**Supplementary Material**

**Untargeted Urine metabolomics assay: sample processing and feature extraction**

Frozen 24-hour urine samples from 995 CRIC participants and a healthy control were thawed, centrifuged and precipitate-free supernatants were diluted 1:50 in double distilled water in 96 well polypropylene storage microplates (AB-1058, Abgene) sealed with easy-peel heat sealing foil (AB-0745, Abgene) and kept frozen until analysis. Diluted urines were shipped on dry ice and stored at -80 Celsius up to 2 weeks prior to data acquisition by mass spectrometry. Samples were injected in duplicate (i.e. technical replicates) with an MPS 3 xt autosampler (Gerstel) coupled to an Agilent 6550 Q-TOF mass spectrometer (Agilent Technologies) by non-targeted flow injection analysis (Fuhrer et al., 2011). Briefly, the flow rate was 150 μL/min of mobile phase consisting of isopropanol/water (60:40, v/v) buffered with 5 mM ammonium fluoride, and for online mass axis correction, homo-taurine and hexakis (1H, 1H, 3H tetrafluoropropoxy) phosphazine (HP-0921, Agilent Technologies) were added to the mobile phase. Profile mass spectra (MS1) were recorded in 4Ghz acquisition mode from 50 to 1000 m/z in negative ionization mode with the following source settings: temperature 225° C, drying gas 11 L/min, nebulizer pressure 20 psig, sheath gas temperature 350° C, sheath gas flow 10 L/min, Vcap voltage 3500 V, nozzle voltage 2000 V, fragmentor voltage 350 V and Oct 1 RF Vpp voltage 750V. All steps of data processing and analysis were performed with Matlab R2017b (The Mathworks) using functions embedded in the bioinformatics, statistics, database, and parallel computing toolboxes. After sample alignment and gap-filling, correction for ion intensity drift over time and between plates was performed, and the common mass axis was recalibrated using known frequently occurring ions. Approximately 15k commonly observed ions masses were annotated based on accurate mass comparison using 1 mDa mass tolerance against the Human Metabolome Database HMDBv4.0, resulting in 1899 annotated ion masses assuming single deprotonation (Supplemental Table S6).

**Targeted Urine metabolomics assay: sample processing and feature extraction**

A subset of 15 candidate metabolites from the untargeted panel were assayed by using a quantitative capillary electrophoresis (CE) coupled to mass spectrometry method (ZipChip-Qexactive) to validate metabolite ion identification and annotations from the untargeted method.

For the ZipChip assay, 10 µL of urine sample or calibration standard mixture was mixed with 90 µL of extraction solution containing 80% methanol, 100 mM ammonium acetate and 1 µM of stable isotope labeled internal standards in a 96 well plate. After mixing, samples or calibration standards were kept in a -20°C freezer for at least one hour and then centrifuged at 5000 rpm for 5 minutes. An 50 µL supernatant was transferred to a clean 96 well plate for analysis. Metabolite separation was achieved with a microfluidic chip which integrates capillary electrophoresis (CE) with nano-electrospray ionization through ZipChip interface (908 Devices, Boston, MA). For each sample, 20 µL solution was placed into the sample well and subsequently injected into the HS chip using a 10-s load time. A field strength of 1000V/cm was applied for separation over 4 minutes using a background electrolyte solution consisting of 2% formic acid in 50% methanol in water. The mass spectrometry acquisition was done with Q-Exactive mass spectrometer (Thermo, San Jose, CA). The resolving power was 17,500 with an AGC target of 3×106, maximum injection time of 20 ms, and scan range of 75–500 m/z. Thermo Scientific’s software Xcalibur-Quan Browser was used for quantitative data processing. Calibration curves for all metabolites were included with each plate. The targeted assay metabolite data were normalized to urine creatinine measured at the CRIC Central Laboratory.

**Untargeted metabolomics data: filtering metabolic features.**

We leveraged technical replicate data for each sample to develop criteria for filtering out metabolite ions that showed poor reproducibility. A total of 1899 annotated metabolite ions were measured for the 995 CRIC subjects along with a pooled urine sample from the healthy subject, as quality control (QC). All data were collected in duplicates. The three QC sample per plate were randomly run within each 96 well plate in duplicates leading to 6 measurements per plate and a total of 198 measurements across 33 plates. The filtering process consists of three steps. In step one, only the QC data was used. Three reliability metrics, the correlation coefficient between the technical duplicates (Spearman and Pearson **QC** **CC**), intraclass correlation (**QC ICC**) and coefficient of variation (**QC CV**) for each metabolite ion abundance were calculated. The QC ICC for each metabolite ion abundance was calculated as the variance between technical duplicates divided by the total variation (including batch and replicate variation); the QC CV was calculated as the standard deviation between technical duplicate abundance divided by the mean of the samples. Low correlations, high ICC or high CV values would indicate poor reliability, i.e., high variability relative to signal. We formalized these criteria and excluded ions for which any of the following was true:

* QC\_Spearman < 0.85 or QC\_Pearson < 0.85
* QC\_CV ≥ 0.05
* QC\_ICC ≥ 0.05

These cut offs are based on standard assay reliability metrics. We then implemented filtering step two using the CRIC samples. Here the objective was to filter out metabolite ions which exhibited low biological variability. To this end we calculated an intraclass correlation (CRIC ICC), as the ratio of between subject to total sample variation; ions with ICC <= 0.35 were further excluded.

Thus, in summary, the final set of 698 retained metabolite ions satisfied all criteria: QC Spearman >=0.85 & QC\_Pearson >= 0.85 & QC\_CV < 0.05 & QC\_ICC < 0.05 & CRIC\_ICC > 0.35. The technical replicates of the metabolite ion abundances (two per sample) were then averaged. In the final filtering step, we excluded metabolite ions with low abundance to exclude non-informative ions in the noise range. The ions that passed our filtering criteria and count threshold, constituted the final metabolite ion feature set for modeling.

**Variability of 15 targeted metabolites**: Of the 13 statistically significant metabolites in the target analysis, 7 had a QC CV of ≤ 5%, 3 had a QC CV of between 5% and up to 10%, and 3 (i.e.,Ornithine, Isoleucine, Betaine), had a QC CV of more than 10%. The 2 non-significant metabolites, DL.Homocystine and Nicotinic acid, were not detected in the QC samples.

**Supplemental Table S1**. **Associations between single metabolite ions\* and eGFR slopes, adjusted for 9 clinical variables**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Ion Index** | **Estimate †** | **Lower** | **Upper** | **P value** | **FDR.P value** | Geometric mean (95%Ci) | **Name** |
| 1098 | -0.44 | -0.68 | -0.2 | 0.000361 | 0.04198 | 25511.72 (25009.12, 26024.42) | 3-(4-Methyl-3-pentenyl)thiophene |
| 1099 | -0.45 | -0.66 | -0.24 | 2.90E-05 | 0.01012 | 16598.07 (16250.48, 16953.1) | C10:3 |
| 281 | 0.27 | 0.14 | 0.41 | 7.19E-05 | 0.01672 | 417279.81 (402283.15, 432835.52) | Furoic acid |
| 30 | 0.3 | 0.15 | 0.46 | 0.00016 | 0.02787 | 10894.52 (10557.28, 11242.53) | Butynal |
| 678 | -0.45 | -0.7 | -0.21 | 0.000335 | 0.04198 | 21007.91 (20618.87, 21404.29) | Cycloheptanecarboxylic acid |
| 9178 | 0.25 | 0.16 | 0.34 | 1.96E-07 | 0.000137 | 18245.82 (17390.49, 19143.22) | 3,4-Dicaffeoyl-1,5-quinolactone |

\*Results for 6 significant metabolites after FDR correction from a total of 698 metabolite ion candidates.

†Estimates are from linear regression models using log2 transformed metabolite ion abundances.

**Supplemental Table S2.** **Associations between single metabolite ion\* and time-to-ESKD, adjusted for 9 clinical variables**

