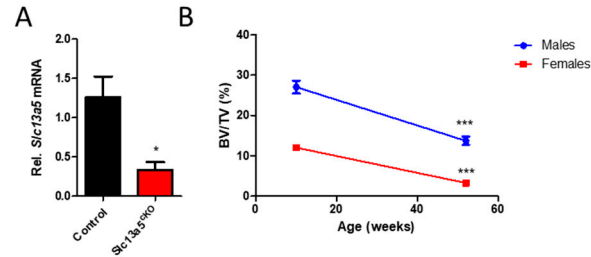
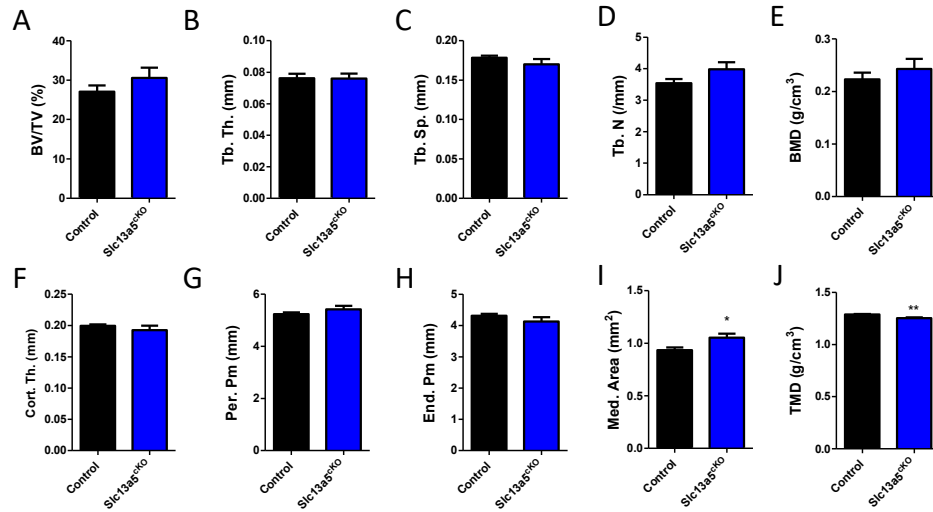


**Figure S1.** Workflow and results of the synthetic clinical trial on osteoporosis.



**Figure S2.** A) Relative *Slc13a5* mRNA expression in full bones of control and *Slc13a5<sup>cKO</sup>* mice (n=4). B) Bone Volume/Tissue Volume (BV/TV) % in male and female control mice at 10 (young) and 52 weeks (middle-aged) of age (n=6-11). All graphs represent mean  $\pm$  SEM; Student's t-test versus control (A) or young (B), \* $p$ <0.05, \*\*\* $p$ <0.001.



**Figure S3. (A-H)** Micro-CT analysis of the femur in 10-week-old control and *Slc13a5<sup>cKO</sup>* male mice (n=8-11) showing Bone Volume/Tissue Volume (BV/TV%, A), Trabecular Thickness (Tb. Th., B), Trabecular Separation (Tb. Sp., C), Trabecular Number (Tb. N., D), Bone Mineral Density (BMD, E) Cortical Thickness (Cort. Th., F), Periosteal Perimeter (Per. Pm, G), Endosteal Perimeter (End. Pm., H), and Medullary Area (Med. Area, I), and Tissue Mineral Density. All graphs represent mean  $\pm$  SEM; Student's t-test versus control, \* $p$ <0.05, \*\* $p$ <0.01.

**Table S1.** Results of the regression on osteoporosis. Significance thresholds are indicated by asterisks, where three asterisks indicate  $p$ -values below 0.001/51, two indicate  $p$ -values below 0.01/51, and one asterisk indicates  $p$ -values below 0.05/51.

| Trait                                | Estimate | SE     | $p$ -value |
|--------------------------------------|----------|--------|------------|
| bmi                                  | -0.0591  | 0.0031 | 2.5332E-83 |
| high_light_scatter_reticulocyte_ct   | -7.6383  | 1.5321 | 6.1851E-07 |
| high_light_scatter_reticulocyte_perc | -0.2015  | 0.0644 | 0.0018     |
| red_blood_cell_ct                    | -0.4964  | 0.0385 | 4.0573E-38 |
| red_blood_cell_distribution_width    | 0.1563   | 0.0152 | 6.6728E-25 |
| mean_reticulocyte_vol                | 0.0178   | 0.0018 | 6.3137E-22 |
| immature_reticulocyte_fraction       | -0.5717  | 0.2372 | 0.0159     |
| reticulocyte_ct                      | -1.9724  | 0.524  | 2E-04      |
| reticulocyte_perc                    | -0.0438  | 0.0188 | 0.0197     |
| nucleated_red_blood_cell_ct          | 0.7691   | 0.6059 | 0.2043     |
| nucleated_red_blood_cell_perc        | 0.0673   | 0.0409 | 0.0999     |
| haemoglobin_concentration            | -0.1599  | 0.0134 | 1.1526E-32 |

