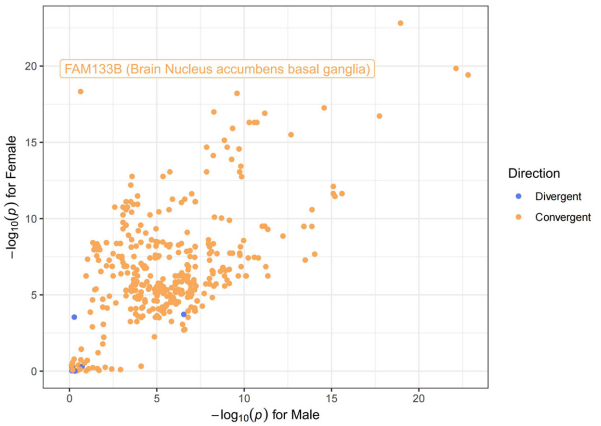


**Figure S1** Comparison of Mendelian randomization results between sexes. The direction "Divergent" indicates that the beta coefficients for males and females have different signs.

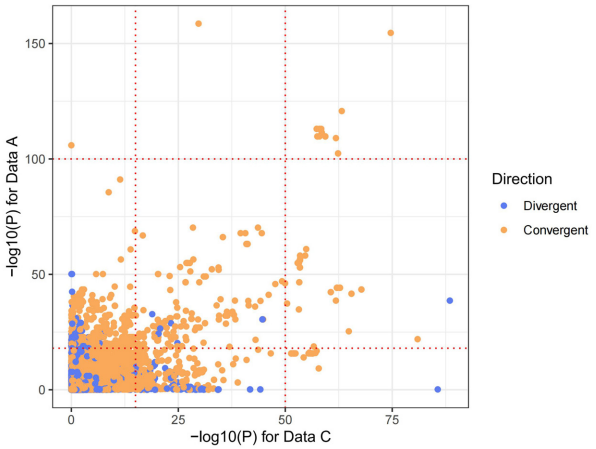


**Figure S2** Comparison of Mendelian randomization results between ancestries. Vertical lines indicate $P=10^{-15}$ and $P=10^{-50}$, and horizontal lines indicate $P=10^{-18}$ and $P=10^{-100}$. The direction "Divergent" indicates that the beta coefficients for Data A and Data C have different signs.

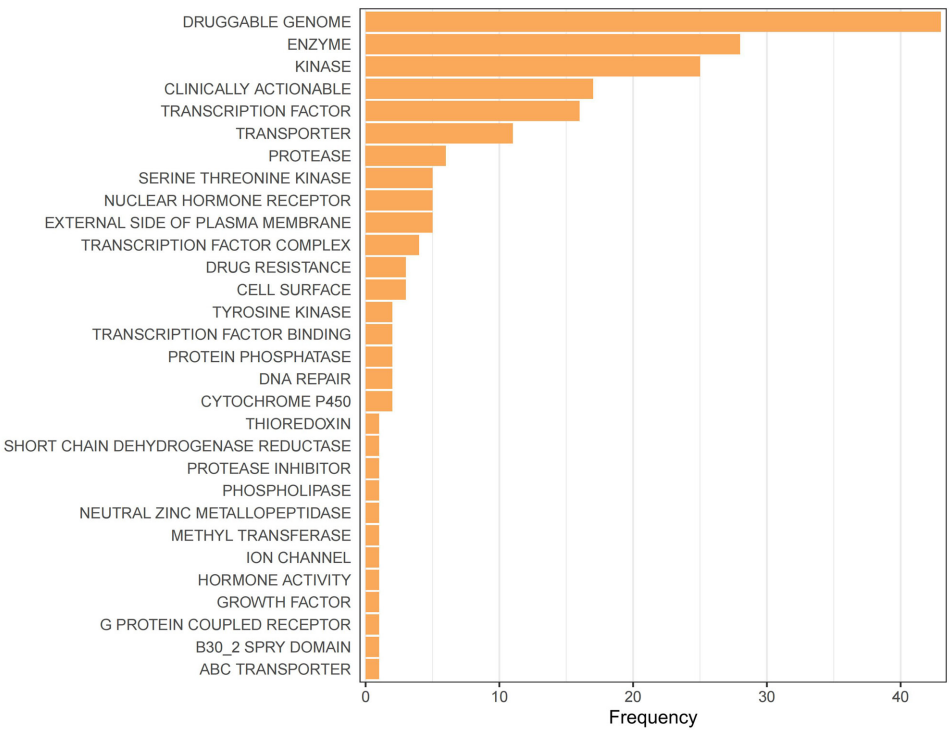


**Figure S3** Druggable categories of selected genes classified by DGIdb.


https://dx.doi.org/10.21037/tp-24-265

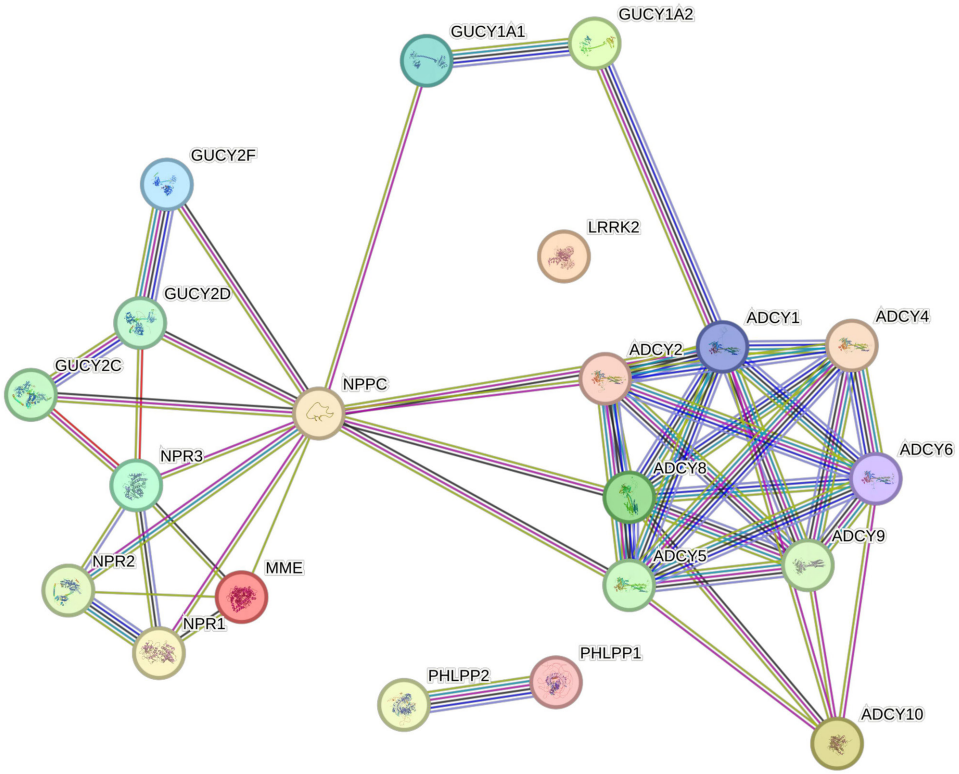


**Figure S4** Known and predicted protein-protein interactions of NPPC (created using the STRING database on September 24, 2023). Nodes represent proteins, and edges represent protein-protein associations.