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
| **Ion Index** | **HR** **†** | **lower** | **upper** | **p** | **FDR.p** | **Geometric Mean  (95%Ci)** | **Name** |
| 1019 | 1.54 | 1.21 | 1.97 | 0 | 0.01 | 193443.23  (189589.41, 197375.38) | Hydroxyadipate |
| 1019 | 1.54 | 1.21 | 1.97 | 0 | 0.01 | 193443.23  (189589.41, 197375.38) | (-)-1-Methylpropyl 1-propenyl disulfide |
| 1022 | 1.47 | 1.15 | 1.87 | 0 | 0.02 | 18222.56  (17852.12, 18600.69) | Cymarose |
| 1036 | 1.38 | 1.12 | 1.69 | 0 | 0.02 | 71019.19  (69557.9, 72511.17) | Acetylcysteine |
| 1075 | 1.27 | 1.07 | 1.5 | 0.01 | 0.05 | 46124.24  (44819.74, 47466.71) | 4-Pyridoxolactone |
| 1079 | 1.48 | 1.21 | 1.8 | 0 | 0.01 | 50991.66  (49719.96, 52295.89) | Phenylalanine |
| 1098 | 1.84 | 1.45 | 2.32 | 0 | 0 | 25511.72  (25009.12, 26024.42) | 3-(4-Methyl-3-pentenyl)thiophene |
| 1127 | 1.31 | 1.08 | 1.59 | 0.01 | 0.04 | 17488.86  (17008.88, 17982.38) | Methyl 1-(methylthio)propyl disulfide |
| 1165 | 1.41 | 1.12 | 1.78 | 0 | 0.03 | 12907.19  (12644.8, 13175.02) | Glycerone sulfate |
| 1167 | 1.32 | 1.08 | 1.62 | 0.01 | 0.05 | 19637.46  (19153.11, 20134.05) | Benzyl methyl disulfide |
| 1167 | 1.32 | 1.08 | 1.62 | 0.01 | 0.05 | 19637.46  (19153.11, 20134.05) | Gallic acid |
| 1293 | 1.42 | 1.16 | 1.74 | 0 | 0.01 | 40878.75  (39843.27, 41941.15) | Berteroin |
| 1293 | 1.42 | 1.16 | 1.74 | 0 | 0.01 | 40878.75  (39843.27, 41941.15) | Acetyl-Asp |
| 1294 | 1.39 | 1.14 | 1.71 | 0 | 0.02 | 24241.14  (23726.58, 24766.87) | Indole-3-acetate |
| 1337 | 1.32 | 1.15 | 1.52 | 0 | 0.01 | 24288.61  (23513.63, 25089.13) | Polyvidone |
| 1337 | 1.32 | 1.15 | 1.52 | 0 | 0.01 | 24288.61  (23513.63, 25089.13) | Formyl-Met |
| 1486 | 1.12 | 1.03 | 1.21 | 0.01 | 0.05 | 1433393.25  (1345812.7, 1526673.22) | 4-Pyridoxate |
| 1695 | 1.38 | 1.13 | 1.69 | 0 | 0.02 | 26895.48  (26270.83, 27534.99) | 5-Hydroxyindoleacetic acid |
| 1983 | 1.34 | 1.09 | 1.66 | 0.01 | 0.05 | 105402.12  (103059.83, 107797.64) | Sebacic acid |
| 2004 | 1.49 | 1.24 | 1.79 | 0 | 0 | 10527.86  (10267.45, 10794.89) | Indolepyruvate |
| 2028 | 1.32 | 1.11 | 1.58 | 0 | 0.02 | 38218.72  (37123.22, 39346.55) | Tryptophan |
| 2030 | 1.49 | 1.15 | 1.92 | 0 | 0.03 | 17238.22  (16913.82, 17568.85) | Serinyl-Valine |
| 2046 | 1.59 | 1.24 | 2.03 | 0 | 0.01 | 38921.25  (38135.27, 39723.42) | N-Methylcalystegine C1 |
| 2046 | 1.59 | 1.24 | 2.03 | 0 | 0.01 | 38921.25  (38135.27, 39723.42) | Dihydro-2,4-dimethyl-6-(2-methylpropyl)-4H-1,3,5-dithiazine |
| 2094 | 1.29 | 1.09 | 1.53 | 0 | 0.03 | 7727.64  (7519.45, 7941.59) | Isoniazid pyruvate |
| 2115 | 1.45 | 1.2 | 1.75 | 0 | 0.01 | 11825.9  (11523.55, 12136.19) | Dihydrolipoate |
| 2115 | 1.45 | 1.2 | 1.75 | 0 | 0.01 | 11825.9  (11523.55, 12136.19) | Aminofurantoin |
| 2115 | 1.45 | 1.2 | 1.75 | 0 | 0.01 | 11825.9  (11523.55, 12136.19) | Methyl 5-(1-Propynyl)-2-thiophenepropanoate |
| 215 | 1.35 | 1.12 | 1.62 | 0 | 0.02 | 31559.9  (30800.84, 32337.67) | Aminobutanoic acid (ABA) |
| 2232 | 1.47 | 1.17 | 1.83 | 0 | 0.02 | 10597.09  (10372.1, 10826.97) | Cucurbic acid |
| 226 | 1.79 | 1.37 | 2.34 | 0 | 0 | 36708.43  (35995.85, 37435.12) | Hydroxybutanoic acid |
| 2360 | 1.36 | 1.13 | 1.65 | 0 | 0.02 | 29428.94  (28673.72, 30204.05) | 1-Isothiocyanato-8-(methylthio)octane |
| 2430 | 1.35 | 1.13 | 1.62 | 0 | 0.02 | 15298.62  (14875.87, 15733.39) | 1-(5-Acetyl-2-hydroxyphenyl)-3-methyl-1-butanone |
| 2456 | 1.49 | 1.21 | 1.83 | 0 | 0.01 | 29508.77  (28839.54, 30193.54) | Methyl 5-hydroxyoxindole-3-acetate |
| 2456 | 1.49 | 1.21 | 1.83 | 0 | 0.01 | 29508.77  (28839.54, 30193.54) | N-lactoyl-Methionine |
| 2480 | 1.29 | 1.1 | 1.51 | 0 | 0.02 | 27796.64  (26998.94, 28617.92) | 3-(6-hydroxy-7-methoxy-2H-1,3-benzodioxol-5-yl)prop-2-enal |
| 2705 | 1.55 | 1.28 | 1.88 | 0 | 0 | 6106.37  (5960.97, 6255.32) | Isoleucyl-Valine |
| 3049 | 1.23 | 1.06 | 1.42 | 0.01 | 0.04 | 7745.56  (7498.43, 8000.84) | Frovatriptan |
| 3078 | 1.48 | 1.22 | 1.8 | 0 | 0.01 | 34343.79  (33610.28, 35093.31) | 1-O-Galloylglycerol |
| 3079 | 1.41 | 1.12 | 1.78 | 0 | 0.03 | 478096.9  (467410.77, 489027.34) | Uridine |
| 3248 | 1.26 | 1.1 | 1.44 | 0 | 0.02 | 11376.16  (10996.85, 11768.56) | 3,5-dihydroxy-4-(sulfooxy)benzoic acid |
| 3310 | 1.32 | 1.09 | 1.61 | 0 | 0.04 | 8357.32  (8162.09, 8557.23) | 5-Hydroxy-N-formylkynurenine |
| 3422 | 1.33 | 1.14 | 1.54 | 0 | 0.01 | 28194.15  (27273.67, 29145.69) | (2R,3S)-Piscidic acid |
| 3425 | 1.37 | 1.15 | 1.62 | 0 | 0.01 | 26614.89  (25857.01, 27394.98) | 3-hydroxy-3-(3,4,5-trimethoxyphenyl)propanoic acid |
| 3429 | 1.46 | 1.19 | 1.79 | 0 | 0.01 | 20227.28  (19750.38, 20715.71) | 1-Methoxy-1-(2,4,5-trimethoxyphenyl)-2-propanol |
| 343 | 1.55 | 1.23 | 1.96 | 0 | 0.01 | 20768.23  (20346.21, 21199) | Indole |
| 3435 | 1.53 | 1.19 | 1.97 | 0 | 0.02 | 1838727.3  (1803916.21, 1874210.15) | C16:0 |
| 344 | 1.5 | 1.2 | 1.86 | 0 | 0.01 | 28340.9  (27753.57, 28940.66) | Valine; Betaine |
| 362 | 1.42 | 1.19 | 1.69 | 0 | 0.01 | 13425.06  (13074.77, 13784.74) | Threonine |
| 3778 | 1.36 | 1.16 | 1.59 | 0 | 0.01 | 9701.78  (9441.69, 9969.03) | 3-(6,7-dimethoxy-2H-1,3-benzodioxol-5-yl)oxirane-2-carboxylic acid |
| 3778 | 1.36 | 1.16 | 1.59 | 0 | 0.01 | 9701.78  (9441.69, 9969.03) | DL-Homocystine |
| 4048 | 1.41 | 1.16 | 1.71 | 0 | 0.01 | 9365.57  (9138.14, 9598.67) | Alpha-CEHC |
| 410 | 1.36 | 1.16 | 1.61 | 0 | 0.01 | 36796.27  (35733.18, 37890.99) | Nicotinate |
| 4152 | 1.39 | 1.14 | 1.69 | 0 | 0.02 | 5575.09  (5449.61, 5703.46) | Lactapiperanol C |
| 4156 | 1.77 | 1.41 | 2.22 | 0 | 0 | 58945.49  (57717.85, 60199.25) | Oleic acid |
| 4207 | 1.51 | 1.26 | 1.82 | 0 | 0 | 20553.41  (20062.09, 21056.76) | 6-Thioinosinic acid |
| 4220 | 1.55 | 1.19 | 2.02 | 0 | 0.02 | 3479145.07  (3414841.67, 3544659.35) | C18:0 |
| 4383 | 1.22 | 1.06 | 1.41 | 0.01 | 0.05 | 11419.74  (11059.39, 11791.84) | Trimethoprim |
| 4406 | 1.25 | 1.09 | 1.43 | 0 | 0.02 | 16400.8  (15850.14, 16970.6) | Hawkinsin |
| 443 | 1.36 | 1.11 | 1.66 | 0 | 0.03 | 14985.02  (14692.13, 15283.75) | 2,3,6-Trihydroxypyridine |
| 4489 | 1.34 | 1.08 | 1.67 | 0.01 | 0.05 | 10075.7  (9857.36, 10298.88) | gamma-Glutamylphenylalanine |
| 4674 | 1.27 | 1.1 | 1.46 | 0 | 0.02 | 56745.9  (54792.05, 58769.41) | Promazine 5-sulfoxide |
| 473 | 1.19 | 1.05 | 1.35 | 0.01 | 0.04 | 16055.15  (15487.99, 16643.08) | Pipecolate |
| 4754 | 1.28 | 1.09 | 1.5 | 0 | 0.02 | 13413.73  (13016.12, 13823.49) | Arginyl-Glutamine |
| 490 | 1.48 | 1.12 | 1.94 | 0 | 0.04 | 19693.72  (19340.71, 20053.16) | 4-Methyl-2-oxopentanoate |
| 4911 | 1.38 | 1.11 | 1.72 | 0 | 0.04 | 16430.09  (16080.87, 16786.9) | D-Erythroascorbic acid 1''-a-D-glucoside |
| 505 | 1.33 | 1.12 | 1.57 | 0 | 0.02 | 7235.05  (7049.86, 7425.09) | (±)-2-Propylthiazolidine |
| 506 | 1.28 | 1.07 | 1.52 | 0.01 | 0.05 | 44228.25  (43041.67, 45447.54) | (Iso)Leucine |
| 5140 | 1.24 | 1.06 | 1.44 | 0.01 | 0.05 | 9888.5  (9595.22, 10190.75) | 10-Hydroxy-8-nor-2-fenchanone glucoside |
| 522 | 1.32 | 1.08 | 1.61 | 0.01 | 0.05 | 12595.79  (12298.74, 12900.01) | Asparagine |
| 526 | 1.31 | 1.13 | 1.51 | 0 | 0.01 | 22896.08  (22182.14, 23633.01) | Ornithine |
| 5302 | 1.28 | 1.09 | 1.52 | 0 | 0.03 | 8421.12  (8211.17, 8636.44) | Zeranol |
| 534 | 1.65 | 1.35 | 2.02 | 0 | 0 | 31057.32  (30386.43, 31743.02) | Aspartate |
| 5392 | 1.46 | 1.11 | 1.93 | 0.01 | 0.05 | 89602.1  (87991.01, 91242.7) | 2-Dodecylbenzenesulfonic acid |
| 5392 | 1.46 | 1.11 | 1.93 | 0.01 | 0.05 | 89602.1  (87991.01, 91242.7) | Heptaethylene glycol |
| 548 | 1.22 | 1.06 | 1.41 | 0.01 | 0.04 | 38889.49  (37600.93, 40222.2) | Malate |
| 548 | 1.22 | 1.06 | 1.41 | 0.01 | 0.04 | 38889.49  (37600.93, 40222.2) | 3,3-Dimethyl-1,2-dithiolane |
| 5566 | 1.25 | 1.08 | 1.45 | 0 | 0.03 | 8522.47  (8248.01, 8806.07) | (R)-Marmin |
| 561 | 1.44 | 1.11 | 1.87 | 0.01 | 0.05 | 31774.95  (31251.39, 32307.27) | Adenine |
| 576 | 1.45 | 1.13 | 1.87 | 0 | 0.03 | 609099.44  (596985.57, 621459.12) | Threonate |
| 576 | 1.45 | 1.13 | 1.87 | 0 | 0.03 | 609099.44  (596985.57, 621459.12) | 1-Pentanesulfenothioic acid |
| 5810 | 1.22 | 1.08 | 1.38 | 0 | 0.02 | 49493.86  (47485.83, 51586.82) | Sulpiride |
| 592 | 1.34 | 1.12 | 1.61 | 0 | 0.02 | 42123.22  (40959.15, 43320.37) | Anthranilate |
| 6153 | 1.3 | 1.08 | 1.57 | 0.01 | 0.05 | 3805.84  (3710.45, 3903.69) | Prostaglandin F2a |
| 628 | 1.14 | 1.06 | 1.24 | 0 | 0.02 | 522340.33  (491410.18, 555217.27) | Gabaculine |
| 6281 | 1.18 | 1.05 | 1.32 | 0 | 0.04 | 15679.07  (15070.75, 16311.94) | Triglochinin |
| 644 | 1.3 | 1.13 | 1.49 | 0 | 0.01 | 99902.18  (96338.97, 103597.17) | 3,4-Diethylthiophene |
| 645 | 1.44 | 1.11 | 1.88 | 0.01 | 0.05 | 41976.88  (41179.21, 42789.99) | cis-1,2-Dihydro-3-ethylcatechol |
| 6653 | 1.23 | 1.11 | 1.37 | 0 | 0.01 | 98556.82  (94215.21, 103098.5) | Geniposidic acid |
| 6757 | 1.42 | 1.15 | 1.76 | 0 | 0.02 | 12946.33  (12688.07, 13209.85) | 18-Hydroxycortisol |
| 6783 | 1.27 | 1.08 | 1.5 | 0 | 0.04 | 9876.1  (9595.41, 10165.01) | 2-(Arabinosylamino)-3-(glucosylamino)propanenitrile |
| 6876 | 1.28 | 1.08 | 1.53 | 0.01 | 0.04 | 8896.2  (8658.52, 9140.39) | Ceftizoxime |
| 6975 | 1.33 | 1.1 | 1.61 | 0 | 0.03 | 8284.61  (8073.53, 8501.22) | 5,6-Dihydroxyprostaglandin F1a |
| 718 | 1.43 | 1.17 | 1.75 | 0 | 0.01 | 26400.56  (25817.42, 26996.87) | 2-Oxoglutaramate |
| 721 | 1.51 | 1.21 | 1.88 | 0 | 0.01 | 126151.85  (123504.2, 128856.27) | 4-Acetamidobutanoate |
| 740 | 1.23 | 1.08 | 1.4 | 0 | 0.02 | 64292.7  (61945.88, 66728.43) | Lysine |
| 753 | 1.31 | 1.09 | 1.57 | 0 | 0.04 | 34166.98  (33287.17, 35070.05) | Indole-3-carbinol |
| 766 | 1.4 | 1.13 | 1.73 | 0 | 0.02 | 221950.22  (216711.34, 227315.74) | Hydroxyglutarate |
| 766 | 1.4 | 1.13 | 1.73 | 0 | 0.02 | 221950.22  (216711.34, 227315.74) | 2-Propenyl propyl disulfide |
| 767 | 1.49 | 1.17 | 1.9 | 0 | 0.02 | 20985.39  (20551.63, 21428.32) | Carbamoyl-Ser |
| 7671 | 1.28 | 1.08 | 1.53 | 0 | 0.04 | 18703.77  (18202.6, 19218.75) | Aminophylline |
| 798 | 1.36 | 1.11 | 1.67 | 0 | 0.03 | 360778.44  (352719.19, 369021.83) | Diisopropyl disulfide |
| 798 | 1.36 | 1.11 | 1.67 | 0 | 0.03 | 360778.44  (352719.19, 369021.83) | Pentose |
| 8568 | 1.16 | 1.05 | 1.28 | 0 | 0.03 | 19442.1  (18500.55, 20431.57) | Cholylglycine |
| 8590 | 1.29 | 1.1 | 1.51 | 0 | 0.02 | 4647.21  (4514.03, 4784.31) | Dolichyl b-D-glucosyl phosphate |
| 866 | 1.49 | 1.18 | 1.89 | 0 | 0.02 | 65807.37  (64500.23, 67141) | 5-(2-carboxylatoethyl)-4-oxo-4,5-dihydro-1H-imidazol-5-ide |
| 9355 | 1.35 | 1.13 | 1.6 | 0 | 0.02 | 6130.01  (5966.76, 6297.73) | 2-(2,4-dihydroxyphenyl)-3-(3,7-dimethylocta-2,6-dien-1-yl)-5,7-dihydroxy-6-(4-hydroxy-3-methylbut-2-en-1-yl)-3,4-dihydro-2H-1-benzopyran-4-one |
| 9355 | 1.35 | 1.13 | 1.6 | 0 | 0.02 | 6130.01  (5966.76, 6297.73) | Argatroban |
| 9464 | 1.33 | 1.14 | 1.57 | 0 | 0.01 | 7841.61  (7614.47, 8075.54) | Capsianoside V |
| 9483 | 1.28 | 1.11 | 1.48 | 0 | 0.01 | 4648.39  (4497.34, 4804.51) | Taurocholic acid |
| 965 | 1.27 | 1.1 | 1.46 | 0 | 0.02 | 22321.34  (21565.53, 23103.63) | L-2-Amino-4-methylenepentanedioic acid |
| 9706 | 1.2 | 1.05 | 1.36 | 0.01 | 0.04 | 7841.06  (7547.01, 8146.56) | N-[(3a,5b,7b)-7-hydroxy-24-oxo-3-(sulfooxy)cholan-24-yl]-Glycine |
| 9728 | 1.53 | 1.17 | 1.99 | 0 | 0.02 | 136209  (133639.67, 138827.72) | Sabadelin |
| 999 | 1.3 | 1.1 | 1.55 | 0 | 0.03 | 54960.27  (53547.78, 56410.02) | 2-Indolecarboxylic acid |

