

Table S1 Information of included studies

| Exposure/outcome | Participants | PubMed ID/Web source |
|-----------------------------|---------------------------------|---|
| Circulating proteins levels | 35,559 Icelanders | 34857953 |
| CRC | 14,886 cases & 622,807 controls | 34594039 |
| | 5,458 cases & 259,583 controls | https://www.finngen.fi/fi |
| Colon cancer | 3,793 cases & 410,350 controls | 32887889 |
| | 3,292 cases & 259,583 controls | https://www.finngen.fi/fi |
| Rectum cancer | 2,091 cases & 410,350 controls | 32887889 |
| | 2,017 cases & 259,583 controls | https://www.finngen.fi/fi |

CRC, colorectal cancer.

Table S2 Mendelian randomization analysis of associations of circulating proteins levels with CRC cis-pQTLs

| Protein | Beta | SE | FDR | OR | LCI | UCI |
|----------|--------------|-------------|-------------|-------------|-------------|-------------|
| ALDH3B1 | -0.304502031 | 0.018395867 | 9.49E-61 | 0.73749053 | 0.711373315 | 0.764566608 |
| ATP1B2 | -0.49104509 | 0.017910705 | 2.71E-164 | 0.611986479 | 0.590875424 | 0.633851798 |
| CASP3 | -0.214740921 | 0.049911463 | 2.91E-05 | 0.806750425 | 0.731566328 | 0.889661297 |
| CCL18 | -0.080123879 | 0.038738574 | 0.038609674 | 0.923001999 | 0.855515144 | 0.995812518 |
| CD46 | -0.143655462 | 0.009794356 | 5.43E-48 | 0.866186131 | 0.849716598 | 0.882974883 |
| ENGASE | -0.085936028 | 0.026526313 | 0.001686338 | 0.917652933 | 0.87116176 | 0.966625195 |
| FUT3 | -0.095692207 | 0.032033759 | 0.003490821 | 0.908743678 | 0.85344142 | 0.967629474 |
| GSS | -0.060981969 | 0.008265639 | 4.54E-13 | 0.940840204 | 0.925720782 | 0.956206566 |
| LGALS3BP | -0.090169431 | 0.041108144 | 0.030463855 | 0.91377635 | 0.843039561 | 0.99044844 |
| MET | -0.176444023 | 0.034438574 | 6.64E-07 | 0.8382457 | 0.783531802 | 0.896780261 |
| MFAP4 | -0.141802819 | 0.048026881 | 0.003757423 | 0.867792352 | 0.789831612 | 0.953448247 |
| MTHFSD | -0.095345112 | 0.019523593 | 2.02E-06 | 0.909059153 | 0.874930036 | 0.944519572 |
| REG4 | -0.148564884 | 0.034693585 | 3.02E-05 | 0.861944079 | 0.805280745 | 0.922594511 |
| SEPW1 | -0.070965657 | 0.004261499 | 2.24E-61 | 0.931493882 | 0.923745946 | 0.939306803 |
| SIGLEC1 | -0.481940851 | 0.05628662 | 4.30E-17 | 0.61758359 | 0.553074467 | 0.689616884 |
| AGT | 0.156404732 | 0.044271765 | 0.000637256 | 1.16929936 | 1.072113649 | 1.27529483 |
| CHRD2 | 0.324765094 | 0.061365122 | 2.89E-07 | 1.383705567 | 1.226898518 | 1.560553761 |
| CLIC5 | 0.619676186 | 0.063269819 | 5.27E-22 | 1.858326192 | 1.641593376 | 2.103673351 |
| FN1 | 0.377854553 | 0.181546179 | 0.038609674 | 1.459150698 | 1.022268362 | 2.082741519 |
| GKN2 | 0.053323916 | 0.024344865 | 0.030463855 | 1.054771247 | 1.005623735 | 1.106320729 |
| GOLM1 | 0.062174808 | 0.014229303 | 2.28E-05 | 1.06414835 | 1.034879893 | 1.094244578 |
| HHIP | 0.452466667 | 0.142039167 | 0.001947621 | 1.572185464 | 1.190138753 | 2.076873077 |
| HP | 0.07202436 | 0.031561307 | 0.025817964 | 1.074681523 | 1.010216029 | 1.14326079 |
| LILRB2 | 0.053782639 | 0.016181235 | 0.001311015 | 1.055255206 | 1.022312705 | 1.08925923 |
| NMB | 0.095595297 | 0.013509053 | 3.82E-12 | 1.100313674 | 1.071562167 | 1.129836623 |
| NQO2 | 0.040583111 | 0.005441829 | 2.73E-13 | 1.041417859 | 1.03036914 | 1.052585055 |
| PLXNB2 | 0.023309378 | 0.002993988 | 2.39E-14 | 1.023583165 | 1.017594147 | 1.029607431 |
| RNAS2 | 0.102104036 | 0.033710843 | 0.003171195 | 1.107498685 | 1.036687759 | 1.18314635 |
| SCUBE3 | 0.192611846 | 0.001413776 | 0 | 1.2124121 | 1.209057155 | 1.215776354 |
| TPST2 | 0.022671708 | 0.000848316 | 2.46E-156 | 1.022930664 | 1.021231252 | 1.024632905 |
| VNN2 | 0.054167074 | 0.010717717 | 8.95E-07 | 1.055660961 | 1.033716281 | 1.078071503 |

CRC, colorectal cancer; pQTLs, protein quantitative trait loci; SE, standard error; FDR, false discovery rate; OR, odds ratio; LCI, lower confidence interval; UCI, upper confidence interval.

Table S3 Mendelian randomization analysis of associations of circulating proteins levels with CRC trans-pQTLs