https://dx.doi.org/10.21037/tp-24-265

**Table S1** Data sources in Mendelian randomization study

| Dataset | Data A | Data A-M | Data A-F | Data B | Data C |
|---|---|---|---|---|---|
| | ieu-a-89 | ieu-a-96 | ieu-a-97 | ukb-b-10787 | bbj-a-70 |
| PMID | 25282103 | 23754948 | 23754948 | 25826379 | 31562340 |
| Year | 2014 | 2013 | 2013 | 2018 | 2019 |
| Population | European | European | European | European | East Asian |
| Sex | Males and Females | Males | Females | Males and Females | Males and Females |
| Sample size | 253,288 | 60,586 | 73,137 | 461,950 | 159,095 |
| Number of SNPs | 2,550,859 | 2,762,798 | 2,748,546 | 9,851,867 | 27,211,524 |
| Author | Wood AR | Randall JC | Randall JC | Ben Elsworth | Ishigaki K |
| Consortium | GIANT | GIANT | GIANT | UK Biobank | BBJ |
| Build | HG19/GRCh37 | HG19/GRCh37 | HG19/GRCh37 | HG19/GRCh37 | HG19/GRCh37 |
| Design | GWAS meta-analysis | GWAS meta-analysis | | Population-based | Patient-based |
| Setting and participants | A GWAS meta-analysis of adult height using summary statistics from 79 studies consisting of 253,288 individuals of European ancestry. | A sex-specific GWAS meta-analysis of adult height using summary statistics from 46 studies consisting of 60,586 men and 73,137 women, of European ancestry. | | UK Biobank is a very large, population-based prospective study, established to allow detailed investigations of the genetic and nongenetic determinants of the diseases of middle and old age, with over 500,000 participants aged 40–69 years when recruited in 2006–2010. | The BBJ is a registry of patients diagnosed with any of 47 target common diseases. Patients were enrolled at 12 cooperative medical institutes all over Japan from June 2003 to March 2008. |
| Anthropometric assessment method | Measured or self-reported | Measured or self-reported | | Measured | Self-reported |
| Summary statistics for height | Refer to Supplementary Table 19 in the original publication. | Refer to Table S5 in the original publication. | | N/A | Height [cm; mean±SD]<br>Male: 165.4 ± 6.6<br>Female: 152.9 ± 6.4 |
| Sample quality control | Specific to studies | Specific to studies | | Described in "UK Biobank Genetic Data: MRC-IEU Quality Control, Version 1 [Updated version at DOI: 10.5523/bris.1ovaau5sxunp2cv8rcy88688v]". | Eligibility criteria: (I) age ≥ 18, (II) available height information, and (III) height within three times the interquartile range of the upper/lower quartile and within ±4 standard deviations.<br>Exclude: (I) lower call rates (<98%); (II) closely related individuals; (III) Individuals not of Japanese origins. |
| Ethical considerations | N/A | N/A | | The UK Biobank resource was approved by the UKBB Research Ethics Committee, and all participants provided written informed consent to participate. | The study protocol for the BBJ Project was approved by the research ethics committees at the Institute of Medical Science, the University of Tokyo, the RIKEN Yokohama Institute, and the 12 cooperating hospitals. All participants gave written consent to participate in the study. |

BBJ, BioBank Japan; GIANT, Genetic Investigation of ANthropometric Traits; GWAS, genome-wide association studies; SD, standard deviation; SNP, single-nucleotide polymorphism.