|                                            |         |        |            |
|--------------------------------------------|---------|--------|------------|
| mean_corpuscular_volume                    | 0.0214  | 0.0032 | 4.2703E-11 |
| mean_corpuscular_haemoglobin               | 0.0225  | 0.0075 | 0.0026     |
| mean_corpuscular_haemoglobin_concentration | -0.0505 | 0.0134 | 2E-04      |
| haematocrit_perc                           | -0.0474 | 0.0046 | 3.1836E-25 |
| platelet_ct                                | 9E-04   | 2E-04  | 1E-04      |
| platelet_distribution_width                | -0.138  | 0.0283 | 1.0439E-06 |
| platelet_crit                              | 0.4769  | 0.2831 | 0.0921     |
| mean_platelet_vol                          | -0.063  | 0.0133 | 2.2162E-06 |
| white_blood_cell_ct                        | 0.033   | 0.0076 | 0          |
| basophill_ct                               | 0.912   | 0.2969 | 0.0021     |
| basophill_perc                             | 0.0393  | 0.0241 | 0.1028     |
| eosinophill_ct                             | 0.123   | 0.107  | 0.2504     |
| eosinophill_perc                           | -0.0034 | 0.0081 | 0.6697     |
| neutrophill_ct                             | 0.0849  | 0.01   | 1.7377E-17 |
| neutrophill_perc                           | 0.0151  | 0.0017 | 2.5068E-19 |
| monocyte_ct                                | 0.1117  | 0.0657 | 0.089      |
| monocyte_perc                              | 7E-04   | 0.0053 | 0.8942     |
| lymphocyte_ct                              | -0.0898 | 0.0203 | 0          |
| lymphocyte_perc                            | -0.0195 | 0.0019 | 1.1704E-24 |
| mean_sphered_cell_vol                      | 0.0266  | 0.0027 | 9.7436E-23 |
| alanine_aminotransferase                   | -0.0047 | 0.0011 | 0          |
| albumin                                    | -0.0326 | 0.0057 | 1.1261E-08 |
| alkaline_phosphate                         | -0.0011 | 5E-04  | 0.015      |
| apolipoprotein_a                           | 0.1709  | 0.0548 | 0.0018     |
| apolipoprotein_b                           | -0.501  | 0.0612 | 2.7207E-16 |
| aspartate_aminotransferase                 | 0.0034  | 0.0014 | 0.0168     |
| direct_bilirubin                           | 0.0195  | 0.0167 | 0.243      |
| total_bilirubin                            | -0.0123 | 0.0037 | 8E-04      |
| c_reactive_protein                         | 0.0126  | 0.0029 | 0          |
| calcium                                    | 0.4157  | 0.1485 | 0.0051     |
| cholesterol                                | -0.0676 | 0.0125 | 6.6418E-08 |
| creatinine                                 | -6E-04  | 7E-04  | 0.3929     |
| cystatin_c                                 | 0.508   | 0.078  | 7.4832E-11 |
| gamma_glutamyltransferase                  | 0.0013  | 3E-04  | 0          |
| glucose                                    | -0.0274 | 0.0131 | 0.0362     |
| glycated_haemoglobin                       | -0.0061 | 0.0023 | 0.0073     |
| hdl_cholesterol                            | 0.2275  | 0.0379 | 1.899E-09  |
| igf_1                                      | -0.0115 | 0.0026 | 9.2223E-06 |
| ldl_direct                                 | -0.1286 | 0.0165 | 5.9561E-15 |
| lipoprotein_a                              | 4E-04   | 3E-04  | 0.2802     |
| oestradiol                                 | -3E-04  | 1E-04  | 0.0805     |
| phosphate                                  | 0.0874  | 0.0975 | 0.37       |
| rheumatoid_factor                          | 0.0043  | 0.0022 | 0.0481     |
| shbg                                       | 0.0077  | 5E-04  | 2.177E-48  |
| testosterone                               | 0.0053  | 0.0034 | 0.1178     |
| total_protein                              | -0.0109 | 0.0036 | 0.0026     |