| Protein | Beta | SE | FDR | OR | LCI | UCI |
|----------|--------------|-------------|-------------|-------------|-------------|-------------|
| AGRN | -0.33997726 | 0.070079131 | 5.10E-06 | 0.711786509 | 0.620436289 | 0.81658672 |
| COL11A2 | -0.250031939 | 0.066643097 | 0.000462856 | 0.778775909 | 0.683415397 | 0.887442571 |
| CTSF | -0.231598381 | 0.077470813 | 0.003858957 | 0.793264649 | 0.681512167 | 0.923341995 |
| DCUN1D1 | -0.103891371 | 0.028621018 | 0.000632497 | 0.901323202 | 0.852153532 | 0.953329985 |
| ERAP1 | -1.5067225 | 0.498905 | 0.003858957 | 0.221635198 | 0.083360867 | 0.589271235 |
| GPNMB | -0.592210015 | 0.271112168 | 0.029968261 | 0.553103566 | 0.325110594 | 0.940983037 |
| ICAM5 | -0.039367453 | 0.000478725 | 0 | 0.961397376 | 0.960495719 | 0.962299879 |
| KNG1 | -0.424962069 | 0.03025913 | 1.21E-43 | 0.653794584 | 0.616146842 | 0.693742674 |
| LCP1 | -0.4662595 | 0.1820805 | 0.012621243 | 0.627344467 | 0.439052062 | 0.896388183 |
| NEU1 | -1.089015 | 0.333341667 | 0.002251804 | 0.33654783 | 0.175105844 | 0.646834164 |
| SNX4 | -0.200490017 | 0.054820496 | 0.000616192 | 0.818329659 | 0.734960745 | 0.911155372 |
| STXBP6 | -0.226442759 | 0.075424138 | 0.003858957 | 0.797364983 | 0.687788384 | 0.924399031 |
| SVEP1 | -0.12105921 | 0.048686654 | 0.014389324 | 0.885981499 | 0.805344573 | 0.974692377 |
| ARL2 | 0.972723333 | 0.333368333 | 0.00444379 | 2.645138252 | 1.376193563 | 5.084136824 |
| CCDC80 | 0.202962141 | 0.091841292 | 0.029118728 | 1.225026089 | 1.023218661 | 1.466635605 |
| LACRT | 0.124121826 | 0.061218291 | 0.042608398 | 1.132153788 | 1.004142532 | 1.276484323 |
| LEPR | 0.882158096 | 0.227163798 | 0.00029877 | 2.416108278 | 1.547927674 | 3.771222201 |
| LTF | 0.091501203 | 0.007255981 | 1.79E-35 | 1.095818095 | 1.080343969 | 1.111513862 |
| NEFL | 1.016513333 | 0.33343 | 0.003858957 | 2.763542394 | 1.437622249 | 5.312359745 |
| NLGN2 | 1.0498375 | 0.26823875 | 0.000292578 | 2.857186787 | 1.688920471 | 4.833570604 |
| PHGDH | 1.219816 | 0.400116 | 0.003858957 | 3.386564548 | 1.545872754 | 7.418993195 |
| PITPNA | 1.199402 | 0.400012 | 0.003858957 | 3.318132086 | 1.514944008 | 7.267595689 |
| ROBO2 | 0.422740427 | 0.039547999 | 6.61E-26 | 1.5261381 | 1.412309558 | 1.649140932 |
| SERPINA4 | 0.477707909 | 0.038091193 | 3.22E-35 | 1.612374455 | 1.496380468 | 1.737359874 |
| STATH | 0.292854286 | 0.116069752 | 0.013494169 | 1.340247483 | 1.067540679 | 1.682618145 |
| TBCA | 0.7295425 | 0.25002625 | 0.00444379 | 2.074131475 | 1.270602313 | 3.385812645 |
| TGM1 | 0.292505307 | 0.096762792 | 0.003858957 | 1.339779847 | 1.108325408 | 1.61956951 |
| TMEM52B | 0.265955486 | 0.032086806 | 5.56E-16 | 1.304676981 | 1.225152525 | 1.389363357 |
| WFDC8 | 0.15555538 | 0.035395559 | 4.02E-05 | 1.168306635 | 1.090002603 | 1.252235903 |

CRC, colorectal cancer; pQTLs, protein quantitative trait loci; SE, standard error; FDR, false discovery rate; OR, odds ratio; LCI, lower confidence interval; UCI, upper confidence interval.

Table S4 Mendelian randomization analysis of associations of circulating proteins levels with colon cancer cis-pQTLs

| Protein | Beta | SE | FDR | OR | LCI | UCI |
|-----------|--------------|-------------|-------------|-------------|-------------|-------------|
| ALDH3B1 | -0.378630029 | 0.060008334 | 9.20E-10 | 0.684798922 | 0.608811634 | 0.770270371 |
| BDNF | -0.343816442 | 0.072274644 | 4.10E-06 | 0.70905907 | 0.615404967 | 0.816965723 |
| CCDC126 | -0.050825627 | 0.014476951 | 0.000733973 | 0.950444388 | 0.923854718 | 0.977799341 |
| CRTAC1 | -0.09186536 | 0.03825231 | 0.01877394 | 0.912227964 | 0.846335109 | 0.983251018 |
| GPCPD1 | -0.145724308 | 0.029524926 | 1.84E-06 | 0.864395977 | 0.815794199 | 0.915893257 |
| HSPG2 | -0.044957722 | 0.003542393 | 3.80E-36 | 0.9560379 | 0.949423033 | 0.962698855 |
| IFI16 | -0.302406328 | 0.046766933 | 3.83E-10 | 0.739037712 | 0.674307179 | 0.809982093 |
| IGFBP7 | -0.077987745 | 0.032214124 | 0.018740617 | 0.924975762 | 0.868378649 | 0.985261627 |
| KLK11 | -0.091180667 | 0.011949217 | 1.08E-13 | 0.912852774 | 0.891721752 | 0.934484535 |
| SERPINA12 | -0.090436252 | 0.001670939 | 0 | 0.913532568 | 0.910545606 | 0.916529329 |
| SULT1A3 | -0.431857849 | 0.184018728 | 0.019795337 | 0.649301669 | 0.452695957 | 0.93129318 |
| SYK | -0.399591292 | 0.092676202 | 3.11E-05 | 0.670594067 | 0.559206397 | 0.804168917 |
| TEK | -0.08996497 | 0.034987439 | 0.012944238 | 0.913963201 | 0.853388528 | 0.978837545 |
| TESC | -0.310508768 | 0.108573806 | 0.006498153 | 0.733073897 | 0.592553907 | 0.906917213 |
| ATXN3 | 0.08322536 | 0.03536601 | 0.019795337 | 1.086786699 | 1.014005146 | 1.164792244 |
| B4GALT1 | 0.17209617 | 0.040797372 | 4.35E-05 | 1.187792058 | 1.096511 | 1.286671973 |
| CHRD2 | 0.347294286 | 0.002833253 | 0 | 1.415233147 | 1.40739589 | 1.423114048 |
| ENPEP | 0.178474483 | 0.080885784 | 0.02734901 | 1.19539238 | 1.020138443 | 1.400753939 |
| GAA | 0.067472357 | 0.004362102 | 4.39E-53 | 1.069800687 | 1.060693179 | 1.078986395 |
| IGF2R | 0.116994058 | 0.018641078 | 9.98E-10 | 1.12411275 | 1.083782834 | 1.16594343 |
| LILRA2 | 0.141431119 | 0.024902545 | 3.45E-08 | 1.151921156 | 1.097047117 | 1.209539982 |
| PPP1R14A | 0.123059299 | 0.04746256 | 0.012881028 | 1.130951483 | 1.030488211 | 1.241209015 |
| SERPINH1 | 0.296971961 | 0.108635792 | 0.009004077 | 1.345777565 | 1.087678718 | 1.665121533 |

pQTLs, protein quantitative trait loci; SE, standard error; FDR, false discovery rate; OR, odds ratio; LCI, lower confidence interval; UCI, upper confidence interval.