**Table S2** List of exposures with the most between-ancestry differences

| Gene | Tissue | East Asian (Data C) | | European (Data A) | | Direction |
|---|---|---|---|---|---|---|
| | | β | $-\log_{10}(p)$ | β | $-\log_{10}(p)$ | |
| *ATXN3* | Adipose Subcutaneous | -0.1016 | 51.39 | -0.0602 | 15.75 | Convergent |
| *ATXN3* | Artery Tibial | -0.1564 | 54.3 | -0.0752 | 14.01 | Convergent |
| *ATXN3* | Colon Sigmoid | -0.064 | 55.45 | -0.0354 | 15.75 | Convergent |
| *ATXN3* | Colon Transverse | -0.1612 | 55.56 | -0.0895 | 15.75 | Convergent |
| *ATXN3* | Esophagus Muscularis | -0.0969 | 52.38 | -0.0568 | 15.75 | Convergent |
| *ATXN3* | Heart Left Ventricle | -0.105 | 51.94 | -0.0619 | 15.75 | Convergent |
| *ATXN3* | Nerve Tibial | -0.0678 | 52.07 | -0.04 | 15.75 | Convergent |
| *ATXN3* | Ovary | -0.0675 | 55.94 | -0.0373 | 15.75 | Convergent |
| *ATXN3* | Pancreas | -0.1149 | 52.05 | -0.0678 | 15.75 | Convergent |
| *ATXN3* | Prostate | -0.0906 | 57.06 | -0.0512 | 15.93 | Convergent |
| *ATXN3* | Spleen | -0.1291 | 55.67 | -0.0639 | 16.1 | Convergent |
| *ATXN3* | Stomach | -0.1232 | 56.4 | -0.0676 | 15.75 | Convergent |
| *ATXN3* | Thyroid | -0.1318 | 55.67 | -0.0653 | 16.1 | Convergent |
| *RP11-529H20.6* | Adipose Subcutaneous | -0.0882 | 56.39 | -0.0483 | 15.75 | Convergent |
| *RP11-529H20.6* | Adipose Visceral Omentum | -0.1149 | 51.39 | -0.0681 | 15.75 | Convergent |
| *RP11-529H20.6* | Artery Coronary | -0.1176 | 56.22 | -0.0645 | 15.75 | Convergent |
| *RP11-529H20.6* | Brain Nucleus accumbens basal ganglia | -0.0961 | 56.4 | -0.0527 | 15.75 | Convergent |
| *RP11-529H20.6* | Cells EBV-transformed lymphocytes | -0.0668 | 55.94 | -0.0369 | 15.75 | Convergent |
| *RP11-529H20.6* | Esophagus Mucosa | -0.0899 | 51.39 | -0.0533 | 15.75 | Convergent |
| *RP11-529H20.6* | Esophagus Muscularis | -0.1026 | 51.39 | -0.0608 | 15.75 | Convergent |
| *RP11-529H20.6* | Heart Left Ventricle | -0.1394 | 57.35 | -0.0788 | 16.83 | Convergent |
| *RP11-529H20.6* | Liver | -0.1212 | 51.94 | -0.0714 | 15.75 | Convergent |
| *RP11-529H20.6* | Nerve Tibial | -0.0781 | 51.39 | -0.0463 | 15.75 | Convergent |
| *RP11-529H20.6* | Small Intestine Terminal Ileum | -0.0862 | 52.03 | -0.0508 | 15.75 | Convergent |
| *RP11-529H20.6* | Spleen | -0.0861 | 55.67 | -0.0426 | 16.1 | Convergent |
| *RP11-529H20.6* | Thyroid | -0.1224 | 56.39 | -0.0671 | 15.75 | Convergent |
| *RP11-529H20.6* | Whole Blood | -0.1396 | 56.4 | -0.0766 | 15.75 | Convergent |
| *SLC39A5* | Nerve Tibial | -0.1175 | 85.64 | 0.0057 | 0.16 | Divergent |
| *TRIP11* | Esophagus Mucosa | -0.3364 | 57.82 | -0.2053 | 9.25 | Convergent |
| *TRIP11* | Lung | -0.2631 | 52.38 | -0.1543 | 15.75 | Convergent |
| *TRIP11* | Pituitary | -0.0946 | 52.14 | -0.0557 | 15.75 | Convergent |
| *TRIP11* | Testis | -0.2198 | 51.69 | -0.1296 | 15.75 | Convergent |
| *ZBTB38* | Thyroid | 0.0013 | 0 | 0.3182 | 105.92 | Convergent |

EBV, Epstein-Barr virus.


https://dx.doi.org/10.21037/tp-24-265

**Table S3** The druggable categories of the selected genes

| Gene | Druggable category | Sources |
|---|---|---|
| *ABCB9* | DRUGGABLE GENOME | RussLampel\|HopkinsGroom |
| *ABCB9* | ABC TRANSPORTER | HopkinsGroom\|GO |
| *ABCB9* | TRANSPORTER | Pharos |
| *ACSL6* | ENZYME | HumanProteinAtlas |
| *ACSL6* | CLINICALLY ACTIONABLE | FoundationOneGenes\|CarisMolecularIntelligence |
| *ACSS2* | ENZYME | Pharos |
| *ACSS2* | TRANSCRIPTION FACTOR | Pharos |
| *ADAMTSL3* | DRUGGABLE GENOME | HingoraniCasas |
| *ADCY3* | DRUGGABLE GENOME | RussLampel\|HopkinsGroom |
| *ADCY3* | ENZYME | Pharos |
| *AMZ1* | NEUTRAL ZINC METALLOPEPTIDASE | GO |
| *AMZ1* | PROTEASE | dGene |
| *ANAPC10* | KINASE | Pharos |
| *ANKIB1* | ENZYME | Pharos |
| *ASXL2* | CLINICALLY ACTIONABLE | MskImpact |
| *ASXL2* | ENZYME | Pharos |
| *ASXL2* | TRANSCRIPTION FACTOR | Pharos |
| *ATP13A2* | TRANSPORTER | HopkinsGroom\|HumanProteinAtlas |
| *ATP13A2* | DRUGGABLE GENOME | HopkinsGroom |
| *BCS1L* | TRANSPORTER | HumanProteinAtlas |
| *BTN2A2* | B30_2 SPRY DOMAIN | HopkinsGroom |
| *BTN2A2* | DRUGGABLE GENOME | HopkinsGroom |
| *BTN2A2* | EXTERNAL SIDE OF PLASMA MEMBRANE | GO |
| *CBFA2T2* | ENZYME | Pharos |
| *CBFA2T2* | TRANSCRIPTION FACTOR | Pharos |
| *CD79B* | CLINICALLY ACTIONABLE | MskImpact\|FoundationOneGenes\|CarisMolecularIntelligence\|Tempus |
| *CD79B* | DRUGGABLE GENOME | HingoraniCasas |
| *CD79B* | EXTERNAL SIDE OF PLASMA MEMBRANE | GO |
| *CD79B* | KINASE | Pharos |
| *CDC14B* | DRUGGABLE GENOME | RussLampel\|HopkinsGroom |
| *CDC14B* | PROTEIN PHOSPHATASE | HopkinsGroom\|dGene |
| *CDC14B* | DNA REPAIR | GO |
| *CDC14B* | KINASE | Pharos |
| *CDK2AP1* | KINASE | Pharos |
| *CDK5RAP1* | KINASE | Pharos |
| *CEP250* | KINASE | Pharos |
| *CHRNB1* | ION CHANNEL | HopkinsGroom\|IDG\|Pharos |
| *CHRNB1* | DRUGGABLE GENOME | HopkinsGroom\|RussLampel\|HingoraniCasas |
| *CHRNB1* | TRANSPORTER | HumanProteinAtlas |
| *CPNE1* | TRANSPORTER | GO |
| *CPNE1* | TRANSCRIPTION FACTOR | Pharos |
| *CSNK2B* | SERINE THREONINE KINASE | GO |
| *CSNK2B* | ENZYME | Pharos |
| *CSNK2B* | KINASE | Pharos |
| *CTC1* | CLINICALLY ACTIONABLE | Tempus |
| *CTC1* | ENZYME | Pharos |
| *CYP21A2* | DRUGGABLE GENOME | HopkinsGroom\|HingoraniCasas\|RussLampel |
| *CYP21A2* | CYTOCHROME P450 | HopkinsGroom |
| *CYP21A2* | ENZYME | HumanProteinAtlas\|Pharos |
| *CYP27A1* | DRUGGABLE GENOME | HopkinsGroom\|HingoraniCasas\|RussLampel |
| *CYP27A1* | CYTOCHROME P450 | HopkinsGroom |
| *CYP27A1* | ENZYME | HumanProteinAtlas\|Pharos |
| *DCAF7* | KINASE | Pharos |
| *DOT1L* | METHYL TRANSFERASE | BaderLabGenes |
| *DOT1L* | DRUGGABLE GENOME | HingoraniCasas |
| *DOT1L* | CLINICALLY ACTIONABLE | MskImpact\|FoundationOneGenes\|CarisMolecularIntelligence\|Tempus |
| *DOT1L* | DNA REPAIR | GO |
| *E2F1* | TRANSCRIPTION FACTOR | Pharos |
| *EDEM2* | DRUGGABLE GENOME | HingoraniCasas |
| *EFEMP1* | DRUGGABLE GENOME | HingoraniCasas |
| *EFEMP1* | GROWTH FACTOR | GO |
| *EFR3B* | KINASE | Pharos |
| *EIF6* | KINASE | Pharos |
| *EIF6* | TRANSCRIPTION FACTOR | Pharos |
| *EPB41L1* | KINASE | Pharos |
| *FGFR4* | KINASE | HopkinsGroom\|dGene\|Pharos |
| *FGFR4* | DRUGGABLE GENOME | HopkinsGroom\|HingoraniCasas\|RussLampel |
| *FGFR4* | CLINICALLY ACTIONABLE | MskImpact\|FoundationOneGenes\|CarisMolecularIntelligence\|Oncomine\|Tempus |
| *FGFR4* | TYROSINE KINASE | dGene |
| *FGFR4* | DRUG RESISTANCE | CIViC |
| *FGFR4* | ENZYME | Pharos |
| *FLOT1* | EXTERNAL SIDE OF PLASMA MEMBRANE | GO |
| *FRS2* | CLINICALLY ACTIONABLE | FoundationOneGenes\|Tempus |
| *FRS2* | KINASE | Pharos |