|                                                                                |         |            |            |
|--------------------------------------------------------------------------------|---------|------------|------------|
| triglycerides                                                                  | -0.0982 | 0.0161     | 1.1269E-09 |
| urage                                                                          | -0.0023 | 2E-04      | 2.4821E-30 |
| urea                                                                           | -0.012  | 0.0096     | 0.2105     |
| vitamin_d                                                                      | 0.0127  | 7E-04      | 7.2396E-72 |
| creatinine_urin                                                                | 0       | 2.8337E-06 | 8.0977E-06 |
| microalbumin_urin                                                              | 3E-04   | 2E-04      | 0.1666     |
| potassium_urin                                                                 | -0.0023 | 4E-04      | 2.5229E-07 |
| sodium_urin                                                                    | -0.0019 | 4E-04      | 2.1553E-07 |
| 3_hydroxybutyrate                                                              | 0.923   | 0.4862     | 0.0577     |
| acetate                                                                        | 1.8136  | 0.9394     | 0.0535     |
| acetoacetate                                                                   | 6.3061  | 2.4014     | 0.0086     |
| acetone                                                                        | 10.8044 | 5.2939     | 0.0413     |
| alanine                                                                        | -0.8108 | 0.3951     | 0.0402     |
| albumin_nmr                                                                    | -0.0266 | 0.0088     | 0.0026     |
| apolipoprotein_a1_nmr                                                          | -0.0315 | 0.1193     | 0.7916     |
| apolipoprotein_b_nmr                                                           | -0.5495 | 0.1443     | 1E-04      |
| apolipoprotein_b_over_apolipoprotein_a1_nmr                                    | -0.6113 | 0.1842     | 9E-04      |
| average_diameter_hdl_particles                                                 | 0.6111  | 0.1388     | 0          |
| average_diameter_idl_particles                                                 | 0.3068  | 0.3469     | 0.3764     |
| average_diameter_vldl_particles                                                | -0.0843 | 0.0244     | 5E-04      |
| cholesterol_in_chylomicrons_and_extremely_large_vldl                           | -1.9122 | 0.7168     | 0.0076     |
| cholesterol_in_idl                                                             | -0.3713 | 0.1313     | 0.0047     |
| cholesterol_in_large_hdl                                                       | 0.4716  | 0.1648     | 0.0042     |
| cholesterol_in_large_ldl                                                       | -0.4102 | 0.1017     | 1E-04      |
| cholesterol_in_large_vldl                                                      | -2.5426 | 0.6264     | 0          |
| cholesterol_in_medium_hdl                                                      | 0.0149  | 0.2387     | 0.9503     |
| cholesterol_in_medium_ldl                                                      | -1.2807 | 0.252      | 3.7137E-07 |
| cholesterol_in_medium_vldl                                                     | -1.4664 | 0.4357     | 8E-04      |
| cholesterol_in_small_hdl                                                       | -2.2138 | 0.4733     | 2.9106E-06 |
| cholesterol_in_small_ldl                                                       | -3.0406 | 0.6681     | 5.3339E-06 |
| cholesterol_in_small_vldl                                                      | -2.0692 | 0.557      | 2E-04      |
| cholesterol_in_very_large_hdl                                                  | 2.3338  | 0.7608     | 0.0022     |
| cholesterol_in_very_large_vldl                                                 | -4.0678 | 1.0483     | 1E-04      |
| cholesterol_in_very_small_vldl                                                 | -1.0505 | 0.5661     | 0.0635     |
| cholesterol_to_total_lipids_in_cylomicrons_and_extremely_large_vldl_percentage | -0.0036 | 0.0026     | 0.1596     |
| cholesterol_to_total_lipids_in_idl_percentage                                  | -0.0211 | 0.01       | 0.0349     |
| cholesterol_to_total_lipids_in_large_hdl_percentage                            | 0.0121  | 0.006      | 0.0438     |
| cholesterol_to_total_lipids_in_large_ldl_percentage                            | -0.0393 | 0.0178     | 0.0274     |
| cholesterol_to_total_lipids_in_large_vldl_percentage                           | 0.0134  | 0.0066     | 0.0409     |
| cholesterol_to_total_lipids_in_medium_hdl_percentage                           | 0.0146  | 0.0101     | 0.149      |
| cholesterol_to_total_lipids_in_medium_ldl_percentage                           | -0.0593 | 0.0178     | 9E-04      |
| cholesterol_to_total_lipids_in_medium_vldl_percentage                          | 0.0067  | 0.0044     | 0.1266     |
| cholesterol_to_total_lipids_in_small_hdl_percentage                            | -0.0198 | 0.0162     | 0.2229     |
| cholesterol_to_total_lipids_in_small_ldl_percentage                            | -0.0672 | 0.0149     | 6.4803E-06 |
| cholesterol_to_total_lipids_in_small_vldl_percentage                           | -3E-04  | 0.0063     | 0.9624     |