Table S5 Mendelian randomization analysis of associations of circulating proteins levels with colon cancer trans-pQTLs

| Protein | Beta | SE | FDR | OR | LCI | UCI |
|---------|--------------|-------------|-------------|-------------|-------------|-------------|
| ACBD6 | -0.149766699 | 0.024588598 | 3.92E-09 | 0.860908804 | 0.820402381 | 0.903415185 |
| DCUN1D1 | -0.130205743 | 0.003597239 | 4.92E-286 | 0.877914788 | 0.871746741 | 0.884126476 |
| CLPSL1 | 0.163663855 | 0.067292548 | 0.015010546 | 1.177818331 | 1.032280529 | 1.343875023 |
| MMP8 | 0.243594802 | 0.075873799 | 0.002318615 | 1.275827263 | 1.099529275 | 1.480392785 |
| NLGN2 | 0.87977 | 0.3401375 | 0.012033678 | 2.410345263 | 1.237509015 | 4.694724822 |
| PRND | 0.498899413 | 0.130901505 | 0.000322609 | 1.646907708 | 1.274217753 | 2.128603994 |
| WFDC6 | 0.239973993 | 0.093553433 | 0.012033678 | 1.271216089 | 1.058242237 | 1.527051454 |

pQTLs, protein quantitative trait loci; SE, standard error; FDR, false discovery rate; OR, odds ratio; LCI, lower confidence interval; UCI, upper confidence interval.

Table S6 Mendelian randomization analysis of associations of circulating proteins levels with rectum cancer cis-pQTLs

| Protein | Beta | SE | FDR | OR | LCI | UCI |
|----------|--------------|-------------|-------------|-------------|-------------|-------------|
| CCL15 | -0.202513464 | 0.054870426 | 0.000571389 | 0.816675487 | 0.733403318 | 0.909402554 |
| CCL18 | -0.209430655 | 0.059164335 | 0.000920945 | 0.811045879 | 0.722243636 | 0.910766653 |
| CPZ | -0.18585404 | 0.03431052 | 2.79E-07 | 0.830394791 | 0.776388174 | 0.88815818 |
| SCARF2 | -0.3782105 | 0.076044465 | 2.16E-06 | 0.685086275 | 0.590221345 | 0.795198628 |
| SERPINF2 | -0.197990577 | 0.089703478 | 0.033050247 | 0.820377584 | 0.688108057 | 0.978072227 |
| SRA1 | -0.346375922 | 0.019259871 | 5.93E-71 | 0.707246568 | 0.681046108 | 0.734454983 |
| SWAP70 | -0.25581267 | 0.065111789 | 0.000245525 | 0.774287002 | 0.681518572 | 0.879683088 |
| TXNDC5 | -0.38756042 | 0.142162737 | 0.012280683 | 0.678710625 | 0.513657086 | 0.896800854 |
| ASRGL1 | 0.324357619 | 0.165125714 | 0.049494485 | 1.383141856 | 1.000711473 | 1.911721258 |
| C1QTNF9 | 0.18721399 | 0.036567358 | 1.17E-06 | 1.205885305 | 1.122481622 | 1.295486126 |
| C5 | 0.359978695 | 0.136562538 | 0.014494754 | 1.433298878 | 1.09671146 | 1.873187021 |
| CHRD2 | 0.261432445 | 0.108012051 | 0.02109895 | 1.298789199 | 1.050986057 | 1.605019755 |
| CNTN2 | 0.723803833 | 0.219928573 | 0.002086757 | 2.062262813 | 1.340099453 | 3.173591259 |
| CPB2 | 0.378643414 | 0.061620047 | 4.61E-09 | 1.46030222 | 1.294168135 | 1.647763158 |
| CPM | 0.14468443 | 0.017487872 | 1.50E-15 | 1.155674816 | 1.116733829 | 1.195973693 |
| DECR2 | 0.257419911 | 0.036770772 | 1.96E-11 | 1.293588205 | 1.203638675 | 1.390259783 |
| F10 | 0.238942801 | 0.117199247 | 0.043357685 | 1.269905897 | 1.009275026 | 1.597840971 |
| FAS | 0.072145746 | 0.029021644 | 0.019812775 | 1.074811982 | 1.015380403 | 1.137722171 |
| FKBP1B | 0.392465747 | 0.149862354 | 0.014494754 | 1.480627148 | 1.103774349 | 1.986145768 |
| GSTM4 | 0.146560411 | 0.068603065 | 0.037548184 | 1.157844875 | 1.012171885 | 1.324483296 |
| IFNAR1 | 0.803035637 | 0.333625241 | 0.02109895 | 2.232307128 | 1.160824078 | 4.292808194 |
| PLEKHA1 | 0.268471711 | 0.130220022 | 0.042975427 | 1.307963976 | 1.013328511 | 1.688267667 |
| SPINK2 | 0.072488347 | 0.030236327 | 0.02109895 | 1.075180277 | 1.013312985 | 1.140824844 |

pQTLs, protein quantitative trait loci; SE, standard error; FDR, false discovery rate; OR, odds ratio; LCI, lower confidence interval; UCI, upper confidence interval.

Table S7 Mendelian randomization analysis of associations of circulating proteins levels with rectum cancer trans-pQTLs

| Protein | Beta | SE | FDR | OR | LCI | UCI |
|---------|--------------|-------------|-------------|-------------|-------------|-------------|
| C1R | -0.163300367 | 0.025995558 | 1.27E-09 | 0.849336038 | 0.807145233 | 0.893732225 |
| CCL25 | -0.304158199 | 0.109204017 | 0.009935285 | 0.737744147 | 0.595592797 | 0.91382305 |
| CTSZ | -0.091282464 | 0.04549173 | 0.044795182 | 0.912759853 | 0.834897551 | 0.99788357 |
| GPNMB | -0.995553408 | 0.493637028 | 0.044795182 | 0.369518893 | 0.140424966 | 0.97236422 |
| ICAM5 | -0.122072427 | 0.007139057 | 1.43E-64 | 0.885084262 | 0.872785918 | 0.897555901 |
| ISG15 | -0.323048744 | 0.139820962 | 0.026427087 | 0.723938566 | 0.550406694 | 0.952181455 |
| MAPK8 | -0.498861285 | 0.032004882 | 5.27E-54 | 0.607221719 | 0.570301076 | 0.646532561 |
| MINPP1 | -0.244499011 | 0.085874576 | 0.009312242 | 0.783096763 | 0.661785906 | 0.926644908 |
| MRC1 | -0.342986515 | 0.005756247 | 0 | 0.709647781 | 0.701686357 | 0.717699536 |
| PCDH10 | -0.119768878 | 0.05178165 | 0.026427087 | 0.887125447 | 0.80150753 | 0.981889165 |
| SEMA7A | -0.367396677 | 0.15787497 | 0.026427087 | 0.692534878 | 0.508224694 | 0.943686056 |
| STOML1 | -0.399132781 | 0.082755292 | 4.47E-06 | 0.670901612 | 0.570448062 | 0.789044619 |
| AKR1C3 | 0.486936091 | 0.230155208 | 0.038415255 | 1.627322605 | 1.036481582 | 2.554969532 |
| DIABLO | 0.371916561 | 0.143197292 | 0.014879926 | 1.450511947 | 1.095542713 | 1.920495553 |
| DLX4 | 0.326111213 | 0.020941038 | 5.27E-54 | 1.385569454 | 1.329850831 | 1.443622598 |
| LEPR | 0.996763196 | 0.306068282 | 0.003059752 | 2.709497507 | 1.487161639 | 4.936502225 |
| NT5E | 0.174612743 | 0.063228984 | 0.009935285 | 1.190784987 | 1.051990343 | 1.347891543 |
| PLXND1 | 0.267940816 | 0.119131407 | 0.029099533 | 1.307269768 | 1.035043297 | 1.651094454 |
| RACGAP1 | 0.036101105 | 0.011554391 | 0.004230787 | 1.036760663 | 1.013545418 | 1.060507653 |

pQTLs, protein quantitative trait loci; SE, standard error; FDR, false discovery rate; OR, odds ratio; LCI, lower confidence interval; UCI, upper confidence interval.

