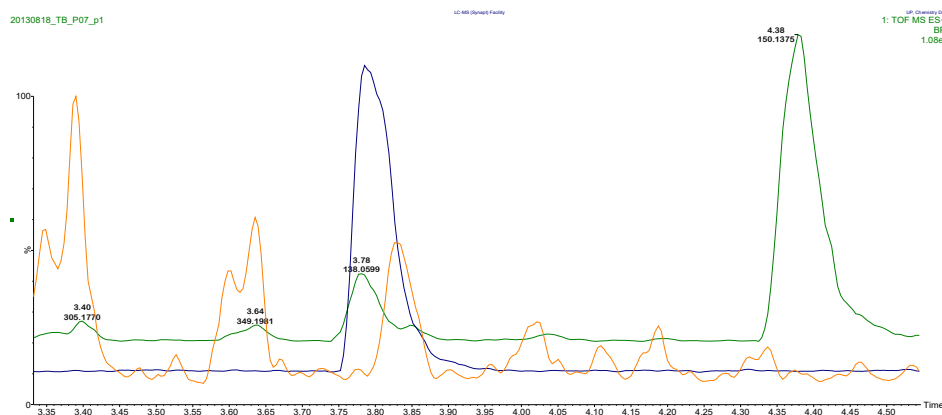
| | | | | | |
|----|-----------------------|---------|----------|--------|----------|
| 17 | 407.23969_12.679_2.89 | -6.7028 | 2.40E-09 | 8.6192 | 1.95E-06 |
| 18 | 425.30481_16.274_3.34 | -6.6578 | 2.93E-09 | 8.5328 | 2.24E-06 |
| 19 | 391.24661_14.069_3.00 | -6.6447 | 3.11E-09 | 8.5077 | 2.25E-06 |
| 20 | 393.22371_13.788_2.83 | -6.5994 | 3.79E-09 | 8.421 | 2.61E-06 |
| 21 | 407.21977_14.073_3.03 | -6.5464 | 4.79E-09 | 8.3197 | 3.14E-06 |
| 22 | 121.02842_12.439_1.11 | -6.4182 | 8.40E-09 | 8.0759 | 5.26E-06 |
| 23 | 283.15391_11.794_2.24 | -6.4029 | 8.98E-09 | 8.0468 | 5.38E-06 |
| 24 | 343.18792_12.331_2.61 | -6.3513 | 1.12E-08 | 7.9492 | 6.33E-06 |
| 25 | 295.22641_14.074_2.42 | -6.3465 | 1.15E-08 | 7.94 | 6.33E-06 |
| 26 | 237.11201_11.794_1.89 | -6.2941 | 1.44E-08 | 7.8411 | 7.38E-06 |
| 27 | 411.28868_15.129_3.17 | -6.2933 | 1.45E-08 | 7.8395 | 7.38E-06 |
| 28 | 437.26564_16.281_3.46 | -6.2609 | 1.67E-08 | 7.7785 | 8.19E-06 |
| 29 | 339.21213_11.796_2.51 | -6.2322 | 1.89E-08 | 7.7244 | 8.96E-06 |
| 30 | 347.18309_11.100_2.57 | -6.2047 | 2.12E-08 | 7.6728 | 9.76E-06 |
| 31 | 361.19953_11.793_2.62 | -6.1904 | 2.26E-08 | 7.646 | 9.91E-06 |
| 32 | 391.36303_14.074_3.00 | -6.1806 | 2.36E-08 | 7.6276 | 9.91E-06 |
| 33 | 361.31174_11.791_2.62 | -6.1791 | 2.37E-08 | 7.6247 | 9.91E-06 |
| 34 | 209.11703_11.794_1.73 | -6.1351 | 2.87E-08 | 7.5423 | 1.16E-05 |
| 35 | 277.17975_13.140_2.18 | -6.1134 | 3.15E-08 | 7.5016 | 1.23E-05 |
| 36 | 467.28342_14.020_3.51 | -6.1079 | 3.23E-08 | 7.4915 | 1.23E-05 |
| 37 | 361.31184_11.459_2.72 | -6.0973 | 3.38E-08 | 7.4717 | 1.26E-05 |
| 38 | 357.24133_14.615_2.86 | -6.0823 | 3.60E-08 | 7.4436 | 1.30E-05 |
| 39 | 228.23186_12.780_2.22 | -6.0768 | 3.69E-08 | 7.4333 | 1.30E-05 |
| 40 | 275.16414_11.459_2.12 | -6.0376 | 4.36E-08 | 7.3604 | 1.50E-05 |
| 41 | 391.24488_14.297_2.94 | -6.0213 | 4.68E-08 | 7.3299 | 1.57E-05 |
| 42 | 588.42474_15.050_4.12 | -6.0051 | 5.01E-08 | 7.2999 | 1.64E-05 |
| 43 | 387.25807_15.906_2.97 | -5.9866 | 5.43E-08 | 7.2654 | 1.72E-05 |
| 44 | 343.22568_14.657_2.84 | -5.982 | 5.53E-08 | 7.257 | 1.72E-05 |
| 45 | 309.20588_14.779_2.46 | -5.9785 | 5.62E-08 | 7.2504 | 1.72E-05 |
| 46 | 361.19988_11.455_2.72 | -5.969 | 5.85E-08 | 7.2329 | 1.75E-05 |
| 47 | 293.17437_11.459_2.31 | -5.955 | 6.21E-08 | 7.2068 | 1.82E-05 |
| 48 | 200.20060_10.800_2.04 | -5.9486 | 6.38E-08 | 7.1951 | 1.83E-05 |
| 49 | 229.15836_11.459_1.93 | -5.9349 | 6.77E-08 | 7.1697 | 1.90E-05 |
| 50 | 405.22322_13.094_2.80 | -5.9252 | 7.05E-08 | 7.1518 | 1.94E-05 |



Supplementary Figure 2: Plot of the permutations' tests using the area under the ROC curve or the predictive accuracy of the model as a measure of performance. The plot shows the AUC of all permutations, highlighting the actual observed AUC in blue, along with showing the empirical p-value.



Supplementary Figure 3: ROC curves of potential TB diagnostic biomarkers with an AUC > 0.8; (A) 150.12878_4.345_1.48, (B) 337.19933_12.016_2.62, (C) 246.18538_13.287_2.18, (D) 288.23464_15.260_2.50, and (E) 232.17070_12.985_2.07.



Supplementary Figure 4: Base peak ion (BPI) overlaid chromatograms. Top (green) trace shows PABA, 138.0599 m/z , at retention time 3.78 min in a TB patient skin sample. Middle (blue) trace shows the PABA reference standard, 10 ppm, at retention time 3.78 min. Bottom (orange) trace shows a pooled control sample, confirming the absence of PABA.