\*Results for 99 significant metabolite ions after FDR correction from a total of 698 metabolite ion candidates.

† Hazards ratios are from Cox regression models using log2 transformed metabolite abundances.

**Supplemental Table S3. Machine learning and penalized regression models predicting eGFR slope:** number of variables selected by each model from among 698 metabolite ions and 9 clinical variables

|  |  |  |  |
| --- | --- | --- | --- |
| **Models\*** | **Inclusion criteria for clinical variables: Forced (F) or Not forced (NF)** | **Number of variables**  **selected** | **Number of Metabolite ions selected** |
| 1-LASSO  (λ.1se) | F | 9 | 0 |
| 2-LASSO  (λ.min) | F | 29 | 20 |
| 3-LASSO (λ.min) | NF | 30 | 24 |
| 4-LASSO  (λ.1se) | NF | 12 | 6 |
| 5-Random Forest | NF | 30 | 25 |
| 6-Random Forest | NF | 12 | 8 |

\*: Likelihood ratio test p-value < 0.001 when comparing each metabolite model (Models 2- 6) to the clinical-features-only model (Model 1).

**Supplemental Table S4. Metabolites (p = 49) selected across six multivariable models for eGFR slope outcome**

|  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Ion Index** | **Tuning parameter choice for Lasso Models** | | | | **Random Forest** | | **# of times a metabolite ion is selected across the six models** | **Metabolite Name** |
| **Force** | | **Not Force** | |
| **λ.1se\*** | **λ.min\*** | **λ.min\*** | **λ.1se\*** | **Top 30\*** | **Top12\*** |
| **Model # (from Table 2)** | **1** | **2** | **3** | **4** | **5** | **6** |  |  |
| 1079 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | Phenylalanine |
| 1098 | 0 | 1 | 1 | 1 | 0 | 0 | 3 | 3-(4-Methyl-3-pentenyl)thiophene |
| 1099 | 0 | 1 | 1 | 1 | 0 | 0 | 3 | C10:3 |
| 1114 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | Zapotidine |
| 1219 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | Glycerol 3-phosphate |
| 1384 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | Hippurate |
| 2202 | 0 | 1 | 1 | 1 | 0 | 0 | 3 | Zalcitabine |
| 2227 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | Glycyl-Histidine |
| 226 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | Hydroxybutanoic acid |
| 2399 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 4-Nitrophenyl sulfate |
| 2480 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 3-(6-hydroxy-7-methoxy-2H-1,3-benzodioxol-5-yl)prop-2-enal |
| 2513 | 0 | 1 | 1 | 0 | 0 | 0 | 2 | 4-(2-Amino-3-hydroxyphenyl)-2,4-dioxobutanoic acid |
| 255 | 0 | 1 | 1 | 0 | 0 | 0 | 2 | Aminophenol |
| 2718 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | Asparaginyl-Valine |
| 2755 | 0 | 0 | 0 | 0 | 1 | 1 | 2 | 2,4-Dihydroxy-acetophenone 5-sulfate |
| 281 | 0 | 1 | 1 | 0 | 0 | 0 | 2 | Furoic acid |
| 30 | 0 | 1 | 1 | 0 | 1 | 1 | 4 | Butynal |
| 3117 | 0 | 1 | 1 | 1 | 0 | 0 | 3 | Asparaginyl-Hydroxyproline |
| 3165 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 2-Hydroxy-acetaminophen sulfate |
| 3193 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | Vanillic acid 4-sulfate |
| 3260 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | Heptabarbital |
| 3380 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | Thiamylal |
| 344 | 0 | 1 | 0 | 0 | 1 | 1 | 3 | Valine; Betaine |
| 3756 | 0 | 1 | 1 | 0 | 0 | 0 | 2 | Adenosine |
| 3756 | 0 | 1 | 1 | 0 | 0 | 0 | 2 | Neuraminic acid |
| 3996 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | [4-(3-hydroxybutyl)-2-methoxyphenyl] oxidanesulfonic acid |
| 3996 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | O-Demethylfonsecin |
| 4207 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 6-Thioinosinic acid |
| 4376 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 5-(4-Acetoxy-3-oxo-1-butynyl)-2,2''-bithiophene |
| 4442 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | Pantoyllactone glucoside |
| 473 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | Pipecolate |
| 4754 | 0 | 1 | 1 | 1 | 0 | 0 | 3 | Arginyl-Glutamine |
| 487 | 0 | 0 | 0 | 0 | 1 | 1 | 2 | Itaconate |
| 506 | 0 | 0 | 0 | 0 | 1 | 1 | 2 | (Iso)Leucine |
| 5196 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | Ubiquinone-2 |
| 526 | 0 | 0 | 1 | 0 | 1 | 0 | 2 | Ornithine |
| 5302 | 0 | 0 | 1 | 0 | 1 | 0 | 2 | Zeranol |
| 534 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | Aspartate |
| 5388 | 0 | 1 | 1 | 0 | 0 | 0 | 2 | Hydroxyhexamide |
| 6333 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | [(5-oxo-1,7-diphenylheptan-2-yl)oxy]sulfonic acid |
| 6478 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 3,4,5-trihydroxy-6-{[3-(hydroxymethyl)-1-oxo-1H-isochromen-7-yl]oxy}oxane-2-carboxylic acid |
| 6512 | 0 | 0 | 0 | 0 | 1 | 1 | 2 | Amisulpride |
| 7244 | 0 | 1 | 1 | 0 | 0 | 0 | 2 | Pipazethate |
| 7671 | 0 | 1 | 1 | 0 | 0 | 0 | 2 | Aminophylline |
| 798 | 0 | 1 | 0 | 0 | 1 | 1 | 3 | Pentose |
| 798 | 0 | 1 | 0 | 0 | 1 | 1 | 3 | Diisopropyl disulfide |
| 8590 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | Dolichyl b-D-glucosyl phosphate |
| 9178 | 0 | 1 | 1 | 1 | 1 | 1 | 5 | 3,4-Dicaffeoyl-1,5-quinolactone |
| 9355 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 2-(2,4-dihydroxy-phenyl)-3-(3,7-dimethylocta-2,6-dien-1-yl)-5,7-dihydroxy-6-(4-hydroxy-3-methylbut-2-en-1-yl)-3,4-dihydro-2H-1-benzopyran-4-one |
| 9355 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | Argatroban |
| 9419 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | 3,7,11,15,23-Pentaoxolanost-8-en-26-oic acid |
| 9464 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | Capsianoside V |
| 983 | 0 | 0 | 0 | 0 | 1 | 0 | 1 | Oxoadipate |

\*0 means not selected and 1 means selected by that model. 49 Metabolites selected across six multivariable models for eGFR slope outcome.