Table S8 Phewas of FUT3

| Beta | P | SE | rsid | EAF | Trait |
|-------------|-----------|-------------|--------------|----------|--|
| 0.8088 | 1.32E-208 | 0.0262 | rs2608894 | 0.7567 | Galactoside 3(4)-L-fucosyltransferase |
| 0.848 | 5.25E-196 | 0.0284 | rs812936 | 0.81494 | Galactoside 3(4)-L-fucosyltransferase |
| 0.5188 | 2.00E-82 | 0.027 | rs4807816 | 0.27648 | Galactoside 3(4)-L-fucosyltransferase |
| 0.5097 | 9.77E-76 | 0.0277 | rs4807052 | 0.25924 | Galactoside 3(4)-L-fucosyltransferase |
| 0.9298 | 8.78E-73 | 0.0473422 | rs778986 | – | Fucosyltransferase 3 |
| 0.4694 | 2.40E-59 | 0.0289 | rs11668191 | 0.23341 | Galactoside 3(4)-L-fucosyltransferase |
| 0.4345 | 2.34E-51 | 0.0288 | rs2608894 | 0.7567 | Alpha-(1,3)-fucosyltransferase 5 |
| -0.6815 | 7.24E-45 | 0.0485 | rs3894326 | 0.06695 | Galactoside 3(4)-L-fucosyltransferase |
| -0.5778 | 5.62E-43 | 0.042 | rs28362459 | 0.09191 | Alpha-(1,3)-fucosyltransferase 5 |
| -0.5644 | 5.37E-41 | 0.0421 | rs28362459 | 0.09191 | Galactoside 3(4)-L-fucosyltransferase |
| 0.279 | 8.32E-30 | 0.0246 | rs2637193 | 0.4487 | Galactoside 3(4)-L-fucosyltransferase |
| 0.2752 | 4.47E-29 | 0.0246 | rs2608892 | 0.45119 | Galactoside 3(4)-L-fucosyltransferase |
| 0.276 | 1.02E-28 | 0.0248 | rs2637194 | 0.45039 | Galactoside 3(4)-L-fucosyltransferase |
| 0.2718 | 1.70E-28 | 0.0245 | rs2608893 | 0.45026 | Galactoside 3(4)-L-fucosyltransferase |
| 0.3041 | 1.41E-27 | 0.0279 | rs4807816 | 0.27648 | Alpha-(1,3)-fucosyltransferase 5 |
| 0.2967 | 3.24E-25 | 0.0286 | rs4807052 | 0.25924 | Alpha-(1,3)-fucosyltransferase 5 |
| 0.3231 | 1.15E-24 | 0.0315 | rs812936 | 0.81494 | Alpha-(1,3)-fucosyltransferase 5 |
| -0.5028 | 1.51E-24 | 0.0492 | rs3894326 | 0.06695 | Alpha-(1,3)-fucosyltransferase 5 |
| -0.487 | 4.57E-24 | 0.0481 | rs150092813 | 0.07289 | Galactoside 3(4)-L-fucosyltransferase |
| 0.3194 | 1.15E-23 | 0.0318 | rs778986 | 0.82324 | Alpha-(1,3)-fucosyltransferase 5 |
| -0.4801 | 2.29E-23 | 0.0482 | rs150092813 | 0.07289 | Alpha-(1,3)-fucosyltransferase 5 |
| -0.7687 | 3.55E-21 | 0.0814 | rs28742587 | 0.02773 | Alpha-(1,3)-fucosyltransferase 5 |
| -0.8808 | 7.24E-21 | 0.094 | rs3745635 | 0.01762 | Alpha-(1,3)-fucosyltransferase 5 |
| -0.6757 | 1.10E-20 | 0.0708429 | rs28362459 | – | Fucosyltransferase 3 |
| 0.2315 | 4.90E-20 | 0.0253 | rs28362450 | 0.43351 | Galactoside 3(4)-L-fucosyltransferase |
| 0.2286 | 1.45E-19 | 0.0253 | rs28362451 | 0.43026 | Galactoside 3(4)-L-fucosyltransferase |
| 0.2248 | 7.76E-19 | 0.0254 | rs11673407 | 0.43525 | Galactoside 3(4)-L-fucosyltransferase |
| 0.2398 | 7.41E-16 | 0.0297 | rs11668191 | 0.23341 | Alpha-(1,3)-fucosyltransferase 5 |
| -0.7087 | 6.03E-14 | 0.0944 | rs3745635 | 0.01762 | Galactoside 3(4)-L-fucosyltransferase |
| -0.036267 | 1.18E-13 | 0.0048884 | rs3894326 | 0.060952 | Aspartate aminotransferase |
| -0.4723 | 1.95E-13 | 0.0642 | rs34493282 | 0.04807 | Galactoside 3(4)-L-fucosyltransferase |
| 0.7217 | 4.57E-13 | 0.0997 | rs117095068 | 0.01808 | Alpha-(1,3)-fucosyltransferase 5 |
| -0.2102 | 1.20E-12 | 0.0296 | rs2608894 | 0.7567 | Protein FAM3B |
| -0.8854 | 7.59E-12 | 0.1293 | rs569641642 | 0.01081 | Alpha-(1,3)-fucosyltransferase 5 |
| -0.0934 | 1.35E-11 | 0.0138 | rs2608894 | 0.7599 | Cholelithiasis, broad definition with cholecystitis |
| 0.027666 | 1.57E-11 | 0.0041038 | rs28362459 | 0.087668 | Alkaline phosphatase |
| -0.8747 | 2.57E-11 | 0.1311 | rs535367747 | 0.01028 | Alpha-(1,3)-fucosyltransferase 5 |
| -0.031301 | 3.46E-11 | 0.0047242 | rs150092813 | 0.064788 | Aspartate aminotransferase |
| -0.00353134 | 8.98E-11 | 0.000544682 | rs2608894 | 0.766543 | Disorders of gallbladder, biliary tract and pancreas |