|                                                                                        |             |           |            |
|----------------------------------------------------------------------------------------|-------------|-----------|------------|
| cholesterol_to_total_lipids_in_very_large_hdl_percentage                               | -0.0291     | 0.0078    | 2E-04      |
| cholesterol_to_total_lipids_in_very_large_vldl_percentage                              | 0.0071      | 0.0035    | 0.0404     |
| cholesterol_to_total_lipids_in_very_small_vldl_percentage                              | -0.0024     | 0.0066    | 0.7164     |
| cholesteryl_esters_in_chylomicrons_and_extremely_large_vldl                            | -3.8764     | 1.2996    | 0.0029     |
| cholesteryl_esters_in_hdl                                                              | 0.1151      | 0.1125    | 0.3064     |
| cholesteryl_esters_in_idl                                                              | -0.5082     | 0.1766    | 0.004      |
| cholesteryl_esters_in_ldl                                                              | -0.4126     | 0.0906    | 5.3097E-06 |
| cholesteryl_esters_in_large_hdl                                                        | 0.607       | 0.2122    | 0.0042     |
| cholesteryl_esters_in_large_ldl                                                        | -0.5767     | 0.1388    | 0          |
| cholesteryl_esters_in_large_vldl                                                       | -4.9747     | 1.2546    | 1E-04      |
| cholesteryl_esters_in_medium_hdl                                                       | 0.0214      | 0.298     | 0.9429     |
| cholesteryl_esters_in_medium_ldl                                                       | -1.7476     | 0.3398    | 2.7066E-07 |
| cholesteryl_esters_in_medium_vldl                                                      | -2.0475     | 0.7458    | 0.006      |
| cholesteryl_esters_in_small_hdl                                                        | -2.8779     | 0.6099    | 2.3733E-06 |
| cholesteryl_esters_in_small_ldl                                                        | -4.172      | 0.8985    | 3.4269E-06 |
| cholesteryl_esters_in_small_vldl                                                       | -3.0908     | 0.8627    | 3E-04      |
| cholesteryl_esters_in_vldl                                                             | -0.7002     | 0.1994    | 4E-04      |
| cholesteryl_esters_in_very_large_hdl                                                   | 2.882       | 0.958     | 0.0026     |
| cholesteryl_esters_in_very_large_vldl                                                  | -8.4317     | 2.0173    | 0          |
| cholesteryl_esters_in_very_small_vldl                                                  | -1.4176     | 0.7931    | 0.0739     |
| cholesteryl_esters_to_total_lipids_in_chylomicrons_and_extremely_large_vldl_percentage | -0.0083     | 0.0037    | 0.0247     |
| cholesteryl_esters_to_total_lipids_in_idl_percentage                                   | -0.0272     | 0.0121    | 0.024      |
| cholesteryl_esters_to_total_lipids_in_large_hdl_percentage                             | 0.0136      | 0.007     | 0.0514     |
| cholesteryl_esters_to_total_lipids_in_large_ldl_percentage                             | -0.0811     | 0.0256    | 0.0015     |
| cholesteryl_esters_to_total_lipids_in_large_vldl_percentage                            | 0.0235      | 0.0083    | 0.0047     |
| cholesteryl_esters_to_total_lipids_in_medium_hdl_percentage                            | 0.0153      | 0.0119    | 0.1966     |
| cholesteryl_esters_to_total_lipids_in_medium_ldl_percentage                            | -0.0498     | 0.0149    | 9E-04      |
| cholesteryl_esters_to_total_lipids_in_medium_vldl_percentage                           | 0.0099      | 0.0058    | 0.0887     |
| cholesteryl_esters_to_total_lipids_in_small_hdl_percentage                             | -0.0283     | 0.0163    | 0.0815     |
| cholesteryl_esters_to_total_lipids_in_small_ldl_percentage                             | -0.0472     | 0.0133    | 4E-04      |
| cholesteryl_esters_to_total_lipids_in_small_vldl_percentage                            | 2E-04       | 0.0106    | 0.9885     |
| cholesteryl_esters_to_total_lipids_in_very_large_hdl_percentage                        | -0.0234     | 0.0107    | 0.0288     |
| cholesteryl_esters_to_total_lipids_in_very_large_vldl_percentage                       | 0.0074      | 0.0043    | 0.0839     |
| cholesteryl_esters_to_total_lipids_in_very_small_vldl_percentage                       | -0.0018     | 0.0073    | 0.8092     |
| citrate                                                                                | -3.2958     | 2.2736    | 0.1472     |
| clinical_ldl_cholesterol                                                               | -0.1653     | 0.0394    | 0          |
| concentration_of_chylomicrons_and_extremely_large_vldl_particles                       | -45409.4535 | 20477.486 | 0.0266     |
| concentration_of_hdl_particles                                                         | -21.7379    | 11.9537   | 0.069      |
| concentration_of_idl_particles                                                         | -1117.1197  | 368.7925  | 0.0025     |
| concentration_of_ldl_particles                                                         | -400.8223   | 102.9526  | 1E-04      |
| concentration_of_large_hdl_particles                                                   | 96.7105     | 36.1449   | 0.0075     |
| concentration_of_large_ldl_particles                                                   | -577.0085   | 164.0951  | 4E-04      |
| concentration_of_large_vldl_particles                                                  | -20873.7074 | 5525.4029 | 2E-04      |
| concentration_of_medium_hdl_particles                                                  | -6.4778     | 31.503    | 0.8371     |
| concentration_of_medium_ldl_particles                                                  | -1731.7673  | 387.5255  | 7.8666E-06 |

