**Supplementary Table** **3**.Differential metabolites for PTR callbacks

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Modle | Name | Normal | Model | Up/down | PTR | Up/down | Metformin | Up/down |
| ESI- | 13-L-Hydroperoxylinoleic acid | 5.23±2.75 | 117.8±70.87 | ↑ | 15.26±21.40 | ↓ | 24.54±29.46 | ↓ |
|  | 13-L-Hydroperoxylinoleic acid | 0.51±0.50 | 38.89±27.04 | ↑ | 4.89±7.15 | ↓ | 25.06±52.20 | ↓ |
|  | 11,12-Epoxyeicosatrienoic acid | 15.99±7.74 | 49.73±13.08 | ↑ | 20.01±13.46 | ↓ | 7.66±5.88 | ↓ |
|  | 5-HETE | 15.99±7.74 | 49.73±13.08 | ↑ | 20.01±13.46 | ↓ | 7.66±5.88 | ↓ |
|  | Leukotriene D4 | 16.42±7.20 | 84.76±37.20 | ↑ | 32.76±38.05 | ↓ | 40.52±35.08 | ↓ |
|  | Prostaglandin H3 | 1.51±1.41 | 227.25±126.75 | ↑ | 30.71±50.87 | ↓ | 138.91±252.25 | ↓ |
|  | 11,12-Epoxyeicosatrienoic acid | 1.96±2.91 | 79.06±97.48 | ↑ | 9.31±12.73 | ↓ | 33.47±53.63 | ↓ |
|  | 5a-Pregnane-3,20-dione | 419.94±110.86 | 1421.76±580.48 | ↑ | 885.82±519.57 | ↓ | 654.02±513.41 | ↓ |
|  | 2-Methoxy-estradiol-17b 3-glucuronide | 51.17±16.50 | 180.9±58.08 | ↑ | 78.79±66.60 | ↓ | 89.81±69.88 | ↓ |
|  | 11b,21-Dihydroxy-3,20-oxo-5b-pregnan-18-al | 9.27±8.25 | 494.54±478.32 | ↑ | 70.37±99.37 | ↓ | 472.08±790.00 | ↓ |
|  | Estrone | 6.35±2.49 | 41.93±17.60 | ↑ | 15.82±18.54 | ↓ | 50.38±94.13 | ↑ |
|  | Cortisol | 59.48±41.72 | 1.38±1.140 | ↓ | 3.19±4.13 | ↑ | 1.22±1.58 | ↓ |
|  | 5-L-Glutamyl-taurine | 303.25±81.12 | 14.06±8.54 | ↓ | 188.23±398.96 | ↑ | 10.53±5.81 | ↓ |
|  | 5-L-Glutamyl-taurine | 215.19±65.25 | 36.6±20.49 | ↓ | 199.43±333.91 | ↑ | 22.44±12.34 | ↓ |
|  | Oxidized glutathione | 4.14±5.43 | 37.54±23.34 | ↑ | 10.67±16.19 | ↓ | 4.13±6.99 | ↓ |
|  | Myristic acid | 49.01±13.99 | 115.44±29.02 | ↑ | 77.58±35.44 | ↓ | 53.59±22.00 | ↓ |
|  | Chitobiose | 47.32±18.41 | 162.84±38.96 | ↑ | 75.88±53.87 | ↓ | 48.67±43.82 | ↓ |
|  | Stearidonic acid | 1.83±3.33 | 143.68±98.35 | ↑ | 31.95±46.10 | ↓ | 8.88±18.96 | ↓ |
|  | 2,3-Diphosphoglyceric acid | 52.06±17.34 | 128.62±29.17 | ↑ | 121.09±41.16 | ↓ | 93.17±33.69 | ↓ |
|  | Deoxyguanosine | 50.19±20.83 | 139.25±31.29 | ↑ | 119.56±49.32 | ↓ | 94.47±39.78 | ↓ |
|  | Glucaric acid | 43.27±19.25 | 4.04±4.20 | ↓ | 7.71±9.82 | ↑ | 2.19±2.04 | ↓ |
|  | Myristic acid | 109.84±27.55 | 468.79±144.10 | ↑ | 222.72±103.53 | ↓ | 128.76±71.83 | ↓ |
|  | Dihomo-gamma-linolenic acid | 92.62±28.55 | 193.39±72.82 | ↑ | 157.38±81.43 | ↓ | 133.39±109.52 | ↓ |
| ESI+ | 12-Keto-tetrahydro-leukotriene B4 | 1048.74±973.85 | 395.47±129.55 | ↓ | 530.97±134.04 | ↑ | 465.45±143.25 | ↑ |