| -0.017199 | 1.28E-10 | 0.002675 | rs2608894 | 0.76652 | Gamma glutamyltransferase |
| -0.5266 | 1.32E-10 | 0.082 | rs28742587 | 0.02773 | Galactoside 3(4)-L-fucosyltransferase |
| 0.030681 | 1.75E-10 | 0.0048077 | rs150092813 | 0.064769 | Alkaline phosphatase |
| 0.024898 | 2.03E-10 | 0.0039154 | rs28362459 | 0.08767 | Gamma glutamyltransferase |
| 0.1094 | 2.76E-10 | 0.0173 | rs3894326 | 0.0664 | E-selectin levels |
| -0.4053 | 3.09E-10 | 0.0644 | rs34493282 | 0.04807 | Alpha-(1,3)-fucosyltransferase 5 |
| -0.064829 | 6.06E-10 | 0.010475 | rs535367747 | 0.013814 | Aspartate aminotransferase |
| -0.064825 | 6.07E-10 | 0.010475 | rs569641642 | 0.013814 | Aspartate aminotransferase |
| -0.0781 | 7.26E-10 | 0.0127 | rs2608894 | 0.7599 | Disorders of gallbladder, biliary tract and pancreas |
| 0.1536 | 7.41E-10 | 0.0249 | rs2637193 | 0.4487 | Alpha-(1,3)-fucosyltransferase 5 |
| 0.7592 | 1.00E-09 | 0.1242 | rs201556334 | 0.98881 | Alpha-(1,3)-fucosyltransferase 5 |
| -0.066112 | 1.09E-09 | 0.010846 | rs201556334 | 0.01317 | Aspartate aminotransferase |
| 0.012706 | 1.42E-09 | 0.002098 | rs874232 | 0.427878 | basophil cell count |
| -0.0818 | 1.53E-09 | 0.0135 | rs4807816 | 0.2755 | Cholelithiasis |
| -0.0818 | 1.59E-09 | 0.0135 | rs4807052 | 0.2755 | Cholelithiasis |
| 0.027663 | 1.63E-09 | 0.0045868 | rs150092813 | 0.064771 | Gamma glutamyltransferase |
| -0.0796 | 1.97E-09 | 0.0133 | rs4807816 | 0.2755 | Cholelithiasis, broad definition with cholecystitis |
| 0.0146054 | 2.02E-09 | 0.00243564 | rs874232 | 0.424927 | Basophil percentage |
| -0.0796 | 2.03E-09 | 0.0133 | rs4807052 | 0.2755 | Cholelithiasis, broad definition with cholecystitis |
| -0.1766 | 2.63E-09 | 0.0296 | rs2608894 | 0.7567 | Lactoperoxidase |
| -0.00286694 | 3.00E-09 | 0.000483328 | rs2608894 | 0.764256 | Operation code: cholecystectomy/gall bladder removal |
| 0.64664 | 4.03E-09 | 0.10992 | rs28362459 | 0.087668 | Alkaline phosphatase |
| 0.1501 | 4.27E-09 | 0.0256 | rs11673407 | 0.43525 | Alpha-(1,3)-fucosyltransferase 5 |
| 0.2286 | 4.27E-09 | 0.0389 | rs34304528 | 0.14126 | Alpha-(1,3)-fucosyltransferase 5 |
| 0.0883 | 4.54E-09 | 0.0151 | rs28362459 | 0.1116 | E-selectin levels |
| 0.75175 | 5.29E-09 | 0.12877 | rs150092813 | 0.064769 | Alkaline phosphatase |
| 0.2871 | 7.59E-09 | 0.0497 | rs3894326 | 0.06695 | Lactoperoxidase |
| 0.1451 | 8.13E-09 | 0.0252 | rs2637194 | 0.45039 | Alpha-(1,3)-fucosyltransferase 5 |
| -0.085 | 8.49E-09 | 0.0148 | rs778986 | 0.8037 | Cholelithiasis, broad definition with cholecystitis |
| -0.0867 | 8.74E-09 | 0.0151 | rs778986 | 0.8037 | Cholelithiasis |
| 0.1424 | 1.12E-08 | 0.0249 | rs2608892 | 0.45119 | Alpha-(1,3)-fucosyltransferase 5 |
| 0.1419 | 1.17E-08 | 0.0249 | rs2608893 | 0.45026 | Alpha-(1,3)-fucosyltransferase 5 |
| 0.1417 | 1.35E-08 | 0.025 | rs2561796 | 0.45067 | Alpha-(1,3)-fucosyltransferase 5 |
| 0.1454 | 1.50E-08 | 0.02568 | rs28362466 | 0.8324 | Alkaline phosphatase |
| 0.018183 | 1.59E-08 | 0.003215 | rs1568412839 | 0.12794 | basophil cell count |
| 0.14 | 1.82E-08 | 0.02488 | rs28362463 | 0.8187 | Alkaline phosphatase |
| 0.0207743 | 2.36E-08 | 0.0037206 | rs34304528 | 0.127684 | Basophil percentage |
| -0.0157811 | 2.40E-08 | 0.00282838 | rs778986 | 0.829658 | Red cell distribution width |
| 0.1415 | 2.82E-08 | 0.0255 | rs28362450 | 0.43351 | Alpha-(1,3)-fucosyltransferase 5 |
| -0.718 | 3.09E-08 | 0.1297 | rs569641642 | 0.01081 | Galactoside 3(4)-L-fucosyltransferase |
| 0.1387 | 3.24E-08 | 0.0251 | rs28742594 | 0.44568 | Alpha-(1,3)-fucosyltransferase 5 |
| 0.1404 | 3.55E-08 | 0.0255 | rs28362451 | 0.43026 | Alpha-(1,3)-fucosyltransferase 5 |
| -0.022103 | 4.26E-08 | 0.0040334 | rs28362459 | 0.087676 | Aspartate aminotransferase |