**Table S3** (*continued*)


https://dx.doi.org/10.21037/tp-24-265

**Table S3** (*continued*)

| Gene | Druggable category | Sources |
|---|---|---|
| *GGT7* | DRUGGABLE GENOME | HingoraniCasas |
| *GGT7* | PROTEASE | dGene |
| *GGT7* | ENZYME | Pharos |
| *GNA12* | CLINICALLY ACTIONABLE | FoundationOneGenes |
| *GNA12* | TRANSCRIPTION FACTOR | Pharos |
| *GPR126* | DRUGGABLE GENOME | RussLampel\|HopkinsGroom |
| *GPR126* | G PROTEIN COUPLED RECEPTOR | HopkinsGroom\|HumanProteinAtlas\|GO\|dGene |
| *GPR126* | CELL SURFACE | GO |
| *GSS* | DRUGGABLE GENOME | HingoraniCasas |
| *HABP4* | DRUGGABLE GENOME | HingoraniCasas |
| *HABP4* | TRANSCRIPTION FACTOR | Pharos |
| *HHIP* | DRUGGABLE GENOME | HingoraniCasas |
| *HHIP* | CELL SURFACE | GO |
| *HIST1H2BD* | CLINICALLY ACTIONABLE | MskImpact |
| *HIST1H2BE* | CLINICALLY ACTIONABLE | MskImpact |
| *HIST1H2BG* | CLINICALLY ACTIONABLE | MskImpact |
| *HIST1H4C* | DRUGGABLE GENOME | HingoraniCasas |
| *HIST1H4E* | DRUGGABLE GENOME | HingoraniCasas |
| *HIST1H4E* | CLINICALLY ACTIONABLE | Tempus |
| *HIST1H4H* | DRUGGABLE GENOME | HingoraniCasas |
| *HLA-C* | DRUGGABLE GENOME | HingoraniCasas |
| *HLA-C* | CELL SURFACE | GO |
| *HLA-C* | CLINICALLY ACTIONABLE | Tempus |
| *HLA-C* | DRUG RESISTANCE | CIViC |
| *HOXA5* | TRANSCRIPTION FACTOR | Pharos |
| *HSD17B3* | DRUGGABLE GENOME | RussLampel\|HopkinsGroom\|HingoraniCasas |
| *HSD17B3* | SHORT CHAIN DEHYDROGENASE REDUCTASE | HopkinsGroom |
| *HSD17B3* | ENZYME | HumanProteinAtlas\|Pharos |
| *ITCH* | ENZYME | HumanProteinAtlas\|Pharos |
| *ITCH* | TRANSCRIPTION FACTOR | Pharos |
| *JAZF1* | CLINICALLY ACTIONABLE | FoundationOneGenes\|CarisMolecularIntelligence |
| *JAZF1* | ENZYME | Pharos |
| *JAZF1* | NUCLEAR HORMONE RECEPTOR | Pharos |
| *LIMD2* | KINASE | Pharos |
| *LYN* | KINASE | BaderLabGenes\|HopkinsGroom\|GO\|dGene\|Pharos |
| *LYN* | DRUGGABLE GENOME | HopkinsGroom\|RussLampel\|HingoraniCasas |
| *LYN* | ENZYME | HumanProteinAtlas |
| *LYN* | CLINICALLY ACTIONABLE | FoundationOneGenes\|Tempus |
| *LYN* | TYROSINE KINASE | GO\|dGene |
| *LYN* | DRUG RESISTANCE | CIViC |
| *MAP3K3* | DRUGGABLE GENOME | HingoraniCasas\|HopkinsGroom\|RussLampel |
| *MAP3K3* | KINASE | HopkinsGroom\|dGene\|Pharos |
| *MAP3K3* | SERINE THREONINE KINASE | GO\|dGene |
| *MFAP2* | DRUGGABLE GENOME | HingoraniCasas |
| *MST1L* | DRUGGABLE GENOME | RussLampel |
| *MST1L* | PROTEASE | dGene |
| *MST1P2* | DRUGGABLE GENOME | RussLampel |
| *MTCH2* | DRUGGABLE GENOME | RussLampel |
| *MTCH2* | TRANSPORTER | Pharos |
| *MYL9* | KINASE | Pharos |
| *NCOA1* | ENZYME | HumanProteinAtlas |
| *NCOA1* | CLINICALLY ACTIONABLE | CarisMolecularIntelligence |
| *NCOA1* | TRANSCRIPTION FACTOR COMPLEX | GO |
| *NCOA1* | TRANSCRIPTION FACTOR | Pharos |
| *NCOA1* | NUCLEAR HORMONE RECEPTOR | Pharos |
| *NCOA6* | TRANSCRIPTION FACTOR COMPLEX | GO |
| *NCOA6* | NUCLEAR HORMONE RECEPTOR | Pharos |
| *NECAB3* | KINASE | Pharos |
| *NFS1* | ENZYME | Pharos |
| *NPPC* | DRUGGABLE GENOME | HingoraniCasas |
| *NPPC* | HORMONE ACTIVITY | GO |
| *NPR3* | DRUGGABLE GENOME | RussLampel\|HopkinsGroom |
| *OTUD4* | ENZYME | Pharos |
| *P4HA2* | ENZYME | HumanProteinAtlas\|Pharos |
| *PACSIN1* | KINASE | Pharos |
| *PITX1* | TRANSCRIPTION FACTOR COMPLEX | GO |
| *PITX1* | TRANSCRIPTION FACTOR | Pharos |
| *PLCD4* | DRUGGABLE GENOME | RussLampel\|HopkinsGroom |
| *PLCD4* | PHOSPHOLIPASE | HopkinsGroom |
| *PLCD4* | ENZYME | Pharos |
| *PLCD4* | KINASE | Pharos |
| *PPARD* | DRUGGABLE GENOME | RussLampel\|HingoraniCasas\|HopkinsGroom |
| *PPARD* | NUCLEAR HORMONE RECEPTOR | BaderLabGenes\|HopkinsGroom\|GO\|dGene\|Pharos |