**Supplemental Table S5. Pathway Enrichment Analysis for 131 Features**

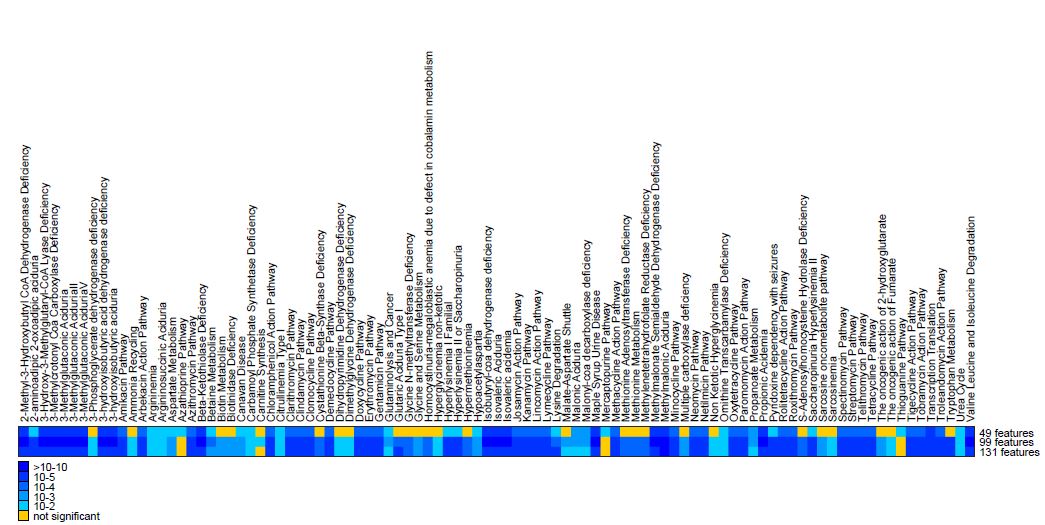
|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
| auc  (-log10 pval) | max  -log10 pval | max  -log10 qval (BH) | Pathway | # of hits | ion indices | annotation of hits |
| 924.6201144 | 9.155605371 | 2.38192E-09 | Transcription Translation | 9 | 344 362 506 522 534 740 1079 2028 | HMDB0000159  HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000182  HMDB0000191  HMDB0000687  HMDB0000883 |
| 848.6396038 | 10.79557417 | 5.91859E-11 | Methylmalonic Aciduria | 8 | 215 226 344 490 506 | HMDB0000008  HMDB0000023  HMDB0000172  HMDB0000491  HMDB0000687  HMDB0000695  HMDB0000883  HMDB0002166 |
| 827.0602089 | 10.25372887 | 1.90897E-10 | 2-Methyl-3-Hydroxybutryl CoA Dehydrogenase Deficiency | 7 | 215 226 344 490 506 | HMDB0000023  HMDB0000172  HMDB0000491  HMDB0000687  HMDB0000695  HMDB0000883  HMDB0002166 |
| 827.0602089 | 10.25372887 | 1.90897E-10 | 3-Hydroxy-3-Methylglutaryl-CoA Lyase Deficiency | 7 | 215 226 344 490 506 | HMDB0000023  HMDB0000172  HMDB0000491  HMDB0000687  HMDB0000695  HMDB0000883  HMDB0002166 |
| 827.0602089 | 10.25372887 | 1.90897E-10 | 3-Methylcrotonyl Coa Carboxylase Deficiency | 7 | 215 226 344 490 506 | HMDB0000023  HMDB0000172  HMDB0000491  HMDB0000687  HMDB0000695  HMDB0000883  HMDB0002166 |
| 827.0602089 | 10.25372887 | 1.90897E-10 | 3-Methylglutaconic Aciduria | 7 | 215 226 344 490 506 | HMDB0000023  HMDB0000172  HMDB0000491  HMDB0000687  HMDB0000695  HMDB0000883  HMDB0002166 |
| 827.0602089 | 10.25372887 | 1.90897E-10 | 3-Methylglutaconic AciduriaII | 7 | 215 226 344 490 506 | HMDB0000023  HMDB0000172  HMDB0000491  HMDB0000687  HMDB0000695  HMDB0000883  HMDB0002166 |
| 827.0602089 | 10.25372887 | 1.90897E-10 | 3-Methylglutaconic AciduriaV | 7 | 215 226 344 490 506 | HMDB0000023  HMDB0000172  HMDB0000491  HMDB0000687  HMDB0000695  HMDB0000883  HMDB0002166 |
| 827.0602089 | 10.25372887 | 1.90897E-10 | 3-hydroxyisobutyric acid dehydrogenase deficiency | 7 | 215 226 344 490 506 | HMDB0000023  HMDB0000172  HMDB0000491  HMDB0000687  HMDB0000695  HMDB0000883  HMDB0002166 |
| 827.0602089 | 10.25372887 | 1.90897E-10 | 3-hydroxyisobutyric aciduria | 7 | 215 226 344 490 506 | HMDB0000023  HMDB0000172  HMDB0000491  HMDB0000687  HMDB0000695  HMDB0000883  HMDB0002166 |
| 827.0602089 | 10.25372887 | 1.90897E-10 | Beta-Ketothiolase Deficiency | 7 | 215 226 344 490 506 | HMDB0000023  HMDB0000172  HMDB0000491  HMDB0000687  HMDB0000695  HMDB0000883  HMDB0002166 |
| 827.0602089 | 10.25372887 | 1.90897E-10 | Isobutyryl-coa dehydrogenase deficiency | 7 | 215 226 344 490 506 | HMDB0000023  HMDB0000172  HMDB0000491  HMDB0000687  HMDB0000695  HMDB0000883  HMDB0002166 |
| 827.0602089 | 10.25372887 | 1.90897E-10 | Isovaleric Aciduria | 7 | 215 226 344 490 506 | HMDB0000023  HMDB0000172  HMDB0000491  HMDB0000687  HMDB0000695  HMDB0000883  HMDB0002166 |
| 827.0602089 | 10.25372887 | 1.90897E-10 | Isovaleric acidemia | 7 | 215 226 344 490 506 | HMDB0000023  HMDB0000172  HMDB0000491  HMDB0000687  HMDB0000695  HMDB0000883  HMDB0002166 |
| 827.0602089 | 10.25372887 | 1.90897E-10 | Maple Syrup Urine Disease | 7 | 215 226 344 490 506 | HMDB0000023  HMDB0000172  HMDB0000491  HMDB0000687  HMDB0000695  HMDB0000883  HMDB0002166 |
| 827.0602089 | 10.25372887 | 1.90897E-10 | Methylmalonate Semialdehyde Dehydrogenase Deficiency | 7 | 215 226 344 490 506 | HMDB0000023  HMDB0000172  HMDB0000491  HMDB0000687  HMDB0000695  HMDB0000883  HMDB0002166 |
| 827.0602089 | 10.25372887 | 1.90897E-10 | Propionic Acidemia | 7 | 215 226 344 490 506 | HMDB0000023  HMDB0000172  HMDB0000491  HMDB0000687  HMDB0000695  HMDB0000883  HMDB0002166 |
| 827.0602089 | 10.25372887 | 1.90897E-10 | Valine Leucine and Isoleucine Degradation | 7 | 215 226 344 490 506 | HMDB0000023  HMDB0000172  HMDB0000491  HMDB0000687  HMDB0000695  HMDB0000883  HMDB0002166 |
| 608.5556453 | 7.054608497 | 2.57957E-07 | 2-aminoadipic 2-oxoadipic aciduria | 5 | 473 721 740 983 | HMDB0000182  HMDB0000225  HMDB0000716  HMDB0001263  HMDB0003405 |
| 608.5556453 | 7.054608497 | 2.57957E-07 | Hyperlysinemia I Familial | 5 | 473 721 740 983 | HMDB0000182  HMDB0000225  HMDB0000716  HMDB0001263  HMDB0003405 |
| 608.5556453 | 7.054608497 | 2.57957E-07 | Hyperlysinemia II or Saccharopinuria | 5 | 473 721 740 983 | HMDB0000182  HMDB0000225  HMDB0000716  HMDB0001263  HMDB0003405 |
| 608.5556453 | 7.054608497 | 2.57957E-07 | Pyridoxine dependency with seizures | 5 | 473 721 740 983 | HMDB0000182  HMDB0000225  HMDB0000716  HMDB0001263  HMDB0003405 |
| 608.5556453 | 7.054608497 | 2.57957E-07 | Saccharopinuria Hyperlysinemia II | 5 | 473 721 740 983 | HMDB0000182  HMDB0000225  HMDB0000716  HMDB0001263  HMDB0003405 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Amikacin Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Chloramphenicol Action Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Clindamycin Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Clomocycline Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Demeclocycline Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Doxycycline Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Erythromycin Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Gentamicin Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Josamycin Action Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Kanamycin Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Lincomycin Action Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Lymecycline Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Methacycline Action Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Minocycline Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Neomycin Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Netilmicin Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Oxytetracycline Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Paromomycin Action Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Rolitetracycline Action Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Roxithromycin Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Spectinomycin Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Streptomycin Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Tetracycline Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Tigecycline Action Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 606.86437 | 7.5150756 | 9.33914E-08 | Tobramycin Action Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 577.5299119 | 7.256291613 | 1.66053E-07 | Arbekacin Action Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 577.5299119 | 7.256291613 | 1.66053E-07 | Azithromycin Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 577.5299119 | 7.256291613 | 1.66053E-07 | Clarithromycin Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 577.5299119 | 7.256291613 | 1.66053E-07 | Telithromycin Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 577.5299119 | 7.256291613 | 1.66053E-07 | Troleandomycin Action Pathway | 5 | 344 362 506 522 | HMDB0000167  HMDB0000168  HMDB0000172  HMDB0000687  HMDB0000883 |
| 566.2013188 | 6.637861909 | 6.7079E-07 | Lysine Degradation | 5 | 473 721 740 983 | HMDB0000182  HMDB0000225  HMDB0000716  HMDB0001263  HMDB0003405 |
| 509.8205521 | 7.091948012 | 2.41458E-07 | Tryptophan Metabolism | 9 | 592 999 1075 1294 1695 2028 2513 3310 | HMDB0000197  HMDB0000763  HMDB0000929  HMDB0001123  HMDB0004073  HMDB0004077  HMDB0004083  HMDB0004086 |
| 507.1681215 | 5.524222572 | 8.68013E-06 | Glutaric Aciduria Type I | 6 | 473 721 740 983 3435 | HMDB0000182  HMDB0000225  HMDB0000716  HMDB0001263  HMDB0003405 |
| 427.3014386 | 4.69903907 | 5.62789E-05 | Methylenetetrahydrofolate Reductase Deficiency | 5 | 215 344 362 1293 3756 | HMDB0000043  HMDB0000092  HMDB0000719 |
| 407.177883 | 4.296911545 | 0.000141524 | Betaine Metabolism | 3 | 215 344 3756 | HMDB0000043  HMDB0000092 |
| 372.94126 | 4.9584832 | 3.10849E-05 | Cystathionine Beta-Synthase Deficiency | 4 | 215 344 362 3756 | HMDB0000043  HMDB0000092  HMDB0000719 |
| 372.94126 | 4.9584832 | 3.10849E-05 | Glycine N-methyltransferase Deficiency | 4 | 215 344 362 3756 | HMDB0000043  HMDB0000092  HMDB0000719 |
| 372.94126 | 4.9584832 | 3.10849E-05 | Homocystinuria-megaloblastic anemia due to defect in cobalamin metabolism | 4 | 215 344 362 3756 | HMDB0000043  HMDB0000092  HMDB0000719 |
| 372.94126 | 4.9584832 | 3.10849E-05 | Hypermethioninemia | 4 | 215 344 362 3756 | HMDB0000043  HMDB0000092  HMDB0000719 |
| 372.94126 | 4.9584832 | 3.10849E-05 | Methionine Adenosyltransferase Deficiency | 4 | 215 344 362 3756 | HMDB0000043  HMDB0000092  HMDB0000719 |
| 372.94126 | 4.9584832 | 3.10849E-05 | Methionine Metabolism | 4 | 215 344 362 3756 | HMDB0000043  HMDB0000092  HMDB0000719 |
| 372.94126 | 4.9584832 | 3.10849E-05 | S-Adenosylhomocysteine Hydrolase Deficiency | 4 | 215 344 362 3756 | HMDB0000043  HMDB0000092  HMDB0000719 |
| 354.5800761 | 4.093274253 | 0.000224493 | Glycine and Serine Metabolism | 5 | 215 344 362 526 2115 | HMDB0000043  HMDB0000092  HMDB0000167  HMDB0000214 |
| 348.1722007 | 3.716543427 | 0.000528545 | Canavan Disease | 4 | 522 534 1293 | HMDB0000168  HMDB0000191  HMDB0000812  HMDB0006483 |
| 348.1722007 | 3.716543427 | 0.000528545 | Hypoacetylaspartia | 4 | 522 534 1293 | HMDB0000168  HMDB0000191  HMDB0000812  HMDB0006483 |