Table S9 Phewas of CHRDL2

| SE | P | Beta | rsid | EAF | Trait |
|------------|----------|-------------|-------------|------------|---|
| 0.0609 | 5.75E-26 | -0.6419 | rs11607100 | 0.04167 | Chordin-like protein 2 |
| 0.0602 | 1.78E-24 | 0.6152 | rs141934331 | 0.95587 | Chordin-like protein 2 |
| 0.0628 | 1.55E-23 | -0.6275 | rs535025308 | 0.0409 | Chordin-like protein 2 |
| 0.0016559 | 3.30E-17 | -0.0139672 | rs11236225 | 0.202108 | Standing height |
| 0.00134066 | 1.90E-15 | 0.0106555 | rs12417156 | 0.396332 | Standing height |
| 0.00134376 | 2.80E-15 | 0.0106162 | rs56187629 | 0.396653 | Standing height |
| 0.00133509 | 5.70E-15 | 0.0104284 | rs4944943 | 0.399955 | Standing height |
| 0.00134659 | 1.00E-14 | 0.010416 | rs12419371 | 0.400094 | Standing height |
| 0.00218907 | 2.54E-14 | -0.0166807 | rs73490624 | 0.199152 | Standing height |
| 0.00148735 | 7.40E-14 | 0.0111256 | rs28515900 | 0.311766 | Standing height |
| 0.0068791 | 1.72E-13 | 0.0507825 | rs190338930 | 0.00170374 | Underlying (primary) cause of death: ICD10: E85.4 Organ-limited amyloidosis |
| 0.00131775 | 2.70E-13 | 0.00963287 | rs4944944 | 0.550734 | Standing height |
| 0.00137838 | 3.00E-13 | -0.0100518 | rs7951634 | 0.35777 | Standing height |
| 0.00131284 | 3.20E-13 | 0.00956264 | rs12576444 | 0.484623 | Standing height |
| 0.0024 | 5.19E-13 | -0.0173 | rs11236225 | 0.2019 | Appendicular lean mass |
| 0.0615 | 1.78E-12 | -0.4334 | rs11607100 | 0.04167 | Bone morphogenetic protein 6 |
| 0.00134088 | 3.20E-12 | 0.0093448 | rs76059845 | 0.421656 | Standing height |
| 0.00372331 | 3.50E-12 | 0.0258975 | rs11236228 | 0.042062 | Hand grip strength (left) |
| 0.00369155 | 1.10E-11 | 0.0250703 | rs34695217 | 0.042198 | Hand grip strength (left) |
| 0.00218893 | 2.79E-11 | -0.0145729 | rs11236225 | 0.200413 | Standing height |
| 0.0608 | 3.89E-11 | 0.4017 | rs141934331 | 0.95587 | Bone morphogenetic protein 6 |
| 0.00176778 | 4.76E-11 | 0.0116295 | rs968305 | 0.400646 | Standing height |
| 0.00176977 | 6.05E-11 | 0.0115793 | rs56187629 | 0.400456 | Standing height |
| 0.00176588 | 6.15E-11 | 0.0115495 | rs12417156 | 0.400123 | Standing height |
| 0.00172899 | 8.42E-11 | 0.0112266 | rs1433771 | 0.503118 | Standing height |
| 0.00177343 | 1.99E-10 | 0.0112828 | rs12419371 | 0.403112 | Standing height |
| 0.00175882 | 2.33E-10 | 0.0111473 | rs4944943 | 0.403335 | Standing height |
| 0.00179584 | 3.16E-10 | 0.0112973 | rs61897000 | 0.361401 | Standing height |
| 0.0615 | 3.98E-10 | -0.3846 | rs11236228 | 0.04378 | Bone morphogenetic protein 6 |
| 0.00178327 | 4.50E-10 | 0.0111203 | rs7948433 | 0.400821 | Standing height |
| 0.00174647 | 5.45E-10 | 0.0108381 | rs55837439 | 0.56831 | Standing height |
| 0.00179812 | 6.57E-10 | 0.0111058 | rs11236233 | 0.361846 | Standing height |
| 0.00172968 | 1.32E-09 | 0.0104899 | rs12576444 | 0.487015 | Standing height |
| 0.00181969 | 1.45E-09 | -0.0110084 | rs4944942 | 0.350861 | Standing height |
| 0.0018193 | 2.35E-09 | -0.0108638 | rs7951634 | 0.355308 | Standing height |
| 0.00373782 | 3.60E-09 | 0.0220553 | rs61389091 | 0.041752 | Hand grip strength (right) |
| 0.00371048 | 4.10E-09 | 0.0218223 | rs76136269 | 0.04222 | Hand grip strength (right) |
| 0.00369614 | 7.10E-09 | 0.0213952 | rs34695217 | 0.042214 | Hand grip strength (right) |
| 0.00372818 | 8.00E-09 | 0.0215045 | rs11236228 | 0.042074 | Hand grip strength (right) |
| 0.00173828 | 1.01E-08 | 0.00995995 | rs4944944 | 0.553075 | Standing height |
| 0.00143974 | 2.30E-08 | -0.00804864 | rs66684251 | 0.305403 | Standing height |
| 0.00176701 | 2.70E-08 | 0.00982475 | rs76059845 | 0.42458 | Standing height |
| 0.00150643 | 3.20E-08 | 0.00833402 | rs1433771 | 0.500448 | Sitting height |
| 0.00439857 | 3.57E-08 | 0.0242414 | rs61389091 | 0.0418447 | Hand grip strength (left) |
| 0.00436576 | 3.66E-08 | 0.0240408 | rs76136269 | 0.0422985 | Hand grip strength (left) |
| 0.00151968 | 4.00E-08 | 0.00834165 | rs55837439 | 0.565004 | Sitting height |
| 0.0020149 | 4.77E-08 | -0.0110013 | rs73490624 | 0.199152 | Leg predicted mass (right) |

FUT3, fucosyltransferase 3; SE, standard error; EAF, effective allele frequency.