|                                                                                      |             |            |            |
|--------------------------------------------------------------------------------------|-------------|------------|------------|
| concentration_of_medium_vldl_particles                                               | -10167.9183 | 2394.6942  | 0          |
| concentration_of_small_hdl_particles                                                 | -110.1021   | 22.014     | 5.6897E-07 |
| concentration_of_small_ldl_particles                                                 | -2981.4067  | 782.6399   | 1E-04      |
| concentration_of_small_vldl_particles                                                | -8125.3695  | 2282.7559  | 4E-04      |
| concentration_of_vldl_particles                                                      | -2347.6642  | 658.3619   | 4E-04      |
| concentration_of_very_large_hdl_particles                                            | 800.0132    | 278.9785   | 0.0041     |
| concentration_of_very_large_vldl_particles                                           | -46601.4422 | 13480.5429 | 5E-04      |
| concentration_of_very_small_vldl_particles                                           | -4373.7729  | 2057.0637  | 0.0335     |
| creatinine_nmr                                                                       | -0.7315     | 2.2247     | 0.7423     |
| degree_of_unsaturation                                                               | -0.2858     | 0.3517     | 0.4165     |
| docosahexaenoic_acid                                                                 | -0.6083     | 0.33       | 0.0653     |
| docosahexaenoic_acid_to_total_fatty_acids_percentage                                 | -0.0076     | 0.0417     | 0.856      |
| free_cholesterol_in_chylomicrons_and_extremely_large_vldl                            | -3.5579     | 1.5795     | 0.0243     |
| free_cholesterol_in_hdl                                                              | 0.3913      | 0.3852     | 0.3098     |
| free_cholesterol_in_idl                                                              | -1.3195     | 0.5009     | 0.0084     |
| free_cholesterol_in_ldl                                                              | -0.9378     | 0.2387     | 1E-04      |
| free_cholesterol_in_large_hdl                                                        | 2.0827      | 0.7329     | 0.0045     |
| free_cholesterol_in_large_ldl                                                        | -1.3352     | 0.3698     | 3E-04      |
| free_cholesterol_in_large_vldl                                                       | -4.9335     | 1.2193     | 1E-04      |
| free_cholesterol_in_medium_hdl                                                       | 0.0285      | 1.1738     | 0.9807     |
| free_cholesterol_in_medium_ldl                                                       | -4.1563     | 0.9077     | 4.6693E-06 |
| free_cholesterol_in_medium_vldl                                                      | -3.9082     | 0.9836     | 1E-04      |
| free_cholesterol_in_small_hdl                                                        | -6.9388     | 1.7953     | 1E-04      |
| free_cholesterol_in_small_ldl                                                        | -8.9174     | 2.3282     | 1E-04      |
| free_cholesterol_in_small_vldl                                                       | -5.9349     | 1.5357     | 1E-04      |
| free_cholesterol_in_vldl                                                             | -1.0523     | 0.2747     | 1E-04      |
| free_cholesterol_in_very_large_hdl                                                   | 11.4436     | 3.5827     | 0.0014     |
| free_cholesterol_in_very_large_vldl                                                  | -7.2989     | 2.1163     | 6E-04      |
| free_cholesterol_in_very_small_vldl                                                  | -3.6974     | 1.8999     | 0.0517     |
| free_cholesterol_to_total_lipids_in_chylomicrons_and_extremely_large_vldl_percentage | 0.0028      | 0.0065     | 0.6707     |
| free_cholesterol_to_total_lipids_in_idl_percentage                                   | -0.0193     | 0.0284     | 0.496      |
| free_cholesterol_to_total_lipids_in_large_hdl_percentage                             | 0.0502      | 0.0302     | 0.096      |
| free_cholesterol_to_total_lipids_in_large_ldl_percentage                             | 1E-04       | 0.0227     | 0.9973     |
| free_cholesterol_to_total_lipids_in_large_vldl_percentage                            | -0.0116     | 0.0196     | 0.5527     |
| free_cholesterol_to_total_lipids_in_medium_hdl_percentage                            | 0.0597      | 0.0421     | 0.1566     |
| free_cholesterol_to_total_lipids_in_medium_ldl_percentage                            | 0.0092      | 0.0159     | 0.5631     |
| free_cholesterol_to_total_lipids_in_medium_vldl_percentage                           | 0.0163      | 0.0168     | 0.331      |
| free_cholesterol_to_total_lipids_in_small_hdl_percentage                             | 0.0783      | 0.0494     | 0.1128     |
| free_cholesterol_to_total_lipids_in_small_ldl_percentage                             | -0.0089     | 0.0151     | 0.5538     |
| free_cholesterol_to_total_lipids_in_small_vldl_percentage                            | -0.0015     | 0.0131     | 0.9081     |
| free_cholesterol_to_total_lipids_in_very_large_hdl_percentage                        | -0.0315     | 0.0104     | 0.0025     |
| free_cholesterol_to_total_lipids_in_very_large_vldl_percentage                       | 0.0436      | 0.0153     | 0.0045     |
| free_cholesterol_to_total_lipids_in_very_small_vldl_percentage                       | -0.0593     | 0.052      | 0.2537     |
| glucose_nmr                                                                          | 0.0083      | 0.0261     | 0.7495     |
| glutamine                                                                            | 0.123       | 0.3731     | 0.7416     |

