**Supplementary Table** **4**.Differential metabolites for Metformin callbacks

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Modle | Name | Normal | Model | Metformin | Up/down |
| ESI- | 13-L-Hydroperoxylinoleic acid | 5.23±2.75 | 117.8±70.87 | 24.54±29.46 | ↓ |
|  | 13-L-Hydroperoxylinoleic acid | 0.51±0.50 | 38.89±27.04 | 25.06±52.20 | ↓ |
|  | 15H-11,12-EETA | 37.48±21.98 | 2.57±2.25 | 3.70±9.26 | ↑ |
|  | Leukotriene D4 | 16.42±7.20 | 84.76±37.20 | 40.52±35.08 | ↓ |
|  | Prostaglandin H3 | 1.51±1.41 | 227.25±126.75 | 138.91±252.25 | ↓ |
|  | 11,12-Epoxyeicosatrienoic acid | 1.96±2.91 | 79.06±97.48 | 33.47±53.63 | ↓ |
|  | 5a-Pregnane-3,20-dione | 419.94±110.86 | 1421.76±580.48 | 654.02±513.41 | ↓ |
|  | 3beta-Hydroxypregn-5-en-20-one sulfate | 18.02±6.83 | 78.37±38.48 | 50.05±103.88 | ↓ |
|  | 2-Methoxy-estradiol-17b 3-glucuronide | 51.17±16.50 | 180.9±58.08 | 89.81±69.88 | ↓ |
|  | Cortisol | 42.05±32.20 | 394.79±497.67 | 116.49±242.76 | ↓ |
|  | 11b,21-Dihydroxy-3,20-oxo-5b-pregnan-18-al | 9.27±8.25 | 494.54±478.32 | 472.08±790.00 | ↓ |
|  | Cortisol | 8.07±8.55 | 103.66±146.81 | 25.99±56.50 | ↓ |
|  | Myristic acid | 49.01±13.99 | 115.44±29.02 | 53.59±22.00 | ↓ |
|  | 2,3-Diphosphoglyceric acid | 52.06±17.34 | 128.62±29.17 | 93.17±33.69 | ↓ |
|  | Deoxyguanosine | 50.19±20.83 | 139.25±31.29 | 94.47±39.78 | ↓ |
|  | PE(18:2(9Z,12Z)/P-18:1(11Z)) | 853.17±690.86 | 108.02±85.89 | 123.19±173.78 | ↑ |
|  | PE(18:2(9Z,12Z)/P-18:1(9Z)) | 853.17±690.86 | 108.02±85.89 | 123.19±173.78 | ↑ |
|  | PE(20:5(5Z,8Z,11Z,14Z,17Z)/18:0) | 42.38±34.01 | 3.38±4.78 | 4.88±6.29 | ↑ |
|  | Tetrahydrofolyl-[Glu](2) | 222.00±144.65 | 50.16±22.42 | 189.22±270.73 | ↑ |
|  | Dihomo-gamma-linolenic acid | 2179.79±443.66 | 4525.65±1071.58 | 2654.01±1489.12 | ↓ |
|  | Myristic acid | 109.84±27.55 | 468.79±144.10 | 128.76±71.83 | ↓ |
|  | Dihomo-gamma-linolenic acid | 92.62±28.55 | 193.39±72.82 | 133.39±109.52 | ↓ |
| ESI+ | 12-Keto-tetrahydro-leukotriene B4 | 1048.74±973.85 | 395.47±129.55 | 465.45±143.25 | ↑ |
|  | LacCer(d18:1/25:0) | 112.72±110.16 | 1676.13±1378.91 | 889.08±635.88 | ↓ |
|  | 3-O-Sulfogalactosylceramide (d18:1/18:1(9Z)) | 24082.3±17753.64 | 68158.93±57739.78 | 37987.34±23998.72 | ↓ |
|  | Cer(d18:1/16:0) | 117.63±55.76 | 399.94±286.03 | 397.75±277.39 | ↓ |
|  | D-Glucose | 601.99±189.28 | 3014.81±953 | 969.77±855.22 | ↓ |
|  | PE(20:3(8Z,11Z,14Z)/P-18:0) | 1464.82±912.57 | 4857.29±3210.04 | 4517.88±4230.66 | ↓ |
|  | PE(20:3(5Z,8Z,11Z)/P-18:0) | 1464.82±912.57 | 4857.29±3210.04 | 4517.88±4230.66 | ↓ |
|  | PE(20:2(11Z,14Z)/P-18:1(11Z)) | 1464.82±912.57 | 4857.29±3210.04 | 4517.88±4230.66 | ↓ |
|  | PE(20:2(11Z,14Z)/P-18:1(9Z)) | 1464.82±912.57 | 4857.29±3210.04 | 4517.88±4230.66 | ↓ |
|  | L-Allothreonine | 231.76±53.49 | 36.28±10.82 | 80.66±26.25 | ↑ |
|  | Dextrin | 455.29±127.05 | 32.62±21.97 | 63.12±49.13 | ↑ |
|  | Farnesol | 209.95±36.21 | 574.61±483.27 | 572.22±453.66 | ↓ |
|  | 3beta-Hydroxy-5-cholestenoic acid | 10.61±12.32 | 552.16±255.49 | 488.98±187.49 | ↓ |
|  | Retinoyl b-glucuronide | 451.78±91.88 | 201.27±55.26 | 206.01±65.41 | ↑ |
|  | Pregnanediol 3-O-glucuronide | 1.16±1.52 | 596.71±1494.4 | 160.17±501.95 | ↓ |
|  | 5-Acetylamino-6-formylamino-3-methyluracil | 25.90±10.73 | 396.87±711.02 | 98.70±166.11 | ↓ |
|  | 5-Acetylamino-6-formylamino-3-methyluracil | 25.90±10.73 | 396.87±711.02 | 98.70±166.11 | ↓ |
|  | PC(22:4(7Z,10Z,13Z,16Z)/P-16:0) | 14591.12±15077.24 | 57314.16±73203.13 | 30779.08±31862.64 | ↓ |
|  | PC(20:4(5Z,8Z,11Z,14Z)/P-18:0) | 14591.12±15077.24 | 57314.16±73203.13 | 30779.08±31862.64 | ↓ |
|  | dUMP | 324.58±123.12 | 103.79±29.58 | 130.73±32.29 | ↑ |
|  | 5-Thymidylic acid | 497.61±544.12 | 2122.12±1346.42 | 1780.46±524.14 | ↓ |
|  | AICAR | 5991.18±3895.68 | 2990.63±976.2 | 2331.56±452.19 | ↓ |
|  | Succinic acid | 157.26±37.15 | 608.65±330.25 | 330.88±157.75 | ↓ |
|  | L-4-Hydroxyglutamate semialdehyde | 365.55±79.29 | 124.77±26.37 | 151.44±53.75 | ↑ |
|  | PC(15:0/18:3(9Z,12Z,15Z)) | 267.03±318.75 | 733±522.52 | 553.37±260.70 | ↓ |
|  | LysoPA(0:0/18:0) | 26.43±15.31 | 245.75±140.45 | 102.08±63.76 | ↓ |
|  | Hydroxykynurenine | 111.64±31.68 | 316.89±71.56 | 180.43±83.52 | ↓ |