Table S10 Phewas of ENPEP

| Variant and risk allele | P value | EAF | Beta | CI | Trait(s) |
|--|----------|-------------|---------------------------|--------------------------|---|
| rs6848906- T | 1E10-8 | 0.1864 | 0.1817 mmHg increase | [0.12–0.24] | pulse pressure measurement |
| rs1879057- C | 5E10-13 | 0.26108 | 0.18 unit decrease | [0.13–0.23] | serum metabolite measurement |
| rs2348206- G | 8E10-11 | 0.179616 | 0.186 unit increase | [0.13–0.24] | serum metabolite measurement |
| rs6825911- C | 3E10-6 | 0.262036474 | 0.25042096 unit increase | [0.14–0.36] | mean arterial pressure |
| rs55821297- G | 4E10-6 | 0.770687 | 0.435 unit increase | [0.25–0.62] | eye color |
| rs6825911- T | 3E10-6 | 0.47 | 0.3608 unit decrease | [0.21–0.51] | systolic blood pressure |
| rs4834497- T | 2E10-8 | 0.5853 | 0.3714 unit decrease | [0.24–0.5] | systolic blood pressure |
| rs2881854- A | 7E10-9 | 0.6006 | 0.2442 unit decrease | [0.16–0.33] | diastolic blood pressure |
| rs2881854- A | 7E10-9 | 0.6006 | 0.2727 unit decrease | [0.18–0.36] | mean arterial pressure |
| rs6825911- T | 2E10-6 | 0.4718 | 0.26 unit decrease | [0.15–0.37] | mean arterial pressure |
| rs7685862- C | 6E10-12 | 0.203951 | 0.06873241 unit increase | [0.049–0.088] | Calcium channel blocker use measurement |
| rs13118687- A | 2E10-12 | 0.470423 | 0.042658705 unit decrease | [0.031–0.055] | Agents acting on the renin-angiotensin system use measurement |
| rs80303578- ? | 6E10-7 | NR | 1.23737 unit increase | [0.76–1.72] | creatinine measurement |
| rs33966350- A | 5E10-10 | 0.012401 | 0.2244912 unit increase | [0.15–0.3] | Calcium channel blocker use measurement |
| rs192667187- C | 2E10-9 | 0.008947 | 0.52 unit increase | [0.35–0.69] | atrial fibrillation |
| rs192833524- T | 9E10-10 | 0.009705 | 0.52 unit increase | [0.35–0.69] | atrial fibrillation |
| rs147535836- ? | 3E10-6 | NR | 1.1076565 unit decrease | [0.65–1.57] | nucleotide measurement |
| rs143212590- T | 3E10-16 | 0.04 | 1.3 unit increase | [0.99–1.61] | protein measurement |
| rs13124075- ? | 6E10-9 | NR | 0.453787 unit decrease | – | systolic blood pressure |
| rs10004516- ? | 1E10-7 | NR | 0.1628 unit increase | – | aspartate measurement |
| rs2348427- T | 5E10-8 | NR | – | – | hypertension, COVID-19 |
| rs2348206- A | 1E10-12 | NR | 0.0172 unit decrease | [0.012–0.022] | diastolic blood pressure |
| rs13124075- ? | 6E10-12 | NR | 0.348409 unit decrease | – | diastolic blood pressure |
| rs13118687- A | 1E10-11 | NR | 0.2466 unit decrease | [0.18–0.32] | systolic blood pressure |
| rs6533521- ? | 1E10-17 | NR | 0.014987 unit decrease | [0.012–0.018] | Antihypertensive use measurement |
| rs2348206- A | 1E10-15 | NR | 0.0188 unit decrease | [0.014–0.023] | mean arterial pressure |
| rs13124075- ? | 1E10-11 | NR | 0.374561 unit decrease | – | mean arterial pressure |
| rs6823889- A | 4E10-10 | NR | 0.0481 unit decrease | [0.033–0.063] | Diuretic use measurement |
| rs6848906- C | 8E10-14 | NR | 0.0504 unit decrease | [0.037–0.064] | Calcium channel blocker use measurement |
| rs13118687- A | 4E10-13 | NR | 0.0358 unit decrease | [0.026–0.045] | Agents acting on the renin-angiotensin system use measurement |
| rs1879056- T | 3E10-16 | NR | 0.2171 unit decrease | [0.17–0.27] | diastolic blood pressure |
| rs33966350- A | 2E10-152 | 0.01 | 1.594 unit decrease | [1.47–1.71] | protein measurement |
| rs3796879- T | 6E10-17 | 0.08 | 0.201 unit increase | [0.15–0.25] | protein measurement |
| rs6833731- A | 1E10-149 | 0.33 | 0.352 unit increase | [0.32–0.38] | protein measurement |
| rs1879056- T | 9E10-46 | 0.8 | 0.23 unit increase | [0.2–0.26] | protein measurement |
| rs7685862- ? | 7E10-13 | NR | – | – | cardiovascular disease |
| rs6815273- A | 6E10-18 | 0.3927 | 0.3283 mmHg decrease | [0.25–0.4] | systolic blood pressure |
| rs11941078- C | 2E10-6 | 0.145914083 | – | [1.061939155–1.15695976] | lung carcinoma |
| rs13113591- T | 4E10-6 | 0.37 | 0.012 unit increase | NR | response to bronchodilator, FEV/FEC ratio |
| rs10488889- A | 4E10-6 | NR | – | – | attempted suicide |
| rs10488888- C | 4E10-6 | NR | – | – | attempted suicide |
| rs244017- T | 8E10-11 | 0.776 | – | [1.04–1.08] | atrial fibrillation |
| rs190797076- G | 4E10-6 | 0.0041 | 0.6349 unit increase | [0.37–0.9] | cognitive decline measurement |
| rs13113591- T | 1E10-17 | 0.349 | 0.018 unit increase | – | response to bronchodilator, FEV/FEC ratio |
| rs190797076- G | 9E10-7 | 0.0041 | 0.6743 unit increase | [0.41–0.94] | cognitive decline measurement |
| rs13148252- G | 6E10-6 | 0.745779246 | 0.171 unit decrease | [0.097–0.245] | serum IgG glycosylation measurement |
| rs244040- A | 2E10-6 | 0.1415 | – | [1.339–2.006] | Ischemic stroke |
| rs34297584- A | 2E10-11 | NR | 0.5281 unit increase | [0.37–0.68] | diastolic blood pressure |
| rs6815273- A | 2E10-12 | NR | 0.0136 unit decrease | [0.0099–0.0173] | systolic blood pressure |
| rs1996603- A | 2E10-6 | 0.779 | 0.450736 unit increase | [0.27–0.63] | eye color |
| rs243946- T | 8E10-6 | 0.480921 | 0.339 unit decrease | [0.19–0.49] | eye color |
| rs10033366- T | 3E10-8 | 0.2169 | 0.0903 unit increase | [0.059–0.122] | hypertension |
| rs6825911- T | 5E10-6 | 0.4718 | 0.0633 unit decrease | [0.036–0.091] | hypertension |
| rs33966350- A | 2E10-11 | 0.01 | 1.661 unit increase | [1.17–2.15] | systolic blood pressure |
| rs6825911- C | 7E10-8 | 0.51 | 0.6 mm Hg increase | [0.38–0.82] | systolic blood pressure |
| rs6825911- C | 9E10-9 | 0.51 | 0.39 mm Hg increase | [0.25–0.53] | diastolic blood pressure |
| rs2087160- G | 7E10-13 | 0.207 | 0.124 unit decrease | [NR] | metabolite measurement |
| rs139051778- G | 4E10-9 | 0.0119741 | 0.16301987 unit increase | [0.11–0.22] | Agents acting on the renin-angiotensin system use measurement |
| rs13134008- G | 9E10-9 | 0.425252 | 0.045851182 unit decrease | [0.03–0.061] | Diuretic use measurement |
| rs13113591- T | 9E10-14 | 0.351 | 0.074 unit increase | NR | forced expiratory volume, response to bronchodilator |
| rs4555715- A | 3E10-6 | 0.07516 | – | – | pursuit maintenance gain measurement |
| rs6533515- ? | 2E10-16 | NR | – | – | systolic blood pressure |

ENPEP, aminopeptidase A; EAF, effective allele frequency; CI, confidence interval.