| 331.5949736 | 3.554061318 | 0.000765523 | Aspartate Metabolism | 4 | 522 534 1293 | HMDB0000168  HMDB0000191  HMDB0006483 |
| 308.9620164 | 4.169405331 | 0.000189104 | The oncogenic action of 2-hydroxyglutarate | 4 | 548 766 | HMDB0000156  HMDB0000606  HMDB0000694  HMDB0059655 |
| 295.2549989 | 3.997605969 | 0.000278771 | Sarcosine oncometabolite pathway | 2 | 215 344 | HMDB0000043  HMDB0000092 |
| 293.5754475 | 3.539817141 | 0.000782386 | Biotin Metabolism | 2 | 740 | HMDB0000182  HMDB0003405 |
| 293.5754475 | 3.539817141 | 0.000782386 | Biotinidase Deficiency | 2 | 740 | HMDB0000182  HMDB0003405 |
| 293.5754475 | 3.539817141 | 0.000782386 | Multiple carboxylase deficiency | 2 | 740 | HMDB0000182  HMDB0003405 |
| 276.7865681 | 3.37440371 | 0.001140913 | Malate-Aspartate Shuttle | 2 | 534 548 | HMDB0000191  HMDB0000744 |
| 238.2026646 | 3.369659926 | 0.001149264 | Glutaminolysis and Cancer | 3 | 506 534 548 | HMDB0000156  HMDB0000191  HMDB0000687 |
| 223.4364272 | 2.431895244 | 0.009380499 | Ammonia Recycling | 3 | 522 534 2115 | HMDB0000168  HMDB0000191  HMDB0012210 |
| 219.3383298 | 2.834073507 | 0.003888278 | The oncogenic action of Fumarate | 3 | 548 766 | HMDB0000156  HMDB0000744  HMDB0059655 |
| 204.426349 | 3.228079384 | 0.001575089 | Malonic Aciduria | 2 | 226 344 | HMDB0000008  HMDB0000883 |
| 204.426349 | 3.228079384 | 0.001575089 | Malonyl-coa decarboxylase deficiency | 2 | 226 344 | HMDB0000008  HMDB0000883 |
| 204.426349 | 3.228079384 | 0.001575089 | Propanoate Metabolism | 2 | 226 344 | HMDB0000008  HMDB0000883 |
| 181.2841414 | 2.279090369 | 0.0131124 | Mycophenolic Acid Metabolism Pathway | 2 | 506 721 | HMDB0060650  HMDB0061156 |
| 179.2126099 | 2.480279127 | 0.008420286 | Argininemia | 2 | 526 534 | HMDB0000191  HMDB0000214 |
| 179.2126099 | 2.480279127 | 0.008420286 | Argininosuccinic Aciduria | 2 | 526 534 | HMDB0000191  HMDB0000214 |
| 179.2126099 | 2.480279127 | 0.008420286 | Carbamoyl Phosphate Synthetase Deficiency | 2 | 526 534 | HMDB0000191  HMDB0000214 |
| 179.2126099 | 2.480279127 | 0.008420286 | Citrullinemia Type I | 2 | 526 534 | HMDB0000191  HMDB0000214 |
| 179.2126099 | 2.480279127 | 0.008420286 | Ornithine Transcarbamylase Deficiency | 2 | 526 534 | HMDB0000191  HMDB0000214 |
| 179.2126099 | 2.480279127 | 0.008420286 | Urea Cycle | 2 | 526 534 | HMDB0000191  HMDB0000214 |
| 179.2033006 | 2.393233535 | 0.010218989 | Carnitine Synthesis | 2 | 740 | HMDB0000182  HMDB0003405 |
| 173.9923595 | 2.524617635 | 0.007762563 | 3-Phosphoglycerate dehydrogenase deficiency | 3 | 215 344 2115 | HMDB0000043  HMDB0000092 |
| 173.9923595 | 2.524617635 | 0.007762563 | Dihydropyrimidine Dehydrogenase Deficiency | 3 | 215 344 2115 | HMDB0000043  HMDB0000092 |
| 173.9923595 | 2.524617635 | 0.007762563 | Dimethylglycine Dehydrogenase Deficiency | 3 | 215 344 2115 | HMDB0000043  HMDB0000092 |
| 173.9923595 | 2.524617635 | 0.007762563 | Hyperglycinemia non-ketotic | 3 | 215 344 2115 | HMDB0000043  HMDB0000092 |
| 173.9923595 | 2.524617635 | 0.007762563 | Non Ketotic Hyperglycinemia | 3 | 215 344 2115 | HMDB0000043  HMDB0000092 |
| 173.9923595 | 2.524617635 | 0.007762563 | Sarcosinemia | 3 | 215 344 2115 | HMDB0000043  HMDB0000092 |
| 171.3442082 | 1.991355132 | 0.023230122 | Aminocaproic Acid Pathway | 1 | 506 | HMDB0001901 |
| 171.3442082 | 1.991355132 | 0.023230122 | Leucine Stimulation on Insulin Signaling | 1 | 506 | HMDB0000687 |
| 158.3765722 | 1.790533482 | 0.034986209 | Beta Ureidopropionase Deficiency | 3 | 215 522 3079 | HMDB0000026  HMDB0003911 |
| 158.3765722 | 1.790533482 | 0.034986209 | Dihydropyrimidinase Deficiency | 3 | 215 522 3079 | HMDB0000026  HMDB0003911 |
| 158.3765722 | 1.790533482 | 0.034986209 | Mitochondrial Neurogastrointestinal Encephalopathy | 3 | 215 522 3079 | HMDB0000026  HMDB0003911 |
| 158.3765722 | 1.790533482 | 0.034986209 | Pyrimidine Metabolism | 3 | 215 522 3079 | HMDB0000026  HMDB0003911 |
| 158.3765722 | 1.790533482 | 0.034986209 | UMP Synthase Deficiency Orotic Aciduria | 3 | 215 522 3079 | HMDB0000026  HMDB0003911 |
| 154.7183257 | 2.369121032 | 0.010729416 | Mercaptopurine Pathway | 5 | 534 561 3756 4207 | HMDB0000034  HMDB0000050  HMDB0000085  HMDB0000191  HMDB0060791 |
| 154.7183257 | 2.369121032 | 0.010729416 | Thioguanine Pathway | 5 | 534 561 3756 4207 | HMDB0000034  HMDB0000050  HMDB0000085  HMDB0000191  HMDB0060791 |
| 153.4040565 | 2.09334326 | 0.019025453 | AICA-Ribosiduria | 4 | 534 561 3756 | HMDB0000034  HMDB0000050  HMDB0000085  HMDB0000191 |
| 153.4040565 | 2.09334326 | 0.019025453 | Adenine phosphoribosyltransferase deficiency | 4 | 534 561 3756 | HMDB0000034  HMDB0000050  HMDB0000085  HMDB0000191 |
| 153.4040565 | 2.09334326 | 0.019025453 | Adenosine Deaminase Deficiency | 4 | 534 561 3756 | HMDB0000034  HMDB0000050  HMDB0000085  HMDB0000191 |
| 153.4040565 | 2.09334326 | 0.019025453 | Adenylosuccinate Lyase Deficiency | 4 | 534 561 3756 | HMDB0000034  HMDB0000050  HMDB0000085  HMDB0000191 |
| 153.4040565 | 2.09334326 | 0.019025453 | Gout or Kelley-Seegmiller Syndrome | 4 | 534 561 3756 | HMDB0000034  HMDB0000050  HMDB0000085  HMDB0000191 |
| 153.4040565 | 2.09334326 | 0.019025453 | Lesch-Nyhan Syndrome | 4 | 534 561 3756 | HMDB0000034  HMDB0000050  HMDB0000085  HMDB0000191 |
| 153.4040565 | 2.09334326 | 0.019025453 | Mitochondrial DNA depletion syndrome | 4 | 534 561 3756 | HMDB0000034  HMDB0000050  HMDB0000085  HMDB0000191 |
| 153.4040565 | 2.09334326 | 0.019025453 | Molybdenum Cofactor Deficiency | 4 | 534 561 3756 | HMDB0000034  HMDB0000050  HMDB0000085  HMDB0000191 |
| 153.4040565 | 2.09334326 | 0.019025453 | Myoadenylate deaminase deficiency | 4 | 534 561 3756 | HMDB0000034  HMDB0000050  HMDB0000085  HMDB0000191 |
| 153.4040565 | 2.09334326 | 0.019025453 | Purine Nucleoside Phosphorylase Deficiency | 4 | 534 561 3756 | HMDB0000034  HMDB0000050  HMDB0000085  HMDB0000191 |
| 153.4040565 | 2.09334326 | 0.019025453 | Xanthine Dehydrogenase Deficiency | 4 | 534 561 3756 | HMDB0000034  HMDB0000050  HMDB0000085  HMDB0000191 |
| 153.4040565 | 2.09334326 | 0.019025453 | Xanthinuria | 4 | 534 561 3756 | HMDB0000034  HMDB0000050  HMDB0000085  HMDB0000191 |
| 153.4040565 | 2.09334326 | 0.019025453 | XanthinuriaI | 4 | 534 561 3756 | HMDB0000034  HMDB0000050  HMDB0000085  HMDB0000191 |
| 151.4460667 | 2.033047783 | 0.021789835 | Threonine and 2-Oxobutanoate Degradation | 1 | 362 | HMDB0000167 |
| 150.3024006 | 2.296714118 | 0.012633342 | Azathioprine Pathway | 5 | 534 561 3756 4207 | HMDB0000034  HMDB0000050  HMDB0000085  HMDB0000191  HMDB0060791 |
| 150.1629127 | 1.997491916 | 0.023136325 | 2-Hydroxyglutric Aciduria | 2 | 215 534 | HMDB0000112  HMDB0000191 |
| 150.1629127 | 1.997491916 | 0.023136325 | 4-Hydroxybutyric Aciduria Succinic Semialdehyde Dehydrogenase Deficiency | 2 | 215 534 | HMDB0000112  HMDB0000191 |
| 150.1629127 | 1.997491916 | 0.023136325 | Glutamate Metabolism | 2 | 215 534 | HMDB0000112  HMDB0000191 |
| 150.1629127 | 1.997491916 | 0.023136325 | Homocarnosinosis | 2 | 215 534 | HMDB0000112  HMDB0000191 |
| 150.1629127 | 1.997491916 | 0.023136325 | Hyperinsulinism-Hyperammonemia Syndrome | 2 | 215 534 | HMDB0000112  HMDB0000191 |
| 150.1629127 | 1.997491916 | 0.023136325 | Succinic semialdehyde dehydrogenase deficiency | 2 | 215 534 | HMDB0000112  HMDB0000191 |
| 148.3102905 | 2.02046685 | 0.022359532 | Purine Metabolism | 4 | 534 561 3756 | HMDB0000034  HMDB0000050  HMDB0000085  HMDB0000191 |
| 145.3246516 | 2.127288723 | 0.018352412 | Beta-Alanine Metabolism | 2 | 522 534 | HMDB0000026  HMDB0000191 |
| 145.3246516 | 2.127288723 | 0.018352412 | Carnosinuria or carnosinemia | 2 | 522 534 | HMDB0000026  HMDB0000191 |
| 145.3246516 | 2.127288723 | 0.018352412 | GABA-Transaminase Deficiency | 2 | 522 534 | HMDB0000026  HMDB0000191 |
| 145.3246516 | 2.127288723 | 0.018352412 | Ureidopropionase Deficiency | 2 | 522 534 | HMDB0000026  HMDB0000191 |
| 129.2333779 | 1.732037525 | 0.039914638 | The oncogenic action of Succinate | 2 | 548 766 | HMDB0000156  HMDB0059655 |
| 127.6080507 | 1.990389575 | 0.023230122 | Ketone Body Metabolism | 1 | 226 | HMDB0000011 |
| 127.6080507 | 1.990389575 | 0.023230122 | Succinyl CoA 3-ketoacid CoA transferase deficiency | 1 | 226 | HMDB0000011 |
| 125.6471327 | 1.692905677 | 0.043551893 | Fatty Acid Biosynthesis | 3 | 226 490 3435 | HMDB0000357  HMDB0010717 |
| 116.5644777 | 1.49510747 | 0.067505426 | Spermidine and Spermine Biosynthesis | 1 | 526 | HMDB0000214 |
| 114.1847236 | 1.791248985 | 0.034986209 | Arginine Glycine Amidinotransferase Deficiency | 2 | 526 534 | HMDB0000191  HMDB0000214 |
| 114.1847236 | 1.791248985 | 0.034986209 | Arginine and Proline Metabolism | 2 | 526 534 | HMDB0000191  HMDB0000214 |
| 114.1847236 | 1.791248985 | 0.034986209 | Creatine deficiency or guanidinoacetate methyltransferase deficiency | 2 | 526 534 | HMDB0000191  HMDB0000214 |
| 114.1847236 | 1.791248985 | 0.034986209 | Guanidinoacetate Methyltransferase Deficiency | 2 | 526 534 | HMDB0000191  HMDB0000214 |
| 114.1847236 | 1.791248985 | 0.034986209 | Hyperornithinemia with gyrate atrophy | 2 | 526 534 | HMDB0000191  HMDB0000214 |
| 114.1847236 | 1.791248985 | 0.034986209 | Hyperornithinemia-hyperammonemia-homocitrullinuria | 2 | 526 534 | HMDB0000191  HMDB0000214 |
| 114.1847236 | 1.791248985 | 0.034986209 | Hyperprolinemia | 2 | 526 534 | HMDB0000191  HMDB0000214 |
