

Supplementary Materials

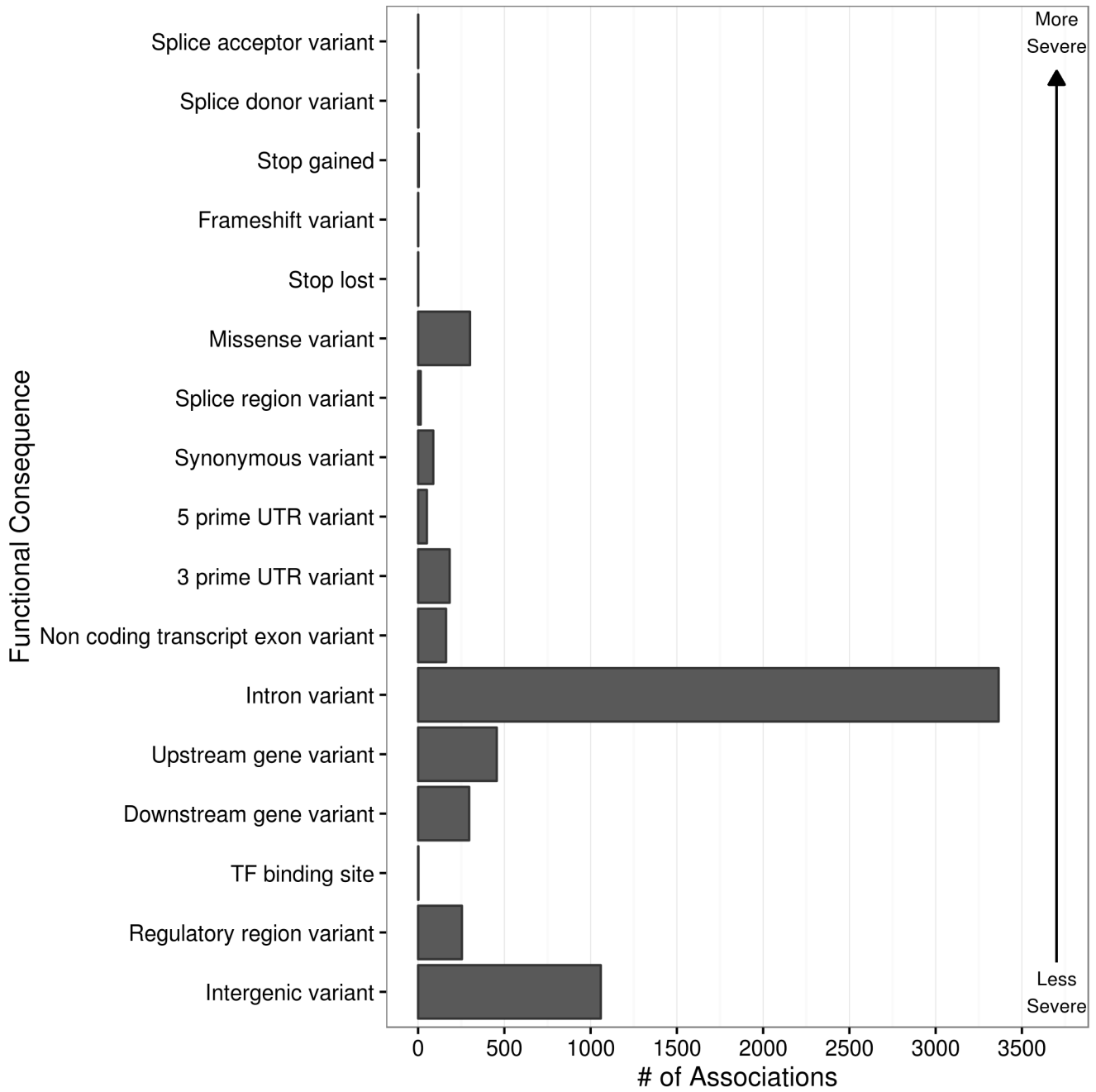


Fig. S1. The distribution of Sequence Ontology functional consequences of GWAS significant variant associations (p-value $\leq 5 \times 10^{-8}$).