|                                                                                   |         |        |            |
|-----------------------------------------------------------------------------------|---------|--------|------------|
| glycine                                                                           | 0.8508  | 0.4291 | 0.0474     |
| glycoprotein_acetyls                                                              | 0.2047  | 0.2496 | 0.412      |
| hdl_cholesterol_nmr                                                               | 0.0901  | 0.0876 | 0.304      |
| histidine                                                                         | -9.7238 | 2.9692 | 0.0011     |
| isoleucine                                                                        | -4.7675 | 1.7326 | 0.0059     |
| ldl_cholesterol                                                                   | -0.2936 | 0.0664 | 9.6519E-06 |
| lactate                                                                           | -0.0418 | 0.027  | 0.1209     |
| leucine                                                                           | -4.9343 | 1.1121 | 9.1318E-06 |
| linoleic_acid                                                                     | -0.1085 | 0.0423 | 0.0103     |
| linoleic_acid_to_total_fatty_acids_percentage                                     | 0.0075  | 0.0087 | 0.3832     |
| monounsaturated_fatty_acids                                                       | -0.0805 | 0.037  | 0.0297     |
| monounsaturated_fatty_acids_to_total_fatty_acids_percentage                       | -0.0016 | 0.0111 | 0.8893     |
| omega_3_fatty_acids                                                               | -0.3154 | 0.1252 | 0.0118     |
| omega_3_fatty_acids_to_total_fatty_acids_percentage                               | -0.0215 | 0.0177 | 0.223      |
| omega_6_fatty_acids                                                               | -0.1366 | 0.0428 | 0.0014     |
| omega_6_fatty_acids_to_omega_3_fatty_acids_ratio                                  | 0.022   | 0.0078 | 0.0047     |
| omega_6_fatty_acids_to_total_fatty_acids_percentage                               | 0.0103  | 0.0086 | 0.2309     |
| phenylalanine                                                                     | -3.0788 | 2.646  | 0.2446     |
| phosphatidylcholines                                                              | -0.1428 | 0.0766 | 0.0622     |
| phosphoglycerides                                                                 | -0.1506 | 0.0726 | 0.0381     |
| phospholipids_in_chylomicrons_and_extremely_large_vldl                            | -2.0958 | 0.9688 | 0.0305     |
| phospholipids_in_hdl                                                              | 0.0578  | 0.091  | 0.5257     |
| phospholipids_in_idl                                                              | -1.0091 | 0.4245 | 0.0174     |
| phospholipids_in_ldl                                                              | -0.9096 | 0.2065 | 0          |
| phospholipids_in_large_hdl                                                        | 0.5031  | 0.1851 | 0.0066     |
| phospholipids_in_large_ldl                                                        | -1.4609 | 0.348  | 0          |
| phospholipids_in_large_vldl                                                       | -2.8722 | 0.7681 | 2E-04      |
| phospholipids_in_medium_hdl                                                       | -0.118  | 0.2931 | 0.6873     |
| phospholipids_in_medium_ldl                                                       | -3.4812 | 0.7038 | 7.5663E-07 |
| phospholipids_in_medium_vldl                                                      | -2.52   | 0.6138 | 0          |
| phospholipids_in_small_hdl                                                        | -1.1578 | 0.3065 | 2E-04      |
| phospholipids_in_small_ldl                                                        | -5.5502 | 1.573  | 4E-04      |
| phospholipids_in_small_vldl                                                       | -3.73   | 0.9661 | 1E-04      |
| phospholipids_in_vldl                                                             | -0.5935 | 0.1639 | 3E-04      |
| phospholipids_in_very_large_hdl                                                   | 2.1754  | 0.602  | 3E-04      |
| phospholipids_in_very_large_vldl                                                  | -3.9716 | 1.1741 | 7E-04      |
| phospholipids_in_very_small_vldl                                                  | -1.6284 | 1.0728 | 0.129      |
| phospholipids_to_total_lipids_in_chylomicrons_and_extremely_large_vldl_percentage | -0.001  | 0.0066 | 0.8798     |
| phospholipids_to_total_lipids_in_idl_percentage                                   | 0.0967  | 0.0321 | 0.0026     |
| phospholipids_to_total_lipids_in_large_hdl_percentage                             | -0.0178 | 0.0108 | 0.0993     |
| phospholipids_to_total_lipids_in_large_ldl_percentage                             | -0.0217 | 0.0383 | 0.5708     |
| phospholipids_to_total_lipids_in_large_vldl_percentage                            | -0.0058 | 0.0076 | 0.4474     |
| phospholipids_to_total_lipids_in_medium_hdl_percentage                            | -0.019  | 0.024  | 0.4298     |
| phospholipids_to_total_lipids_in_medium_ldl_percentage                            | 0.0392  | 0.0354 | 0.2675     |
| phospholipids_to_total_lipids_in_medium_vldl_percentage                           | 0.0141  | 0.0162 | 0.3839     |