**Table S3** (*continued*)


https://dx.doi.org/10.21037/tp-24-265

**Table S3** (*continued*)

| Gene | Druggable category | Sources |
|---|---|---|
| *PPARD* | TRANSCRIPTION FACTOR | Pharos |
| *PRKG2* | KINASE | HopkinsGroom\|dGene\|Pharos |
| *PRKG2* | DRUGGABLE GENOME | HopkinsGroom\|RussLampel\|HingoraniCasas |
| *PRKG2* | SERINE THREONINE KINASE | dGene |
| *PSMC5* | TRANSCRIPTION FACTOR BINDING | GO |
| *PSMC5* | PROTEASE | dGene |
| *PTPRN* | PROTEIN PHOSPHATASE | HopkinsGroom\|dGene |
| *PTPRN* | DRUGGABLE GENOME | HopkinsGroom\|RussLampel\|HingoraniCasas |
| *PTPRN* | TRANSCRIPTION FACTOR BINDING | GO |
| *PTPRN* | ENZYME | Pharos |
| *PTRHD1* | ENZYME | Pharos |
| *QSOX2* | DRUGGABLE GENOME | HingoraniCasas\|HopkinsGroom |
| *QSOX2* | THIOREDOXIN | HopkinsGroom |
| *RBM39* | NUCLEAR HORMONE RECEPTOR | Pharos |
| *RFT1* | TRANSPORTER | HumanProteinAtlas |
| *RFT1* | ENZYME | Pharos |
| *SCAND1* | TRANSCRIPTION FACTOR | Pharos |
| *SDHB* | CLINICALLY ACTIONABLE | MskImpact\|FoundationOneGenes\|CarisMolecularIntelligence\|Tempus |
| *SDHB* | ENZYME | HumanProteinAtlas\|Pharos |
| *SEC11A* | PROTEASE | GO\|dGene |
| *SERPINH1* | PROTEASE INHIBITOR | HopkinsGroom\|dGene |
| *SERPINH1* | DRUGGABLE GENOME | HopkinsGroom\|RussLampel |
| *SLC22A4* | DRUGGABLE GENOME | RussLampel\|HingoraniCasas |
| *SLC22A4* | EXTERNAL SIDE OF PLASMA MEMBRANE | GO |
| *SLC22A4* | TRANSPORTER | Pharos |
| *SLC22A5* | DRUGGABLE GENOME | HingoraniCasas\|RussLampel |
| *SLC22A5* | TRANSPORTER | HumanProteinAtlas\|Pharos |
| *SLC22A5* | EXTERNAL SIDE OF PLASMA MEMBRANE | GO |
| *SLC38A9* | TRANSPORTER | Pharos |
| *SLC44A4* | DRUGGABLE GENOME | HingoraniCasas |
| *SLC44A4* | TRANSPORTER | HumanProteinAtlas\|Pharos |
| *SOGA1* | DRUGGABLE GENOME | HingoraniCasas |
| *STK36* | DRUGGABLE GENOME | RussLampel\|HopkinsGroom\|HingoraniCasas |
| *STK36* | KINASE | HopkinsGroom\|IDG\|dGene\|Pharos |
| *STK36* | SERINE THREONINE KINASE | GO\|dGene |
| *STK36* | ENZYME | Pharos |
| *STK36* | TRANSCRIPTION FACTOR | Pharos |
| *STRADA* | ENZYME | HumanProteinAtlas |
| *STRADA* | SERINE THREONINE KINASE | dGene |
| *STRADA* | KINASE | dGene\|Pharos |
| *TBX2* | TRANSCRIPTION FACTOR COMPLEX | GO |
| *TBX2* | TRANSCRIPTION FACTOR | Pharos |
| *TMEM198* | KINASE | Pharos |
| *TP53INP2* | KINASE | Pharos |
| *UBE2V1* | ENZYME | Pharos |
| *USP37* | PROTEASE | dGene |


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**Table S4** Drug-gene interactions for the selected genes