| 114.1847236 | 1.791248985 | 0.034986209 | HyperprolinemiaI | 2 | 526 534 | HMDB0000191  HMDB0000214 |
| 114.1847236 | 1.791248985 | 0.034986209 | L-arginine glycine amidinotransferase deficiency | 2 | 526 534 | HMDB0000191  HMDB0000214 |
| 114.1847236 | 1.791248985 | 0.034986209 | Ornithine Aminotransferase Deficiency | 2 | 526 534 | HMDB0000191  HMDB0000214 |
| 114.1847236 | 1.791248985 | 0.034986209 | Prolidase Deficiency | 2 | 526 534 | HMDB0000191  HMDB0000214 |
| 114.1847236 | 1.791248985 | 0.034986209 | Prolinemia Type II | 2 | 526 534 | HMDB0000191  HMDB0000214 |
| 104.1656705 | 1.374883965 | 0.088532267 | D-Arginine and D-Ornithine Metabolism | 1 | 526 | HMDB0003374 |
| 99.31712624 | 1.316067756 | 0.100520084 | Benzocaine Pathway | 1 | 1079 | HMDB0004992 |
| 98.70060525 | 1.521036951 | 0.063970333 | Nicotinate and Nicotinamide Metabolism | 1 | 410 | HMDB0001488 |
| 92.8071419 | 1.466373261 | 0.071918537 | Zalcitabine Action Pathway | 1 | 2202 | HMDB0015078 |
| 92.42578199 | 1.243211693 | 0.117562799 | Transfer of Acetyl Groups into Mitochondria | 1 | 548 | HMDB0000156 |
| 89.09819785 | 1.246174988 | 0.117087713 | Folate Metabolism | 1 | 1293 | HMDB0003470 |
| 89.09819785 | 1.246174988 | 0.117087713 | Folate malabsorption hereditary | 1 | 1293 | HMDB0003470 |
| 89.09819785 | 1.246174988 | 0.117087713 | Methotrexate Pathway | 1 | 1293 | HMDB0003470 |
| 88.21213575 | 1.519703089 | 0.063970333 | D-glyceric acidura | 2 | 1219 3435 | HMDB0000126  HMDB0000220 |
| 88.21213575 | 1.519703089 | 0.063970333 | Familial lipoprotein lipase deficiency | 2 | 1219 3435 | HMDB0000126  HMDB0000220 |
| 88.21213575 | 1.519703089 | 0.063970333 | Glycerol Kinase Deficiency | 2 | 1219 3435 | HMDB0000126  HMDB0000220 |
| 88.21213575 | 1.519703089 | 0.063970333 | Glycerolipid Metabolism | 2 | 1219 3435 | HMDB0000126  HMDB0000220 |
| 77.28960609 | 1.089900705 | 0.147334432 | Glycerol Phosphate Shuttle | 1 | 1219 | HMDB0000126 |
| 77.28960609 | 1.089900705 | 0.147334432 | Mitochondrial Electron Transport Chain | 1 | 1219 | HMDB0000126 |
| 73.38018341 | 0.917925298 | 0.206811072 | Tyrosinemia | 2 | 534 1079 | HMDB0000159  HMDB0000191 |
| 71.29861049 | 1.008722183 | 0.172157625 | 2-ketoglutarate dehydrogenase complex deficiency | 1 | 548 | HMDB0000156 |
| 71.29861049 | 1.008722183 | 0.172157625 | Citric Acid Cycle | 1 | 548 | HMDB0000156 |
| 71.29861049 | 1.008722183 | 0.172157625 | Congenital lactic acidosis | 1 | 548 | HMDB0000156 |
| 71.29861049 | 1.008722183 | 0.172157625 | Fructose-16-diphosphatase deficiency | 1 | 548 | HMDB0000744 |
| 71.29861049 | 1.008722183 | 0.172157625 | Fumarase deficiency | 1 | 548 | HMDB0000156 |
| 71.29861049 | 1.008722183 | 0.172157625 | Gluconeogenesis | 1 | 548 | HMDB0000744 |
| 71.29861049 | 1.008722183 | 0.172157625 | Glycogen Storage Disease Type 1A or Von Gierke Disease | 1 | 548 | HMDB0000744 |
| 71.29861049 | 1.008722183 | 0.172157625 | Mitochondrial complex II deficiency | 1 | 548 | HMDB0000156 |
| 71.29861049 | 1.008722183 | 0.172157625 | Phosphoenolpyruvate carboxykinase deficiency | 1 | 548 | HMDB0000744 |
| 71.29861049 | 1.008722183 | 0.172157625 | Pyruvate dehydrogenase deficiency | 1 | 548 | HMDB0000156 |
| 71.29861049 | 1.008722183 | 0.172157625 | Triosephosphate isomerase | 1 | 548 | HMDB0000744 |
| 68.47735206 | 0.950670487 | 0.193126138 | Phenylalanine and Tyrosine Metabolism | 1 | 1079 | HMDB0000159 |
| 68.47735206 | 0.950670487 | 0.193126138 | Phenylketonuria | 1 | 1079 | HMDB0000159 |
| 68.0491199 | 0.968161737 | 0.187240245 | Leigh Syndrome | 1 | 548 | HMDB0000156 |
| 68.0491199 | 0.968161737 | 0.187240245 | Pyruvate Decarboxylase E1 Component Deficiency | 1 | 548 | HMDB0000156 |
| 68.0491199 | 0.968161737 | 0.187240245 | Pyruvate Dehydrogenase Complex Deficiency | 1 | 548 | HMDB0000156 |
| 68.0491199 | 0.968161737 | 0.187240245 | Pyruvate kinase deficiency | 1 | 548 | HMDB0000156 |
| 65.29086232 | 0.931966615 | 0.20115853 | Pyruvate Metabolism | 1 | 548 | HMDB0000156 |
| 63.6736347 | 0.951274007 | 0.193126138 | Hypophosphatasia | 1 | 1486 | HMDB0000017 |
| 63.6736347 | 0.951274007 | 0.193126138 | Vitamin B6 Metabolism | 1 | 1486 | HMDB0000017 |
| 62.55990175 | 0.842495833 | 0.242133228 | Glucose-6-phosphate dehydrogenase deficiency | 1 | 798 | HMDB0000283 |
| 62.55990175 | 0.842495833 | 0.242133228 | Pentose Phosphate Pathway | 1 | 798 | HMDB0000283 |
| 62.55990175 | 0.842495833 | 0.242133228 | Ribose-5-phosphate isomerase deficiency | 1 | 798 | HMDB0000283 |
| 62.55990175 | 0.842495833 | 0.242133228 | Transaldolase deficiency | 1 | 798 | HMDB0000283 |
| 62.04903687 | 0.893284628 | 0.218381039 | Phospholipid Biosynthesis | 1 | 1219 | HMDB0000126 |
| 60.92632858 | 0.869812628 | 0.229979802 | Primary Hyperoxaluria | 1 | 548 | HMDB0000156 |
| 59.87523419 | 0.844020111 | 0.242133228 | Valproic Acid Metabolism Pathway | 1 | 645 | HMDB0060682 |
| 56.47902602 | 0.795234908 | 0.268751056 | Glycogenosis | 1 | 548 | HMDB0000744 |
| 55.93997338 | 1.36770446 | 0.089754452 | Zidovudine Action Pathway | 1 | 3756 | HMDB0014638 |
| 55.41659506 | 0.774106644 | 0.281513483 | Warburg Effect | 1 | 548 | HMDB0000156 |
| 52.46320188 | 0.643177297 | 0.365737542 | Disulfiram Pathway | 1 | 534 | HMDB0000191 |
| 52.41711061 | 0.654667239 | 0.356960901 | Alkaptonuria | 1 | 534 | HMDB0000191 |
| 52.41711061 | 0.654667239 | 0.356960901 | Dopamine beta-hydroxylase deficiency | 1 | 534 | HMDB0000191 |
| 52.41711061 | 0.654667239 | 0.356960901 | Hawkinsinuria | 1 | 534 | HMDB0000191 |
| 52.41711061 | 0.654667239 | 0.356960901 | Monoamine oxidase-a deficiency | 1 | 534 | HMDB0000191 |
| 52.41711061 | 0.654667239 | 0.356960901 | Tyrosine Metabolism | 1 | 534 | HMDB0000191 |
| 48.57732351 | 0.74536795 | 0.293297454 | Felbamate Metabolism Pathway | 1 | 1695 | HMDB0060400 |
| 46.48386401 | 1.332094498 | 0.097150338 | Plasmalogen Synthesis | 1 | 4220 | HMDB0000827 |
| 37.20167053 | 0.92856997 | 0.202269755 | Selenoamino Acid Metabolism | 1 | 3756 | HMDB0000050 |
| 36.36606167 | 1.051722873 | 0.160091666 | Mitochondrial Beta-Oxidation of Long Chain Saturated Fatty Acids | 1 | 4220 | HMDB0000827 |
| 33.60310407 | 0.827878779 | 0.249854839 | Long-chain-3-hydroxyacyl-coa dehydrogenase deficiency | 1 | 3435 | HMDB0000220 |
| 30.31782951 | 0.749697321 | 0.291872576 | Carnitine palmitoyl transferase deficiency | 1 | 3435 | HMDB0000220 |
| 30.31782951 | 0.749697321 | 0.291872576 | Ethylmalonic Encephalopathy | 1 | 3435 | HMDB0000220 |
| 30.31782951 | 0.749697321 | 0.291872576 | Fatty Acid Elongation In Mitochondria | 1 | 3435 | HMDB0000220 |
| 30.31782951 | 0.749697321 | 0.291872576 | Fatty Acid Metabolism | 1 | 3435 | HMDB0000220 |
| 30.31782951 | 0.749697321 | 0.291872576 | Long chain acyl-CoA dehydrogenase deficiency | 1 | 3435 | HMDB0000220 |
| 30.31782951 | 0.749697321 | 0.291872576 | Medium chain acyl-coa dehydrogenase deficiency | 1 | 3435 | HMDB0000220 |
| 30.31782951 | 0.749697321 | 0.291872576 | Short Chain Acyl CoA Dehydrogenase Deficiency | 1 | 3435 | HMDB0000220 |
| 30.31782951 | 0.749697321 | 0.291872576 | Trifunctional protein deficiency | 1 | 3435 | HMDB0000220 |
| 30.31782951 | 0.749697321 | 0.291872576 | Very-long-chain acyl coa dehydrogenase deficiency | 1 | 3435 | HMDB0000220 |
| 29.56813219 | 0.744715678 | 0.293297454 | Insulin Signalling | 1 | 3756 | HMDB0000050 |
| 22.78978613 | 0.746960113 | 0.293071001 | Hydroxylase deficiency | 3 | 3435 8568 9483 | HMDB0000036  HMDB0000138  HMDB0000220 |
| 22.54872191 | 1.162389104 | 0.129093544 | Acetylsalicylic Acid Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Antipyrine Action Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Antrafenine Action Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Bromfenac Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Carprofen Action Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Celecoxib Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Diclofenac Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Diflunisal Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Etoricoxib Action Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Fenoprofen Action Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Flurbiprofen Action Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Indomethacin Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Ketoprofen Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Ketorolac Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Leukotriene C4 Synthesis Deficiency | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Lornoxicam Action Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Lumiracoxib Action Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Magnesium salicylate Action Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Mefanamic Acid Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Nabumetone Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Nepafenac Action Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Oxaprozin Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Phenylbutazone Action Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Piroxicam Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Rofecoxib Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Salicylate-sodium Action Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Salsalate Action Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Sulindac Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Suprofen Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Tenoxicam Action Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Tiaprofenic Acid Action Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Tolmetin Action Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Trisalicylate-choline Action Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.54872191 | 1.162389104 | 0.129093544 | Valdecoxib Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 22.11193707 | 1.106374541 | 0.142895931 | Cerebrotendinous Xanthomatosis | 3 | 3435 8568 9483 | HMDB0000036  HMDB0000138  HMDB0000220 |