|                                                                  |          |         |            |
|------------------------------------------------------------------|----------|---------|------------|
| phospholipids_to_total_lipids_in_small_hdl_percentage            | 0.0825   | 0.0248  | 9E-04      |
| phospholipids_to_total_lipids_in_small_ldl_percentage            | 0.0596   | 0.0157  | 2E-04      |
| phospholipids_to_total_lipids_in_small_vldl_percentage           | 0.0019   | 0.014   | 0.8912     |
| phospholipids_to_total_lipids_in_very_large_hdl_percentage       | 0.0243   | 0.0059  | 0          |
| phospholipids_to_total_lipids_in_very_large_vldl_percentage      | 0.0031   | 0.0104  | 0.7689     |
| phospholipids_to_total_lipids_in_very_small_vldl_percentage      | 0.0836   | 0.034   | 0.014      |
| polyunsaturated_fatty_acids                                      | -0.1234  | 0.0361  | 6E-04      |
| polyunsaturated_fatty_acids_to_monounsaturated_fatty_acids_ratio | 0.043    | 0.0847  | 0.6113     |
| polyunsaturated_fatty_acids_to_total_fatty_acids_percentage      | 0.0045   | 0.008   | 0.5722     |
| pyruvate                                                         | -0.2292  | 0.7248  | 0.7518     |
| remnant_cholesterol                                              | -0.2488  | 0.0685  | 3E-04      |
| saturated_fatty_acids                                            | -0.0926  | 0.0319  | 0.0037     |
| saturated_fatty_acids_to_total_fatty_acids_percentage            | -0.0143  | 0.0157  | 0.3632     |
| sphingomyelins                                                   | -0.7341  | 0.3973  | 0.0647     |
| total_cholesterol                                                | -0.0997  | 0.0303  | 0.001      |
| total_cholesterol_minus_hdl_c                                    | -0.1404  | 0.0342  | 0          |
| total_cholines                                                   | -0.1404  | 0.0701  | 0.0451     |
| total_concentration_of_branched_chain_amino_acids                | -1.7803  | 0.3686  | 1.3638E-06 |
| total_concentration_of_lipoprotein_particles                     | -26.6505 | 11.4401 | 0.0198     |
| total_esterified_cholesterol                                     | -0.1359  | 0.0421  | 0.0013     |
| total_fatty_acids                                                | -0.0385  | 0.0126  | 0.0022     |
| total_free_cholesterol                                           | -0.3594  | 0.1061  | 7E-04      |
| total_lipids_in_chylomicrons_and_extremely_large_vldl            | -0.3346  | 0.153   | 0.0288     |
| total_lipids_in_hdl                                              | 0.0318   | 0.0449  | 0.4789     |
| total_lipids_in_idl                                              | -0.268   | 0.0974  | 0.0059     |
| total_lipids_in_ldl                                              | -0.2141  | 0.0486  | 0          |
| total_lipids_in_large_hdl                                        | 0.2396   | 0.0863  | 0.0055     |
| total_lipids_in_large_ldl                                        | -0.3101  | 0.0763  | 0          |
| total_lipids_in_large_vldl                                       | -0.6905  | 0.174   | 1E-04      |
| total_lipids_in_lipoprotein_particles                            | -0.0649  | 0.0176  | 2E-04      |
| total_lipids_in_medium_hdl                                       | -0.0407  | 0.1304  | 0.7548     |
| total_lipids_in_medium_ldl                                       | -0.9012  | 0.1794  | 5.0871E-07 |
| total_lipids_in_medium_vldl                                      | -0.6341  | 0.1446  | 0          |
| total_lipids_in_small_hdl                                        | -0.7808  | 0.1805  | 0          |
| total_lipids_in_small_ldl                                        | -1.9604  | 0.4546  | 0          |
| total_lipids_in_small_vldl                                       | -0.8334  | 0.2238  | 2E-04      |
| total_lipids_in_vldl                                             | -0.1292  | 0.0351  | 2E-04      |
| total_lipids_in_very_large_hdl                                   | 1.122    | 0.3347  | 8E-04      |
| total_lipids_in_very_large_vldl                                  | -0.788   | 0.2294  | 6E-04      |
| total_lipids_in_very_small_vldl                                  | -0.5844  | 0.3186  | 0.0666     |
| total_phospholipids_in_lipoprotein_particles                     | -0.1576  | 0.061   | 0.0098     |
| total_triglycerides_nmr                                          | -0.1652  | 0.0533  | 0.002      |
| triglycerides_in_chylomicrons_and_extremely_large_vldl           | -0.4805  | 0.2401  | 0.0454     |
| triglycerides_in_hdl                                             | -1.0883  | 0.608   | 0.0734     |
| triglycerides_in_idl                                             | -1.3729  | 1.1195  | 0.22       |
| triglycerides_in_ldl                                             | -1.5089  | 0.7322  | 0.0393     |