| Target | Interaction drugs | Drug |
|---|---|---|
| *ATAD5* | 283 | (E)-2-STYRYLCHROMONE, (R)-PIA, (R,S)-INDATRALINE, [3H]-PHORBOL 12,13-DIBUTYRATE, 1,2-BIS(3-FLUOROBENZYLIDENE)HYDRAZINE, 1,2-DIMETHOXY-ANTHRAQUINONE, 1,4-BIS(2,6-DIFLUOROPHENYLSULFONYL)PIPERAZINE, 2-(3,4-METHYLENEDIOXYPHENYL)BENZOTHIAZOLE, 2-(3',4'-METHYLENEDIOXYPHENYL) QUINOLINE, 2-(4-METHOXYPHENYL)BENZO[D]THIAZOLE, 2-HYDROXY-NAPHTHALDEHYDE THIOSEMICARBAZONE, 2-METHOXY-1,4-NAPHTHOQUINONE, 3,4-METHYLENEDIOXYB-NITROSTYRENE, 3,5-DIPHENYLISOXAZOLE, 4,5,6,7-TETRABROMOBENZIMIDAZOLE, 4'-HYDROXYPHENYL-BENZO[D]THIAZOLE, 4'-METHOXY-AURONE, 4'-METHOXYFLAVONE, 4-PHENYLAMINO-[1,2]NAPHTHOQUINONE, 5,8-DIPRENYLOXYPSORALEN, 5-FLUOROURIDINE, 5-METHOXYFLAVONE, 5-NITRO-[1,10] PHENANTHROLINE, 6-BROMOFLAVONE, 6-HYDROXYFLAVONE, 7,12-DIMETHYL-BENZO[A]ANTHRACENE, 7-METHOXY-BAPTIGENIN, 8-FLUOROTRYPTANTHRIN, 8-PHENOXYCAFFEINE, 9,10-PHENANTHRENEQUINONE, ABT-702, ACRIDIN-1-YLAMINE, AG1295, ALBENDAZOLE, ALPHA,BETA-DEHYDROCURVULARIN, AMSACRINE, ANGUIDIN, ANISOMYCIN, APOMORPHINE HYDROCHLORIDE HEMIHYDRATE, AURIN, AZACITIDINE, AZATHIOPRINE, BAY-11-7082, BETA-TOXICAROL, BIOCHANIN, BIX-01294, BROMOENOL LACTONE, CAFFEIC ACID PHENETHYL ESTER, CALCIMYCIN, CALYCOSIN, CAMPTOTHECIN, CANTHARIDIC_ACID, CGP-60474, CHLOROXINE, CHRYSIN DIMETHYL ETHER, CID 1225609, CID 2056784, CID 4101591, CID 5310801, CID 649849, CID 670282, CID 739615, CID 893238, CID 94381, CINOBUFAGIN, COLCHICINE, CP-55940, CUCURBITACIN B, CV-1808, CYCLOASPEPTIDE A, DAIDZEIN, DAIDZIN, DAPH, DAUNORUBICIN HYDROCHLORIDE, DICHLORORIBOBENZIMIDAZOLE, DIGITOXIN, DIGOXIN, DILAZEP, DIMETHYL 2-(2-NITROBENZYLIDENE)MALONATE, DINALINE, DIPHENYLENEIODONIUM, DIPYRIDAMOLE, DNDI1416955, DNDI1417013, DNDI1417031, DNDI1417032, DNDI1417083, DNDI1417085, DNDI1417132, DNDI1417157, DNDI1417181, DNDI1417195, DNDI1417215, DNDI1417263, DNDI1417264, DNDI1417300, DNDI1417368, DNDI1417420, DNDI1417457, DNDI1417614, DNDI1417701, DNDI1417941, DOMPERIDONE, DOXAZOSIN, ELLIPTECINE, EMETINE, EMETINE HYDROCHLORIDE, ENOXIMONE, ENTINOSTAT, EUPAFOLIN, FASUDIL HYDROCHLORIDE, FIDUXOSIN, FLAVONE, FLUNARIZINE, GALANGIN, GELDANAMYCIN, GENISTEIN, GNF-PF-1008, GNF-PF-1083, GNF-PF-1094, GNF-PF-1134, GNF-PF-1307, GNF-PF-1644, GNF-PF-1813, GNF-PF-1872, GNF-PF-1947, GNF-PF-1969, GNF-PF-2272, GNF-PF-2335, GNF-PF-254, GNF-PF-2657, GNF-PF-2776, GNF-PF-3037, GNF-PF-3286, GNF-PF-3407, GNF-PF-3501, GNF-PF-3546, GNF-PF-3756, GNF-PF-4012, GNF-PF-4046, GNF-PF-4078, GNF-PF-4418, GNF-PF-4463, GNF-PF-4590, GNF-PF-4814, GNF-PF-5007, GNF-PF-5159, GNF-PF-5183, GNF-PF-5217, GNF-PF-5251, GNF-PF-5297, GNF-PF-67, GNF-PF-710, GNF-PF-78, GNF-PF-860, GNF-PF-910, GR-127935, GW405833, HARMALINE, HARMAN, HARMINE HYDROCHLORIDE, HELENALIN, HISPIDULIN, HYDRALAZINE, IDARUBICIN, IPRIFLAVONE, ISOLIQUIRITIGENIN, ISOVELLERAL, JNJ-1661010, KAMEBANIN, KN-62, L-162313, LASSBIO-294, LEFLUNOMIDE, METHOXYVONE, MIBEFRADIL, MICHLER'S KETONE, MITOXANTRONE, MMV009085, MMV020651, MMV085203, N,N-HEXAMETHYLENEAMILORIDE, N6-METHYLADENOSINE, N6-PHENYLADENOSINE, NICARDIPINE, NIFEDIPINE, NILE RED, NIMODIPINE, NITROBENZYLMERCAPTOPURINE RIBONUCLEOSIDE, NOCODAZOLE, N-PHENETHYLCINNAMAMIDE, N-PHENETHYL-NICOTINAMIDE, NSC-102042, NSC-102045, NSC-105827, NSC-139257, NSC-234945, NSC-319994, NSC-353720, NSC-636948, NSC-656158, NSC-92207, NU-6027, OCTAVERINE, ONONIN, OUABAIN, OXOPURPUREINE, PD-98059, PECTOLINARIGENIN, P-HYDROXYPHENETHYL ANISATE, PICEATANNOL, PIFEXOLE, PIFITHRIN-ALPHA, PIPERINE, PROTOAPIGENONE, PYROGALLOL RED, QUINACRINE, RAC-GONIOTHALAMIN, RESERPINE, RESVERATROL, RO-5-3335, RUTAECARPINE, S-(2,4-DICHLOROBENZYL) ISOTHIOUREA HYDROBROMIDE, SB-205384, SEW-03621, SHINJULACTONE