| 22.11193707 | 1.106374541 | 0.142895931 | Congenital Bile Acid Synthesis Defect Type | 3 | 3435 8568 9483 | HMDB0000036  HMDB0000138  HMDB0000220 |
| 22.11193707 | 1.106374541 | 0.142895931 | Congenital Bile Acid Synthesis Defect TypeI | 3 | 3435 8568 9483 | HMDB0000036  HMDB0000138  HMDB0000220 |
| 22.11193707 | 1.106374541 | 0.142895931 | Familial Hypercholanemia | 3 | 3435 8568 9483 | HMDB0000036  HMDB0000138  HMDB0000220 |
| 22.11193707 | 1.106374541 | 0.142895931 | Zellweger Syndrome | 3 | 3435 8568 9483 | HMDB0000036  HMDB0000138  HMDB0000220 |
| 21.95777522 | 1.131937086 | 0.13640355 | Acetaminophen Action Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 21.95777522 | 1.131937086 | 0.13640355 | Arachidonic Acid Metabolism | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 21.95777522 | 1.131937086 | 0.13640355 | Etodolac Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 21.95777522 | 1.131937086 | 0.13640355 | Ibuprofen Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 21.95777522 | 1.131937086 | 0.13640355 | Meloxicam Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 21.95777522 | 1.131937086 | 0.13640355 | Salicylic Acid Action Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 21.88727716 | 1.062680283 | 0.156482836 | Bile Acid Biosynthesis | 3 | 3435 8568 9483 | HMDB0000036  HMDB0000138  HMDB0000220 |
| 21.40073399 | 1.103138821 | 0.143611702 | Naproxen Pathway | 4 | 6153 | HMDB0001139  HMDB0004684  HMDB0004694  HMDB0011137 |
| 6.726414512 | 1.229675391 | 0.120949716 | Argatroban Pathway | 1 | 9355 | HMDB0014423 |
| 0 | 0 | 1 | 11-beta-hydroxylase deficiency | 0 |  |  |
| 0 | 0 | 1 | 17-Beta Hydroxysteroid Dehydrogenase III Deficiency | 0 |  |  |
| 0 | 0 | 1 | 17-alpha-hydroxylase deficiency | 0 |  |  |
| 0 | 0 | 1 | 3-Beta-Hydroxysteroid Dehydrogenase Deficiency | 0 |  |  |
| 0 | 0 | 1 | 3-Methylthiofentanyl Action Pathway | 0 |  |  |
| 0 | 0 | 1 | 5-Oxoprolinuria | 0 |  |  |
| 0 | 0 | 1 | 5-oxoprolinase deficiency | 0 |  |  |
| 0 | 0 | 1 | Acebutolol Pathway | 0 |  |  |
| 0 | 0 | 1 | Acetaminophen Metabolism Pathway | 0 |  |  |
| 0 | 0 | 1 | Acute Intermittent Porphyria | 0 |  |  |
| 0 | 0 | 1 | Adrenal Hyperplasia or Congenital Adrenal Hyperplasia | 0 |  |  |
| 0 | 0 | 1 | Adrenoleukodystrophy X-linked | 0 |  |  |
| 0 | 0 | 1 | Alanine Metabolism | 0 |  |  |
| 0 | 0 | 1 | Alendronate pathway | 0 |  |  |
| 0 | 0 | 1 | Alfentanil Pathway | 0 |  |  |
| 0 | 0 | 1 | Alimemazine H1-Antihistamine Action | 0 |  |  |
| 0 | 0 | 1 | Alpha Linolenic Acid and Linoleic Acid Metabolism | 0 |  |  |
| 0 | 0 | 1 | Alprenolol Pathway | 0 |  |  |
| 0 | 0 | 1 | Alvimopan Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Amiloride Pathway | 0 |  |  |
| 0 | 0 | 1 | Amino Sugar Metabolism | 0 |  |  |
| 0 | 0 | 1 | Androgen and Estrogen Metabolism | 0 |  |  |
| 0 | 0 | 1 | Androstenedione Metabolism | 0 |  |  |
| 0 | 0 | 1 | Anileridine Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Apparent mineralocorticoid excess syndrome | 0 |  |  |
| 0 | 0 | 1 | Aromatase deficiency | 0 |  |  |
| 0 | 0 | 1 | Aromatic L-Aminoacid Decarboxylase Deficiency | 0 |  |  |
| 0 | 0 | 1 | Artemether Metabolism Pathway | 0 |  |  |
| 0 | 0 | 1 | Atenolol Pathway | 0 |  |  |
| 0 | 0 | 1 | Atorvastatin Pathway | 0 |  |  |
| 0 | 0 | 1 | Bendroflumethiazide Pathway | 0 |  |  |
| 0 | 0 | 1 | Beta Oxidation of Very Long Chain Fatty Acids | 0 |  |  |
| 0 | 0 | 1 | Beta-mercaptolactate-cysteine disulfiduria | 0 |  |  |
| 0 | 0 | 1 | Betahistine H1-Antihistamine Action | 0 |  |  |
| 0 | 0 | 1 | Betazole Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Bisoprolol Pathway | 0 |  |  |
| 0 | 0 | 1 | Blue diaper syndrome | 0 |  |  |
| 0 | 0 | 1 | Bumetanide Pathway | 0 |  |  |
| 0 | 0 | 1 | Bupivacaine Pathway | 0 |  |  |
| 0 | 0 | 1 | Buprenorphine Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Butyrate Metabolism | 0 |  |  |
| 0 | 0 | 1 | CHILD Syndrome | 0 |  |  |
| 0 | 0 | 1 | Caffeine Metabolism | 0 |  |  |
| 0 | 0 | 1 | Captopril Pathway | 0 |  |  |
| 0 | 0 | 1 | Carbamazepine Metabolism Pathway | 0 |  |  |
| 0 | 0 | 1 | Cardiolipin Biosynthesis | 0 |  |  |
| 0 | 0 | 1 | Carfentanil Pathway | 0 |  |  |
| 0 | 0 | 1 | Carnitine-acylcarnitine translocase deficiency | 0 |  |  |
| 0 | 0 | 1 | Catecholamine Biosynthesis | 0 |  |  |
| 0 | 0 | 1 | Cerivastatin Pathway | 0 |  |  |
| 0 | 0 | 1 | Chloroprocaine Pathway | 0 |  |  |
| 0 | 0 | 1 | Chlorothiazide Pathway | 0 |  |  |
| 0 | 0 | 1 | Chlorthalidone Pathway | 0 |  |  |
| 0 | 0 | 1 | Cholesteryl ester storage disease | 0 |  |  |
| 0 | 0 | 1 | Chondrodysplasia Punctata II X Linked Dominant | 0 |  |  |
| 0 | 0 | 1 | Cimetidine Pathway | 0 |  |  |
| 0 | 0 | 1 | Citalopram Pathway | 0 |  |  |
| 0 | 0 | 1 | Cocaine Pathway | 0 |  |  |
| 0 | 0 | 1 | Codeine Pathway | 0 |  |  |
| 0 | 0 | 1 | Congenital Erythropoietic Porphyria or Gunther Disease | 0 |  |  |
| 0 | 0 | 1 | Congenital Lipoid Adrenal Hyperplasia or Lipoid CAH | 0 |  |  |
| 0 | 0 | 1 | Congenital disorder of glycosylation CDG-IId | 0 |  |  |
| 0 | 0 | 1 | Corticosterone methyl oxidase deficiency | 0 |  |  |
| 0 | 0 | 1 | Corticotropin Activation of Cortisol Production | 0 |  |  |
| 0 | 0 | 1 | Cyclophosphamide Pathway | 0 |  |  |
| 0 | 0 | 1 | Cyclothiazide Pathway | 0 |  |  |
| 0 | 0 | 1 | Cysteine Metabolism | 0 |  |  |
| 0 | 0 | 1 | Cystinosis ocular nonnephropathic | 0 |  |  |
| 0 | 0 | 1 | Cystinuria | 0 |  |  |
| 0 | 0 | 1 | De Novo Triacylglycerol Biosynthesis | 0 |  |  |
| 0 | 0 | 1 | Desipramine Pathway | 0 |  |  |
| 0 | 0 | 1 | Desmosterolosis | 0 |  |  |
| 0 | 0 | 1 | Dezocine Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Dibucaine Pathway | 0 |  |  |
| 0 | 0 | 1 | Dihydromorphine Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Dimethylthiambutene Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Diphenoxylate Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Dopa-responsive dystonia | 0 |  |  |
| 0 | 0 | 1 | Dopamine Activation of Neurological Reward System | 0 |  |  |
| 0 | 0 | 1 | Doxepin H1-Antihistamine Action | 0 |  |  |
| 0 | 0 | 1 | Doxepin Metabolism Pathway | 0 |  |  |
| 0 | 0 | 1 | Emedastine H1-Antihistamine Action | 0 |  |  |
| 0 | 0 | 1 | Enalapril Metabolism Pathway | 0 |  |  |
| 0 | 0 | 1 | Enalapril Pathway | 0 |  |  |
| 0 | 0 | 1 | Eplerenone Pathway | 0 |  |  |
| 0 | 0 | 1 | Escitalopram Pathway | 0 |  |  |
| 0 | 0 | 1 | Estrone Metabolism | 0 |  |  |
| 0 | 0 | 1 | Ethacrynic Acid pathway | 0 |  |  |
| 0 | 0 | 1 | Ethanol Degradation | 0 |  |  |
| 0 | 0 | 1 | Ethylmorphine Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Excitatory Neural Signalling Through 5-HTR and Serotonin | 0 |  |  |
| 0 | 0 | 1 | Fabry disease | 0 |  |  |
| 0 | 0 | 1 | Fanconi-bickel syndrome | 0 |  |  |
| 0 | 0 | 1 | Fc Epsilon Receptor I Signaling in Mast Cells | 0 |  |  |
| 0 | 0 | 1 | Fentanyl Pathway | 0 |  |  |
| 0 | 0 | 1 | Fexofenadine H1-Antihistamine Action | 0 |  |  |
| 0 | 0 | 1 | Fluoxetine Pathway | 0 |  |  |
| 0 | 0 | 1 | Fluvastatin Pathway | 0 |  |  |
| 0 | 0 | 1 | Fosphenytoin Antiarrhythmic Pathway | 0 |  |  |
| 0 | 0 | 1 | Fructose and Mannose Degradation | 0 |  |  |
| 0 | 0 | 1 | Fructose intolerance hereditary | 0 |  |  |
| 0 | 0 | 1 | Fructosuria | 0 |  |  |
| 0 | 0 | 1 | Furosemide Pathway | 0 |  |  |
| 0 | 0 | 1 | GLUT-1 deficiency syndrome | 0 |  |  |
| 0 | 0 | 1 | GM2-Gangliosidosis Variant B Tay-sachs disease | 0 |  |  |
| 0 | 0 | 1 | Galactose Metabolism | 0 |  |  |
| 0 | 0 | 1 | Galactosemia | 0 |  |  |
| 0 | 0 | 1 | Gamma-Glutamyltransferase Deficiency | 0 |  |  |
| 0 | 0 | 1 | Gamma-cystathionase deficiency | 0 |  |  |
| 0 | 0 | 1 | Gamma-glutamyl-transpeptidase deficiency | 0 |  |  |
| 0 | 0 | 1 | Gaucher Disease | 0 |  |  |
| 0 | 0 | 1 | Glibenclamide Pathway | 0 |  |  |
| 0 | 0 | 1 | Gliclazide Pathway | 0 |  |  |
| 0 | 0 | 1 | Globoid Cell Leukodystrophy | 0 |  |  |
| 0 | 0 | 1 | Glucose Transporter Defect | 0 |  |  |
| 0 | 0 | 1 | Glucose-Alanine Cycle | 0 |  |  |
| 0 | 0 | 1 | Glutathione Metabolism | 0 |  |  |
| 0 | 0 | 1 | Glutathione Synthetase Deficiency | 0 |  |  |
| 0 | 0 | 1 | Glycogen synthetase deficiency | 0 |  |  |
| 0 | 0 | 1 | Glycolysis | 0 |  |  |
| 0 | 0 | 1 | Hartnup Disorder | 0 |  |  |
| 0 | 0 | 1 | Hereditary Coproporphyria | 0 |  |  |
| 0 | 0 | 1 | Heroin Pathway | 0 |  |  |
| 0 | 0 | 1 | Histidine Metabolism | 0 |  |  |
| 0 | 0 | 1 | Histidinemia | 0 |  |  |
| 0 | 0 | 1 | Homocysteine Degradation | 0 |  |  |
| 0 | 0 | 1 | Homocystinuria cystathionine beta-synthase deficiency | 0 |  |  |
| 0 | 0 | 1 | Hydrochlorothiazide Pathway | 0 |  |  |
| 0 | 0 | 1 | Hydrocodone Pathway | 0 |  |  |