|                                                                                   |          |         |             |
|-----------------------------------------------------------------------------------|----------|---------|-------------|
| triglycerides_in_large_hdl                                                        | 0.775    | 2.3349  | 0.74        |
| triglycerides_in_large_ldl                                                        | -2.1222  | 1.1585  | 0.067       |
| triglycerides_in_large_vldl                                                       | -1.3128  | 0.3383  | 1E-04       |
| triglycerides_in_medium_hdl                                                       | -2.8625  | 1.4956  | 0.0556      |
| triglycerides_in_medium_ldl                                                       | -6.9647  | 2.9493  | 0.0182      |
| triglycerides_in_medium_vldl                                                      | -1.1131  | 0.2643  | 0           |
| triglycerides_in_small_hdl                                                        | -4.799   | 1.6426  | 0.0035      |
| triglycerides_in_small_ldl                                                        | -12.7609 | 5.432   | 0.0188      |
| triglycerides_in_small_vldl                                                       | -1.4529  | 0.4927  | 0.0032      |
| triglycerides_in_vldl                                                             | -0.2104  | 0.0641  | 0.001       |
| triglycerides_in_very_large_hdl                                                   | -2.573   | 10.9259 | 0.8138      |
| triglycerides_in_very_large_vldl                                                  | -1.2159  | 0.3807  | 0.0014      |
| triglycerides_in_very_small_vldl                                                  | -1.995   | 1.3678  | 0.1447      |
| triglycerides_to_phosphoglycerides_ratio                                          | -0.3544  | 0.141   | 0.012       |
| triglycerides_to_total_lipids_in_chylomicrons_and_extremely_large_vldl_percentage | 0.0029   | 0.0023  | 0.1964      |
| triglycerides_to_total_lipids_in_idl_percentage                                   | 0.0177   | 0.0123  | 0.1496      |
| triglycerides_to_total_lipids_in_large_hdl_percentage                             | -0.0216  | 0.0109  | 0.0469      |
| triglycerides_to_total_lipids_in_large_ldl_percentage                             | 0.0435   | 0.0177  | 0.0142      |
| triglycerides_to_total_lipids_in_large_vldl_percentage                            | -0.0044  | 0.0046  | 0.3353      |
| triglycerides_to_total_lipids_in_medium_hdl_percentage                            | -0.0291  | 0.0163  | 0.0742      |
| triglycerides_to_total_lipids_in_medium_ldl_percentage                            | 0.0588   | 0.0195  | 0.0025      |
| triglycerides_to_total_lipids_in_medium_vldl_percentage                           | -0.0049  | 0.0035  | 0.1586      |
| triglycerides_to_total_lipids_in_small_hdl_percentage                             | -0.03    | 0.0224  | 0.1794      |
| triglycerides_to_total_lipids_in_small_ldl_percentage                             | 0.0176   | 0.0167  | 0.292       |
| triglycerides_to_total_lipids_in_small_vldl_percentage                            | 0        | 0.0044  | 0.9919      |
| triglycerides_to_total_lipids_in_very_large_hdl_percentage                        | -0.0172  | 0.0091  | 0.0597      |
| triglycerides_to_total_lipids_in_very_large_vldl_percentage                       | -0.0072  | 0.0034  | 0.0339      |
| triglycerides_to_total_lipids_in_very_small_vldl_percentage                       | -9E-04   | 0.0074  | 0.8984      |
| tyrosine                                                                          | -7.2349  | 2.0353  | 4E-04       |
| vldl_cholesterol                                                                  | -0.4329  | 0.1171  | 2E-04       |
| valine                                                                            | -4.1388  | 0.7392  | 2.1572E-08  |
| neutrophil_ct_over_lymphocyte_ct                                                  | 0.1446   | 0.0121  | 7.9316E-33  |
| platelet_ct_over_lymphocyte_ct                                                    | 0.0012   | 2E-04   | 8.5269E-08  |
| asp_over_ala_aminotransferase                                                     | 0.3165   | 0.0338  | 7.7711E-21  |
| non_albumin_protein                                                               | 0.0028   | 0.004   | 0.4894      |
| eGFR                                                                              | 6E-04    | 0.0154  | 0.9688      |
| Heel BMD                                                                          | -5.2377  | 0.1832  | 7.2089E-180 |

**Table S2.** The F statistic and their probabilities  $\Pr(>F)$  values of traits determined in drop-one analysis. Significance thresholds are indicated by asterisks, where three asterisks indicate  $p$ -values below 0.001/14, two indicate  $p$ -values below 0.01/14, and one asterisk indicates  $p$ -values below 0.05/14.

| Trait                                  | F statistic | $\Pr(>F)$  |
|----------------------------------------|-------------|------------|
| Heel BMD                               | 116.0749    | 2.5901E-26 |
| Vitamin D                              | 26.2202     | 3.3544E-07 |
| Neutrophil count over lymphocyte count | 15.5852     | 1E-04      |
| Concentration of small HDL particles   | 6.9742      | 0.0083     |

|                                               |        |        |
|-----------------------------------------------|--------|--------|
| <b>Albumin</b>                                | 6.0833 | 0.0137 |
| <b>Mean spheroid cell volume</b>              | 5.7844 | 0.0163 |
| <b>Gamma glutamyltransferase</b>              | 5.0162 | 0.0252 |
| <b>Urate</b>                                  | 2.2205 | 0.1364 |
| <b>Erythrocyte count</b>                      | 1.3253 | 0.2498 |
| <b>High light scatter reticulocyte count</b>  | 1.2846 | 0.2572 |
| <b>C-reactive protein</b>                     | 1.0525 | 0.3051 |
| <b>Asp over Ala aminotransferase</b>          | 1.0293 | 0.3104 |
| <b>BMI</b>                                    | 1.0146 | 0.3139 |
| <b>Lymphocyte count</b>                       | 0.9478 | 0.3304 |
| <b>SHBG</b>                                   | 0.5583 | 0.4551 |
| <b>Sodium in urine</b>                        | 0.3987 | 0.5278 |
| <b>Mean platelet volume</b>                   | 0.3771 | 0.5392 |
| <b>Concentration of medium VLDL particles</b> | 0.3452 | 0.5569 |
| <b>Platelet count over lymphocyte count</b>   | 0.2547 | 0.6138 |
| <b>IGF-1</b>                                  | 0.1503 | 0.6983 |
| <b>Leucine</b>                                | 0.0847 | 0.7711 |
| <b>Cystatin C</b>                             | 0.0802 | 0.7771 |
| <b>Platelet distribution width</b>            | 0.0555 | 0.8138 |
| <b>Potassium in urine</b>                     | 0.0319 | 0.8583 |
| <b>Platelet count</b>                         | 0.0042 | 0.9482 |
| <b>Erythrocyte distribution width</b>         | 0.0013 | 0.9711 |