Table S11 Phewas of ASRGL1

| Beta | P | SE | rsid | EAF | Trait |
|------------|----------|------------|-------------|-----------|--|
| 0.164479 | 2.20E-12 | 0.023226 | rs74810260 | 0.075815 | Ratio of bisallylic groups to double bonds |
| 0.0453772 | 2.90E-12 | 0.00663345 | – | 0.896863 | Degree of unsaturation |
| 0.160377 | 4.41E-12 | 0.022968 | rs76382649 | 0.079234 | Ratio of bisallylic groups to double bonds |
| 0.105602 | 1.67E-11 | 0.015553 | rs192562757 | 0.285374 | Ratio of bisallylic groups to double bonds |
| –0.101103 | 4.00E-11 | 0.0154913 | rs145347066 | 0.017744 | Degree of unsaturation |
| 0.156581 | 4.00E-11 | 0.023538 | rs74810260 | 0.075771 | Ratio of bisallylic groups to total fatty acids |
| 0.151285 | 1.12E-10 | 0.023286 | rs76382649 | 0.079123 | Ratio of bisallylic groups to total fatty acids |
| 0.0743584 | 2.30E-10 | 0.0116945 | rs11606114 | 0.0299 | Degree of unsaturation |
| 0.0729612 | 3.80E-10 | 0.011632 | rs117829209 | 0.030375 | Degree of unsaturation |
| 0.14086 | 3.90E-10 | 0.0228072 | rs80200394 | 0.008402 | Omega-3 fatty acids |
| 0.0491677 | 4.00E-10 | 0.00788258 | – | 0.909069 | Degree of unsaturation |
| –0.084084 | 5.18E-10 | 0.013532 | rs2513051 | 0.0068658 | Gamma glutamyltransferase |
| 0.0760102 | 7.10E-10 | 0.0120654 | rs11606114 | 0.0299 | Ratio of omega-3 fatty acids to total fatty acids |
| –0.0560512 | 7.30E-10 | 0.00920516 | rs72923236 | 0.051372 | Omega-3 fatty acids |
| 0.082529 | 7.85E-10 | 0.013424 | rs11231062 | 0.993026 | Gamma glutamyltransferase |
| –0.138884 | 8.20E-10 | 0.0229324 | rs80200394 | 0.008402 | Ratio of omega-6 fatty acids to omega-3 fatty acids |
| 0.082382 | 8.81E-10 | 0.01344 | rs7127401 | 0.993062 | Gamma glutamyltransferase |
| 0.195313 | 1.02E-09 | 0.031712 | rs181065888 | 0.04286 | Ratio of bisallylic groups to double bonds |
| –0.0967097 | 1.10E-09 | 0.0159827 | rs145347066 | 0.017744 | Ratio of omega-3 fatty acids to total fatty acids |
| 0.0743469 | 1.20E-09 | 0.012001 | rs117829209 | 0.030375 | Ratio of omega-3 fatty acids to total fatty acids |
| 0.0361059 | 1.40E-09 | 0.00617972 | rs11608211 | 0.113372 | Degree of unsaturation |
| 0.0549524 | 1.90E-09 | 0.00932484 | – | 0.949686 | Omega-3 fatty acids |
| 0.0348221 | 3.20E-09 | 0.00611745 | rs11605965 | 0.115667 | Degree of unsaturation |
| –0.033349 | 3.75E-09 | 0.0056571 | rs116996749 | 0.040056 | Gamma glutamyltransferase |
| 0.054588 | 3.80E-09 | 0.00925571 | rs72923236 | 0.051372 | Ratio of omega-6 fatty acids to omega-3 fatty acids |
| 0.0370285 | 3.90E-09 | 0.0063115 | rs11605965 | 0.115667 | Ratio of omega-3 fatty acids to total fatty acids |
| 0.0403398 | 4.30E-09 | 0.00684387 | – | 0.896863 | Ratio of omega-3 fatty acids to total fatty acids |
| 0.0345187 | 4.30E-09 | 0.00610925 | rs72472161 | 0.11601 | Degree of unsaturation |
| 0.132084 | 4.50E-09 | 0.0227369 | rs80200394 | 0.008402 | Ratio of omega-3 fatty acids to total fatty acids |
| –0.136581 | 4.69E-09 | 0.023222 | rs74810260 | 0.075807 | Average number of methylene groups per double bond |
| 0.135195 | 5.20E-09 | 0.022972 | rs76382649 | 0.079235 | Other polyunsaturated fatty acids than 18:2 |
| 0.0364488 | 6.80E-09 | 0.00630304 | rs72472161 | 0.11601 | Ratio of omega-3 fatty acids to total fatty acids |
| –0.358799 | 7.58E-09 | 0.061633 | rs188815973 | 0.012745 | Other polyunsaturated fatty acids than 18:2 |
| 0.091764 | 7.97E-09 | 0.015791 | rs192562757 | 0.285293 | Ratio of bisallylic groups to total fatty acids |
| 0.0366147 | 9.30E-09 | 0.00637575 | rs11608211 | 0.113372 | Ratio of omega-3 fatty acids to total fatty acids |
| –0.0522525 | 9.30E-09 | 0.00917681 | rs72923236 | 0.051372 | Ratio of omega-3 fatty acids to total fatty acids |
| 0.0463597 | 9.60E-09 | 0.00813263 | – | 0.909069 | Ratio of omega-3 fatty acids to total fatty acids |
| –0.0536153 | 9.90E-09 | 0.00937605 | – | 0.949686 | Ratio of omega-6 fatty acids to omega-3 fatty acids |
| 0.185722 | 9.98E-09 | 0.032172 | rs181065888 | 0.04271 | Ratio of bisallylic groups to total fatty acids |
| –0.101456 | 1.10E-08 | 0.0177424 | rs192357698 | 0.006373 | Heel quantitative ultrasound index (QUI), direct entry |
| –0.012907 | 1.15E-08 | 0.0022616 | rs35105438 | 0.40222 | Gamma glutamyltransferase |
| 0.0803385 | 1.20E-08 | 0.0139892 | rs191756451 | 0.022184 | Ratio of omega-3 fatty acids to total fatty acids |
| 0.0517049 | 1.90E-08 | 0.00929612 | – | 0.949686 | Ratio of omega-3 fatty acids to total fatty acids |
| 0.0781497 | 2.00E-08 | 0.0135591 | rs191756451 | 0.022184 | Degree of unsaturation |
| –0.348275 | 2.15E-08 | 0.061669 | rs188815973 | 0.012748 | Ratio of bisallylic groups to double bonds |
| –0.128424 | 2.55E-08 | 0.022964 | rs76382649 | 0.079224 | Average number of methylene groups per double bond |
| 0.129539 | 3.15E-08 | 0.023235 | rs74810260 | 0.075823 | Other polyunsaturated fatty acids than 18:2 |
| 0.124822 | 3.49E-08 | 0.022616 | rs74810260 | 0.068937 | Average number of double bonds in a fatty acid chain |
| –0.0688192 | 4.10E-08 | 0.0121691 | rs11606114 | 0.0299 | Ratio of omega-6 fatty acids to omega-3 fatty acids |

ASRGL1, asparaginase-like protein 1; SE, standard error; EAF, effective allele frequency.

Table S12 Identification of druggable targets

| Target | Drug name | Status |
|--------|-----------------------------|--|
| IGF2R | alpha-D-mannose 6-phosphate | Experimental |
| | Mecasermin | Approved, investigational |
| | Cerliponase alfa | Approved, investigational |
| | Mecasermin rinfabate | Approved |
| | Avalglucosidase alfa | Approved, investigational |
| | Cipaglucoisidase alfa | Investigational |
| ENPEP | Glutamic acid | Approved, nutraceutical |
| ASRGL1 | Aspartic acid | Approved, nutraceutical |
| | Asparagine | Approved, investigational, nutraceutical |

IGF2R, insulin-like growth factor 2 receptor; ENPEP, aminopeptidase A; ASRGL1, asparaginase-like protein 1.