| 0 | 0 | 1 | Hydroflumethiazide Pathway | 0 |  |  |
| 0 | 0 | 1 | Hydromorphone Pathway | 0 |  |  |
| 0 | 0 | 1 | Hyper-IgD syndrome | 0 |  |  |
| 0 | 0 | 1 | Hypercholesterolemia | 0 |  |  |
| 0 | 0 | 1 | Hyperphenylalaniemia due to guanosine triphosphate cyclohydrolase deficiency | 0 |  |  |
| 0 | 0 | 1 | Hyperphenylalaninemia due to 6-pyruvoyltetrahydropterin synthase deficiency | 0 |  |  |
| 0 | 0 | 1 | Hyperphenylalaninemia due to dhpr-deficiency | 0 |  |  |
| 0 | 0 | 1 | Ibandronate Pathway | 0 |  |  |
| 0 | 0 | 1 | Ifosfamide Pathway | 0 |  |  |
| 0 | 0 | 1 | Iminoglycinuria | 0 |  |  |
| 0 | 0 | 1 | Imipramine Pathway | 0 |  |  |
| 0 | 0 | 1 | Indapamide Pathway | 0 |  |  |
| 0 | 0 | 1 | Inositol Metabolism | 0 |  |  |
| 0 | 0 | 1 | Inositol Phosphate Metabolism | 0 |  |  |
| 0 | 0 | 1 | Irbesartan Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Isoprenaline Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Joubert syndrome | 0 |  |  |
| 0 | 0 | 1 | Ketobemidone Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Kidney Function | 0 |  |  |
| 0 | 0 | 1 | Krabbe disease | 0 |  |  |
| 0 | 0 | 1 | Labetalol Pathway | 0 |  |  |
| 0 | 0 | 1 | Lactic Acidemia | 0 |  |  |
| 0 | 0 | 1 | Lactose Degradation | 0 |  |  |
| 0 | 0 | 1 | Lactose Intolerance | 0 |  |  |
| 0 | 0 | 1 | Lactose Synthesis | 0 |  |  |
| 0 | 0 | 1 | Lamivudine Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Lamivudine Metabolism Pathway | 0 |  |  |
| 0 | 0 | 1 | Levallorphan Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Levobunolol Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Levobupivacaine Pathway | 0 |  |  |
| 0 | 0 | 1 | Levomethadyl Acetate Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Levorphanol Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Lidocaine Pathway | 0 |  |  |
| 0 | 0 | 1 | Lisinopril Pathway | 0 |  |  |
| 0 | 0 | 1 | Lovastatin Pathway | 0 |  |  |
| 0 | 0 | 1 | Lysinuric Protein Intolerance | 0 |  |  |
| 0 | 0 | 1 | Lysosomal Acid Lipase Deficiency | 0 |  |  |
| 0 | 0 | 1 | Mepivacaine Pathway | 0 |  |  |
| 0 | 0 | 1 | Metachromatic Leukodystrophy | 0 |  |  |
| 0 | 0 | 1 | Methadone Pathway | 0 |  |  |
| 0 | 0 | 1 | Methadyl Acetate Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Methyclothiazide Pathway | 0 |  |  |
| 0 | 0 | 1 | Methylhistidine Metabolism | 0 |  |  |
| 0 | 0 | 1 | Metolazone Pathway | 0 |  |  |
| 0 | 0 | 1 | Mevalonic aciduria | 0 |  |  |
| 0 | 0 | 1 | Mitochondrial Beta-Oxidation of Medium Chain Saturated Fatty Acids | 0 |  |  |
| 0 | 0 | 1 | Mitochondrial Beta-Oxidation of Short Chain Saturated Fatty Acids | 0 |  |  |
| 0 | 0 | 1 | Morphine Pathway | 0 |  |  |
| 0 | 0 | 1 | Mucopolysaccharidosis Sly syndrome | 0 |  |  |
| 0 | 0 | 1 | Nalbuphine Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Naloxone Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Naltrexone Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Nateglinide Pathway | 0 |  |  |
| 0 | 0 | 1 | Nevirapine Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Nevirapine Metabolism Pathway | 0 |  |  |
| 0 | 0 | 1 | Nicotine Pathway | 0 |  |  |
| 0 | 0 | 1 | Nifedipine Pathway | 0 |  |  |
| 0 | 0 | 1 | Nucleotide Sugars Metabolism | 0 |  |  |
| 0 | 0 | 1 | Omeprazole Metabolism Pathway | 0 |  |  |
| 0 | 0 | 1 | Omeprazole Pathway | 0 |  |  |
| 0 | 0 | 1 | Orphenadrine H1-Antihistamine Action | 0 |  |  |
| 0 | 0 | 1 | Oxidation of Branched Chain Fatty Acids | 0 |  |  |
| 0 | 0 | 1 | Oxybuprocaine Pathway | 0 |  |  |
| 0 | 0 | 1 | Oxycodone Pathway | 0 |  |  |
| 0 | 0 | 1 | Oxymorphone Pathway | 0 |  |  |
| 0 | 0 | 1 | PE Test | 0 |  |  |
| 0 | 0 | 1 | Pamidronate Pathway | 0 |  |  |
| 0 | 0 | 1 | Pancreas Function | 0 |  |  |
| 0 | 0 | 1 | Pantothenate and CoA Biosynthesis | 0 |  |  |
| 0 | 0 | 1 | Pentazocine Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Perindopril Pathway | 0 |  |  |
| 0 | 0 | 1 | Phenindamine H1-Antihistamine Action | 0 |  |  |
| 0 | 0 | 1 | Phenylacetate Metabolism | 0 |  |  |
| 0 | 0 | 1 | Phenytoin Antiarrhythmic Pathway | 0 |  |  |
| 0 | 0 | 1 | Phosphatidylcholine Biosynthesis | 0 |  |  |
| 0 | 0 | 1 | Phosphatidylethanolamine Biosynthesis | 0 |  |  |
| 0 | 0 | 1 | Phosphatidylinositol Phosphate Metabolism | 0 |  |  |
| 0 | 0 | 1 | Phytanic Acid Peroxisomal Oxidation | 0 |  |  |
| 0 | 0 | 1 | Pindolol Pathway | 0 |  |  |
| 0 | 0 | 1 | Polythiazide Pathway | 0 |  |  |
| 0 | 0 | 1 | Porphyria Variegata | 0 |  |  |
| 0 | 0 | 1 | Porphyrin Metabolism | 0 |  |  |
| 0 | 0 | 1 | Practolol Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Pravastatin Pathway | 0 |  |  |
| 0 | 0 | 1 | Prilocaine Pathway | 0 |  |  |
| 0 | 0 | 1 | Procaine Pathway | 0 |  |  |
| 0 | 0 | 1 | Promethazine H1-Antihistamine Action | 0 |  |  |
| 0 | 0 | 1 | Proparacaine Pathway | 0 |  |  |
| 0 | 0 | 1 | Propoxyphene Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Propranolol Pathway | 0 |  |  |
| 0 | 0 | 1 | Pterine Biosynthesis | 0 |  |  |
| 0 | 0 | 1 | Pyruvaldehyde Degradation | 0 |  |  |
| 0 | 0 | 1 | Pyruvate Carboxylase Deficiency | 0 |  |  |
| 0 | 0 | 1 | Quetiapine H1-Antihistamine Action | 0 |  |  |
| 0 | 0 | 1 | Quinapril Metabolism Pathway | 0 |  |  |
| 0 | 0 | 1 | Quinapril Pathway | 0 |  |  |
| 0 | 0 | 1 | Quinethazone Pathway | 0 |  |  |
| 0 | 0 | 1 | Quinidine Pathway | 0 |  |  |
| 0 | 0 | 1 | Ranitidine Pathway | 0 |  |  |
| 0 | 0 | 1 | Refsum Disease | 0 |  |  |
| 0 | 0 | 1 | Remifentanil Pathway | 0 |  |  |
| 0 | 0 | 1 | Repaglinide Pathway | 0 |  |  |
| 0 | 0 | 1 | Retinol Metabolism | 0 |  |  |
| 0 | 0 | 1 | Riboflavin Metabolism | 0 |  |  |
| 0 | 0 | 1 | Risedronate Pathway | 0 |  |  |
| 0 | 0 | 1 | Ropivacaine Pathway | 0 |  |  |
| 0 | 0 | 1 | Rosiglitazone Metabolism Pathway | 0 |  |  |
| 0 | 0 | 1 | Rosuvastatin Pathway | 0 |  |  |
| 0 | 0 | 1 | Roxatidine acetate Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Salla Disease Infantile Sialic Acid Storage Disease | 0 |  |  |
| 0 | 0 | 1 | Segawa syndrome | 0 |  |  |
| 0 | 0 | 1 | Sepiapterin reductase deficiency | 0 |  |  |
| 0 | 0 | 1 | Short-chain 3-hydroxyacyl-CoA dehydrogenase deficiency | 0 |  |  |
| 0 | 0 | 1 | Sialuria or French Type Sialuria | 0 |  |  |
| 0 | 0 | 1 | Simvastatin Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Smith-Lemli-Opitz Syndrome | 0 |  |  |
| 0 | 0 | 1 | Sotalol Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Sphingolipid Metabolism | 0 |  |  |
| 0 | 0 | 1 | Spironolactone Pathway | 0 |  |  |
| 0 | 0 | 1 | Starch and Sucrose Metabolism | 0 |  |  |
| 0 | 0 | 1 | Stavudine Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Steroid Biosynthesis | 0 |  |  |
| 0 | 0 | 1 | Steroidogenesis | 0 |  |  |
| 0 | 0 | 1 | Sucrase-isomaltase deficiency | 0 |  |  |
| 0 | 0 | 1 | Sufentanil Pathway | 0 |  |  |
| 0 | 0 | 1 | Sulfate Sulfite Metabolism | 0 |  |  |
| 0 | 0 | 1 | Sulfite oxidase deficiency | 0 |  |  |
| 0 | 0 | 1 | Tamoxifen Pathway | 0 |  |  |
| 0 | 0 | 1 | Taurine and Hypotaurine Metabolism | 0 |  |  |
| 0 | 0 | 1 | Tay-Sachs Disease | 0 |  |  |
| 0 | 0 | 1 | Thiamine Metabolism | 0 |  |  |
| 0 | 0 | 1 | Thioguanine Metabolism Pathway | 0 |  |  |
| 0 | 0 | 1 | Thyroid hormone synthesis | 0 |  |  |
| 0 | 0 | 1 | Torsemide Pathway | 0 |  |  |
| 0 | 0 | 1 | Tramadol Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Tramadol Metabolism Pathway | 0 |  |  |
| 0 | 0 | 1 | Tranexamic Acid Pathway | 0 |  |  |
| 0 | 0 | 1 | Trehalose Degradation | 0 |  |  |
| 0 | 0 | 1 | Triamterene Pathway | 0 |  |  |
| 0 | 0 | 1 | Trichlormethiazide Pathway | 0 |  |  |
| 0 | 0 | 1 | Triprolidine H1-Antihistamine Action | 0 |  |  |
| 0 | 0 | 1 | Tyrosine hydroxylase deficiency | 0 |  |  |
| 0 | 0 | 1 | Ubiquinone Biosynthesis | 0 |  |  |
| 0 | 0 | 1 | Valsartan Action Pathway | 0 |  |  |
| 0 | 0 | 1 | Vasopressin Regulation of Water Homeostasis | 0 |  |  |
| 0 | 0 | 1 | Venlafaxine Metabolism Pathway | 0 |  |  |
| 0 | 0 | 1 | Verapamil Pathway | 0 |  |  |
| 0 | 0 | 1 | Vitamin A Deficiency | 0 |  |  |
| 0 | 0 | 1 | Vitamin K Metabolism | 0 |  |  |
| 0 | 0 | 1 | Warfarin Pathway | 0 |  |  |
| 0 | 0 | 1 | Wolman disease | 0 |  |  |
| 0 | 0 | 1 | Zoledronate Pathway | 0 |  |  |

**Supplemental Figure S1. Boxplot of cross-validated concordance (C-statistics) for time-to-ESKD for each model in Supplemental Table S3**

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The numbers on X axis denote the fitted model as specified in Supplemental Table S3. Model 1 is the clinical- variable only model.

Note: R2 of 6 survival models are 0.46, 0.50, 0.50, 0.47, 0.50, 0.41, respectively.

**Supplemental Figure S2. Pathway enrichment analysis using metabolite ions selected in adjusted single metabolite and/or multiple metabolite models**

Top row: 49 metabolite ions selected in multivariable models for eGFR slope outcome (Supplemental Table S4);

Middle row: 99 metabolite ions significant in adjusted Cox model, testing associations between single metabolite ion and time-to-ESKD, adjusted for 9 clinical variables (Supplemental Table S2);

Bottom row: 131 metabolites merged from the 49-metabolite-ion and 99-metabolite-ion sets.

**Supplementary References**

Fuhrer, T, Heer D, Begemann B, et al. High-throughput, accurate mass metabolome profiling of cellular extracts by flow injection-time-of-flight mass spectrometry. Anal Chem, 2011. **83**(18): p. 7074-80.