|  | Inosinic acid | 566.82±272.11 | 192.92±126.99 | ↑ | 305.71±118.47 | ↑ | 174.12±137.58 | ↓ |
|  | LacCer(d18:1/25:0) | 112.72±110.16 | 1676.13±1378.91 | ↑ | 811.7±593.07 | ↓ | 889.08±635.88 | ↓ |
|  | 3-O-Sulfogalactosylceramide (d18:1/18:1(9Z)) | 24082.3±17753.64 | 68158.93±57739.78 | ↑ | 40884.38±23442.19 | ↓ | 37987.34±23998.72 | ↓ |
|  | Corticosterone | 611.76±703.62 | 2536.35±830.51 | ↑ | 2073.39±576.52 | ↓ | 3278.3±650.40 | ↑ |
|  | 5-Methoxyindoleacetate | 209.06±41.23 | 493.89±120.13 | ↑ | 346.96±104.56 | ↓ | 715.01±262.34 | ↑ |
|  | D-Glucose | 601.99±189.28 | 3014.81±953 | ↑ | 2211.98±676.49 | ↓ | 969.77±855.22 | ↓ |
|  | Octanoyl-CoA | 136.04±289.67 | 525.94±449.6 | ↑ | 373.51±590.75 | ↓ | 1748.45±4602.18 | ↑ |
|  | PE(20:3(8Z,11Z,14Z)/P-18:0) | 1464.82±912.57 | 4857.29±3210.04 | ↑ | 3287.19±2746.80 | ↓ | 4517.88±4230.66 | ↓ |
|  | PE(20:3(5Z,8Z,11Z)/P-18:0) | 1464.82±912.57 | 4857.29±3210.04 | ↑ | 3287.19±2746.80 | ↓ | 4517.88±4230.66 | ↓ |
|  | PE(20:2(11Z,14Z)/P-18:1(11Z)) | 1464.82±912.57 | 4857.29±3210.04 | ↑ | 3287.19±2746.80 | ↓ | 4517.88±4230.66 | ↓ |
|  | PE(20:2(11Z,14Z)/P-18:1(9Z)) | 1464.82±912.57 | 4857.29±3210.04 | ↑ | 3287.19±2746.80 | ↓ | 4517.88±4230.66 | ↓ |
|  | L-Allothreonine | 231.76±53.49 | 36.28±10.82 | ↓ | 50.96±10.34 | ↑ | 80.66±26.25 | ↑ |
|  | L-Valine | 490.05±171.81 | 98.10±38.54 | ↓ | 108.54±35.96 | ↑ | 64.24±26.57 | ↓ |
|  | 3beta-Hydroxy-5-cholestenoic acid | 10.61±12.32 | 552.16±255.49 | ↑ | 323.88±128.62 | ↓ | 488.98±187.49 | ↓ |
|  | LysoPA(P-16:0/0:0) | 1887.12±335.93 | 798.35±135 | ↓ | 972.99±122 | ↑ | 567.32±152.96 | ↓ |
|  | Retinoyl b-glucuronide | 451.78±91.88 | 201.27±55.26 | ↓ | 205.83±28.27 | ↑ | 206.01±65.41 | ↑ |
|  | Pregnanediol 3-O-glucuronide | 1.16±1.52 | 596.71±1494.4 | ↑ | 435.65±950.30 | ↓ | 160.17±501.95 | ↓ |
|  | 5-Acetylamino-6-formylamino-3-methyluracil | 25.90±10.73 | 396.87±711.02 | ↑ | 27.97±4.55 | ↓ | 98.70±166.11 | ↓ |
|  | 5-Acetylamino-6-formylamino-3-methyluracil | 25.90±10.73 | 396.87±711.02 | ↑ | 27.97±4.55 | ↓ | 98.70±166.11 | ↓ |
|  | PC(22:4(7Z,10Z,13Z,16Z)/P-16:0) | 14591.12±15077.24 | 57314.16±73203.13 | ↑ | 26963.18±24312.5 | ↓ | 30779.08±31862.64 | ↓ |
|  | PC(20:4(5Z,8Z,11Z,14Z)/P-18:0) | 14591.12±15077.24 | 57314.16±73203.13 | ↑ | 26963.18±24312.50 | ↓ | 30779.08±31862.64 | ↓ |
|  | dUMP | 324.58±123.12 | 103.79±29.58 | ↓ | 184.69±37.50 | ↑ | 130.73±32.29 | ↑ |
|  | 7alpha-Hydroxycholesterol | 405.93±336.97 | 127.24±17.68 | ↓ | 130.11±19.53 | ↑ | 116.53±16.78 | ↓ |
|  | 24-Hydroxycalcitriol | 192.29±72.50 | 441.69±111.43 | ↑ | 401.48±101.01 | ↓ | 740.14±180.84 | ↑ |