B, SIB-1757, SIB-1893, SJ000018298, SJ000024939, SJ000044417, SJ000044511, SJ000047241, SJ000072340, SJ000082805, SJ000113257, SJ000128325, SJ000149318, STREPTONIGRIN, SU-4312, SULFURETIN, TCMDC-123641, TCMDC-123748, TCMDC-123770, TCMDC-123781, TCMDC-123808, TCMDC-123927, TCMDC-123951, TCMDC-124307, TCMDC-124353, TCMDC-124356, TCMDC-124381, TCMDC-124422, TCMDC-124522, TCMDC-124573, TCMDC-124585, TCMDC-125195, TCMDC-125204, TCMDC-125465, TCMDC-125602, TCMDC-125630, TCMDC-125738, TCMDC-125756, TCMDC-125784, TCMDC-125821, TDR77225, TETRABROMOBENZOTRIAZOLE, THIOINOSINE, THUNBERGINOL E, TOLONIUM CHLORIDE, TPCK, TRANILAST, TREQUINSIN, TRICHOSTATIN, TRIMETHOBENZAMIDE HYDROCHLORIDE, TRIPHENYLSTANNYL ACETATE, TYRPHOSTIN A9, TYRPHOSTIN AG-1478, VANOXERINE, VINCAMINE, WIN-62577, ZEARALENONE, ZERANOL |
| *PPARD* | 130 | (R)-16 [PMID: 32267688], 12-HYDROXY-OCTADECANOIC ACID, 2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-PENTADECAFLUORO-OCTANOIC ACID, 2-BROMO-HEXADECANOIC ACID, 3-METHOXY-MORPHANIN HCL, 3R14S-OCHRATOXIN A, 4-TERT-BUTYLCATECHOL, ABAMECTIN, ALPHA-TERTHIENYL, APIGENIN, ASCORBYL PALMITATE, ASTEMIZOLE, ATORVASTATIN, AVE0847, BAZEDOXIFENE ACETATE, BEZAFIBRATE, BIFENAZATE, BIFONAZOLE, BIOALLETHRIN S-CYCLOPENTENYL ISOMER, BIS(DIMETHYLAMINETHIOCARBONYL)MONOSULFIDE, BISPHENOL A, BITHIONOL, CER-002, CHLORANIL, CHLORHEXIDINE, CHLORPHRIFOS OXON, CHLORPROMAZINE HYDROCHLORIDE, CIGLITAZONE, CINACALCET HYDROCHLORIDE, CLOCAPRAMINE, CLOFLUCARBAN, CLOMIPRAMINE, CLOTRIMAZOLE, CLOXYQUIN, CYCLOHEXANONE OXIME, DACTINOMYCIN, DB959, DB-959, DECA-1,9-DIENE, DESLORATADINE, DIBUTYLDICHLOROSTANNANE, DICHLOROPHEN, DIFENOCONAZOLE, DINOSEB, DIPHENYLSULFANE, DOXORUBICIN HYDROCHLORIDE, E319, EMETINE DIHYDROCHLORIDE, ENCLOMIPHENE, ETHYL EICOSAPENTAENOIC ACID, ETOXAZOLE, FENOFIBRIC ACID, FENTICLOR, FLUOXETINE HYDROCHLORIDE, FOLPET, FTORMETAZINE, GBR-12909, GFT-505, GSK0660, GSK3787, GTF505, GW0742, GW0742X, GW2433, GW501516, GW7647, GW9578, HEXACHLOROPHENE, HOMIDIUM BROMIDE, HYCANTHONE, HYDRALAZINE HYDROCHLORIDE, HYDRAMETHYLNON, HYMECROMONE, IDARUBICIN HYDROCHLORIDE, IDEBENONE, INDEGLITAZAR, IPCONAZOLE, ISOCONAZOLE, ISOXABEN, KD3010, KD-3020, L-165041, L-783483, L-796449, MBX-8025, MENADIONE, MOSAPRAMINE, MURAGLITAZAR, N'-(2-HYDROXYBENZYLIDENE)ISONICOTINOHYDRAZIDE, NITROXOLINE, NSC-67746, NSC-747267, NSC-747270, OCTYL_GALLATE, ORYZALIN, PAZOPANIB, PENFLURIDOL, PHENYLMERCURIC ACETATE, PMID25416646-COMPOUND-FIGURE5-C, PROGLUMETACIN, PROMETHAZINE HYDROCHLORIDE, PROPACHLOR, PROPRANOLOL HYDROCHLORIDE, PROSTAGLANDIN D2, RALOXIFENE HYDROCHLORIDE, RETINAL, ROSIGLITAZONE MALEATE, ROTENONE, SANGUINARIUM, SAR351034, SERATRODAST, SJ000299520, SODELGLITAZAR, T3D-959, TAMOXIFEN CITRATE, TCMDC-123920, TETRADECYLTHIOACETIC ACID, THALIDOMIDE, THIORIDAZINE, THIOSEMICARBAZIDE, TPKI-24, TRETINOIN, TRIAMTERENE, TRIBROMSALAN, TRIBUTYLTIN-OXIDE, TRICLOCARBAN, TRIPARANOL, TROVAFLOXACIN MESYLATE, VITAMIN K3H2, ZIRAM |
| *LYN* | 44 | ACALABRUTINIB, ALKYNYL-SUBSTITUTED PYRIMIDINYL-PYRROLE DERIVATIVE 1, ALSTERPAULLONE, AS703569, AZD-1152-HQPA, BAFETINIB, BOSUTINIB, CEDIRANIB, CENISERTIB, COMPOUND 23 [PMID: 17600705], COMPOUND 36 [PMID: 21958547], CYC-116, DORAMAPIMOD, ECF506, ENTRECTINIB, GNF-PF-2301, GO-6976, GW441756X, GW459057A, GW559768X, IBRUTINIB, ILORASERTIB, JNJ-26483327, LINIFANIB, MASITINIB, MLN-8054, NG-25, NILOTINIB, OSI-632, PEXMETINIB, PF-562271, RG-1530, SB-220025, SORAFENIB, SP-600125, SU6656, TAE-684, TAMATINIB, TG100-801, TOLIMIDONE, TOZASERTIB, XILIERTINIB, XL-228, ZIPRASIDONE |
| *FGFR4* | 39 | ACTB1003, ARQ-087, AZD4547, AZD-4547, BAY-1163877, BGJ398, BLU-9931, BRIVANIB, BRIVANIB ALANINATE, CP-459632, CVBT-141B, CVBT-141H, CYCLOPHOSPHAMIDE, DEBIO1347, ENMD-2076, ERDAFITINIB, EVEROLIMUS, FGF/VEGF RECEPTOR TYROSINE KINASE INHIBITOR, PD173074, FGF401, FGF-6, FGFR INHIBITOR AZD4547, FISOGATINIB, FLUOROURACIL, FP-1039, FUTIBATINIB, HESPERADIN, INCB62079, INFIGRATINIB, ISIS-FGFR4RX, LY2874455, LY-2874455, NINTEDANIB ESYLATE, ORANTINIB, PALIFERMIN, PONATINIB, PRN1371, ROBLITINIB, TRAFERMIN, XL-999 |