|  | 5-Thymidylic acid | 497.61±544.12 | 2122.12±1346.42 | ↑ | 1677.69±988.40 | ↓ | 1780.46±524.14 | ↓ |
|  | Succinic acid | 157.26±37.15 | 608.65±330.25 | ↑ | 528.56±258.75 | ↓ | 330.88±157.75 | ↓ |
|  | Hydroxykynurenine | 111.64±31.68 | 316.89±71.56 | ↑ | 213.53±53.80 | ↓ | 180.43±83.52 | ↓ |
|  | 9,10-EOA | 118.33±62.50 | 462.34±103.71 | ↑ | 28.93±81.12 | ↓ | 66.14±83.12 | ↓ |
|  | 12,13-EpOME | 83.80±20.47 | 169.71±59.65 | ↑ | 44.00±48.94 | ↓ | 21.05±25.15 | ↓ |
|  | Spermine | 83.80±20.47 | 169.71±59.65 | ↑ | 44.00±48.94 | ↓ | 21.05±25.15 | ↓ |
|  | SM(d18:1/26:1(17Z)) | 7.72±9.63 | 40.34±19.40 | ↑ | 4.56±7.20 | ↓ | 4.00±6.65 | ↓ |
|  | 3beta-Hydroxypregn-5-en-20-one sulfate | 18.02±6.83 | 78.37±38.48 | ↑ | 1.30±2.23 | ↓ | 50.05±103.88 | ↓ |
|  | Dehydroepiandrosterone sulfate | 24.16±9.49 | 74.72±26.30 | ↑ | 18.96±16.24 | ↓ | 17.46±12.49 | ↓ |
|  | Cortisol | 42.05±32.20 | 394.79±497.67 | ↑ | 39.61±64.27 | ↓ | 116.49±242.76 | ↓ |
|  | Cortisol | 8.07±8.55 | 103.66±146.81 | ↑ | 5.42±13.13 | ↓ | 25.99±56.50 | ↓ |
|  | 11b,21-Dihydroxy-3,20-oxo-5b-pregnan-18-al | 171.58±41.18 | 345.22±146.90 | ↑ | 74.19±92.74 | ↓ | 86.54±108.68 | ↓ |
|  | Taurocholic acid | 2715.54±987.72 | 8668.35±2877.01 | ↑ | 701.56±2109.59 | ↓ | 233.06±531.20 | ↓ |
|  | 5-Methoxyindoleacetate | 299.31±90.20 | 769.36±312.72 | ↑ | 30.51±51.14 | ↓ | 182.68±372.96 | ↓ |
|  | LysoPC(20:4(8Z,11Z,14Z,17Z)/0:0) | 22.00±9.33 | 55.07±20.99 | ↑ | 7.69±12.84 | ↓ | 15.50±26.03 | ↓ |
|  | Indoleacetaldehyde | 61.75±22.08 | 173.26±79.66 | ↑ | 8.87±11.35 | ↓ | 37.88±78.20 | ↓ |
|  | Orotidylic acid | 39.57±15.98 | 99.37±41.60 | ↑ | 18.57±19.24 | ↓ | 27.95±40.34 | ↓ |
|  | 7,8-Dihydro-7-hydroxy-8-S-glutathionyl-benzo[a]pyrene | 46.17±17.39 | 115.08±35.02 | ↑ | 45.15±35.96 | ↓ | 26.31±23.61 | ↓ |
|  | Tetrahydrofolyl-[Glu](2) | 222.00±144.65 | 50.16±22.42 | ↓ | 525.67±333.74 | ↑ | 189.22±270.73 | ↑ |
|  | Riboflavin reduced | 151.59±88.03 | 446.37±371.84 | ↑ | 23.07±26.04 | ↓ | 61.37±59.39 | ↓ |
|  | Dihomo-gamma-linolenic acid | 2179.79±443.66 | 4525.65±1071.58 | ↑ | 1809.02±1706.24 | ↓ | 2654.01±1489.12 | ↓ |
|  | Melibiitol | 23.57±8.00 | 59.05±20.91 | ↑ | 13.33±21.05 | ↓ | 14.57±22.27 | ↓ |
|  | Taurochenodesoxycholic acid | 93.71±35.81 | 662.2±939.04 | ↑ | 54.44±90.91 | ↓ | 23.87±63.64 | ↓ |
|  | Inosine | 45.56±9.49 | 100.34±54.31 | ↑ | 6.70±13.05 | ↓ | 23.83±48.44 | ↓ |
|  | LysoPA(18:1(9Z)/0:0) | 33.34±13.90 | 81.2±21.10 | ↑ | 14.86±20.26 | ↓ | 23.48±33.83 | ↓ |
|  | Indoleacetic acid | 27.02±8.03 | 85.85±40.24 | ↑ | 12.86±21.31 | ↓ | 113.38±233.99 | ↑ |