| *HLA-C* | 21 | ACETAMINOPHEN, ALLOPURINOL, AMOXICILLIN, CLAVULANATE, CLOZAPINE, DRUGS FOR TREATMENT OF TUBERCULOSIS, FLUCLOXACILLIN, INFLIXIMAB, LAMOTRIGINE, LAPATINIB, METHAZOLAMIDE, NEVIRAPINE, PEGINTERFERON ALFA-2B, PHENYTOIN, RIBAVIRIN, RUBELLA VACCINES, SULFAMETHOXAZOLE / TRIMETHOPRIM, THERAPEUTIC TUMOR INFILTRATING LYMPHOCYTES, TICLOPIDINE, TUMOR NECROSIS FACTOR ALPHA (TNF-ALPHA) INHIBITORS, VALPROIC ACID |
| *E2F1* | 19 | 12-O-TETRADECANOYLPHORBOL-13-ACETATE, 17 BETA-ESTRADIOL, 5-FLUOROURACIL, ADRIAMYCIN, ARQ-171, BCNU, GP-120, HGF, HOECHST 33258, IRINOTECAN, LARGAZOLE, MTX, NAC, NERVE GROWTH FACTOR, NICOTINE, PRIMAQUINE, PS-341, RAS INHIBITORS, VITAMIN C |
| *CHRNB1* | 18 | ATRACURIUM BESYLATE, CISATRACURIUM BESYLATE, DECAMETHONIUM BROMIDE, DOXACURIUM CHLORIDE, ECULIZUMAB, EFGARTIGIMOD ALFA, GALLAMINE TRIETHIODIDE, METOCURINE IODIDE, MIVACURIUM CHLORIDE, PANCURONIUM BROMIDE, PIPECURONIUM BROMIDE, RAPACURONIUM BROMIDE, RAVULIZUMAB, ROCURONIUM BROMIDE, SUCCINYLCHOLINE CHLORIDE, TUBOCURARINE CHLORIDE, VARENICLINE, VECURONIUM BROMIDE |
| *NPPC* | 11 | ANDROSTENEDIONE, ANTISERUM, BMN-111, CORTISOL, DEXAMETHASONE, ETHER, IMMUNOMODULATORS, PMA, PROGESTERONE, STAUROSPORINE, TESTOSTERONE |
| *NPR3* | 9 | [125I]ANP (HUMAN), ANX-042, AP811, CANF4-23, CARDIODILATIN, M372049, NESIRITIDE, OSTEOCRIN, PL-3994 |
| *ATAD5, PPARD* | 8 | CYCLOHEXIMIDE, DISULFIRAM, FLUSPIRILENE, GOSSYPOL, IDAZOXAN, MITOXANTRONE DIHYDROCHLORIDE, PHENANTHROLINE, PIMOZIDE |
| *DOT1L* | 7 | BROMO-DEAZA-SAH, CANDESARTAN, COMPOUND 13 [CHEN ET AL., 2016], EPZ004777, HYDROCHLOROTHIAZIDE, PINOMETOSTAT, SGC0946 |
| *CYP27A1* | 6 | CHOLESTYRAMINE, CHOLIC ACID, COMPOUND 4D [PMID: 20655626], MK-24, PHYTOSTEROLS, RETINOID |
| *PSMC5* | 5 | BORTEZOMIB, CARFILZOMIB, IXAZOMIB, IXAZOMIB CITRATE, OPROZOMIB |
| *CD79B* | 4 | DCDS-4501A, MGD010, POLATUZUMAB VEDOTIN, RG7596 |
| *SDHB* | 4 | ANTIBIOTIC, CORTICOSTEROIDS, DOXORUBICIN, GENTAMYCIN |
| *FGFR4, LYN* | 3 | DOVITINIB, ENMD-981693, NINTEDANIB |
| *PRKG2* | 3 | COMPOUND 32 [PMID: 20471253], GSK-269962A, PHA-767491 |
| *ACSS2, HLA-C, PRRC2A* | 2 | CARBOPLATIN, GEMCITABINE |
| *ACSS2, PPARD* | 2 | DOCETAXEL, ETHANOL |
| *ATAD5, NCOA1* | 2 | METHYLTHIONINIUM CHLORIDE, TCMDC-123764 |
| *E2F1, NPPC* | 2 | DES, VASOPRESSIN |
| *NCOA1* | 2 | COMPOUND 26 [PMID: 21733693], TAMOXIFEN |
| *SLC22A5* | 2 | SUNITINIB |
| *STK36* | 2 | RO-0505124, SB-202190 |
| *ACSS2* | 1 | EXAMPLE 265 [WO2019097515A1] |
| *ACSS2, E2F1* | 1 | PACLITAXEL |
| *ACSS2, E2F1, PPARD* | 1 | CISPLATIN |
| *ARF1* | 1 | AFATINIB |
| *ARF1, FGFR4, LYN* | 1 | ERLOTINIB |
| *ARF1, LYN* | 1 | GEFITINIB |
| *ATAD5, E2F1* | 1 | QUERCETIN |
| *ATAD5, LYN* | 1 | KENPAULLONE |
| *BAG6, HLA-C, PRRC2A* | 1 | CARBAMAZEPINE |
| *CYP27A1, E2F1* | 1 | URSODEOXYCHOLIC ACID |
| *CYP27A1, E2F1, NPPC* | 1 | HORMONES |

**Table S4** (*continued*)


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**Table S4** (*continued*)

| Target | Interaction drugs | Drug |
|---|---|---|
| *E2F1, NCOA1* | 1 | ETOPOSIDE |
| *E2F1, SERPINH1* | 1 | ANTISENSE OLIGONUCLEOTIDES |
| *HLA-C, FGFR4* | 1 | METHOTREXATE |
| *HLA-C, SLC22A4* | 1 | USTEKINUMAB |
| *HSD17B3* | 1 | CURCUMIN |
| *L3MBTL3* | 1 | UNC1215 |
| *LYN, PPARD* | 1 | DASATINIB |
| *LYN, SLC22A4, SLC22A5* | 1 | IMATINIB |
| *MAP3K3* | 1 | COMPOUND 5N [PMID: 20483621] |
| *MYH7B* | 1 | OMECAMTIV MECARBIL |
| *NFKBIL1* | 1 | IFN |
| *SERPINH1* | 1 | 11D10 |
| *SLC22A4, SLC22A5* | 1 | PROPIONYL-L-CARNITINE |
| *SLC44A4* | 1 | ASG-5ME |
| *TBX2* | 1 | ATENOLOL |


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