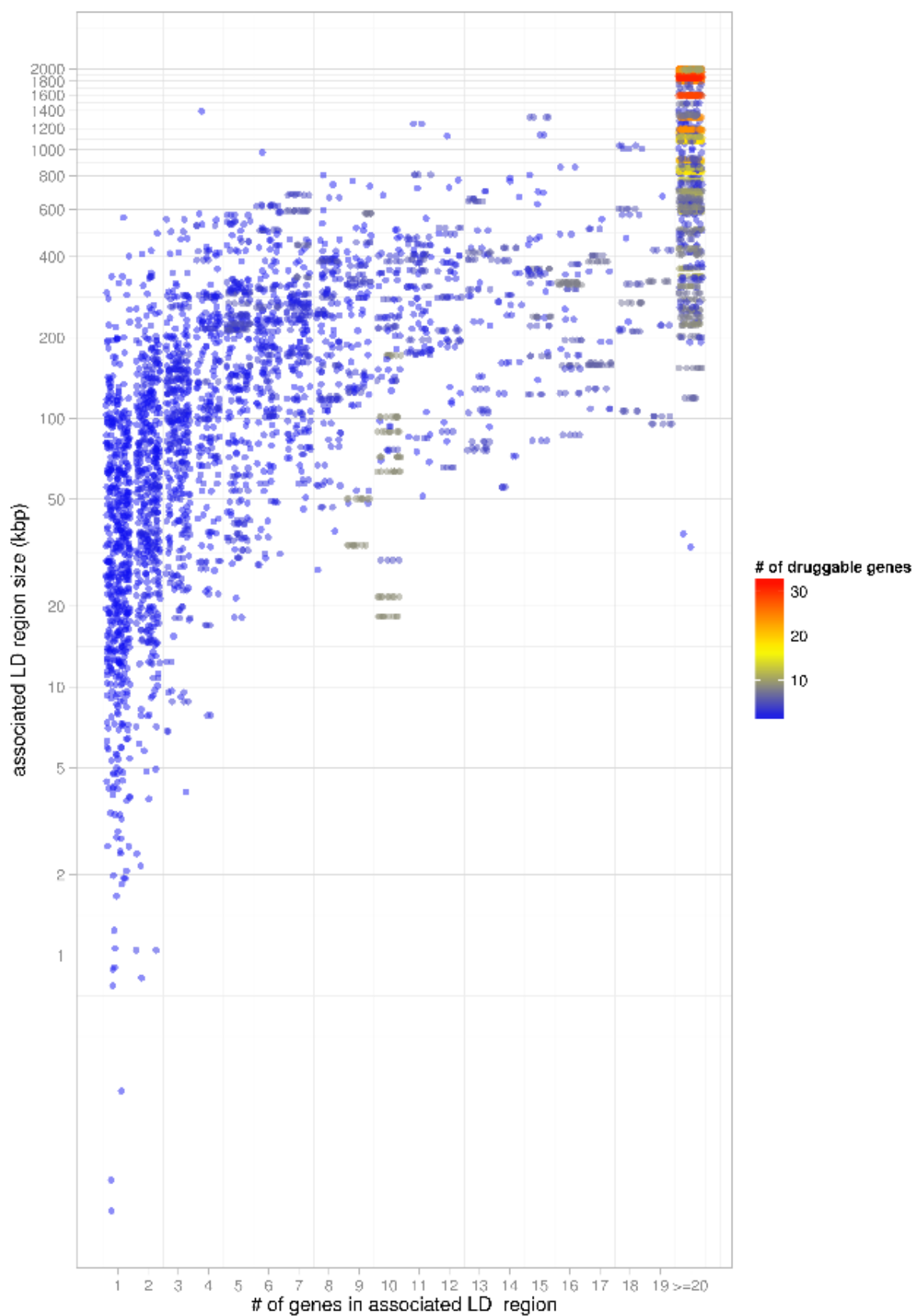


Fig. S2. Number of protein-coding genes in LD region. Shown above is a jittered line plot, where each point represents an LD region, its position on the x-axis is the number of protein-coding genes found in the region, and its position on the y-axis is the length (in kbp) of the region. The number of druggable genes within the region is color-coded.

Diseases (N=184)	Digestive System Diseases				Neoplasms				Nervous System Diseases				Cardiovascular Diseases																			
Studies (N=609)	106 (Est. Samples=234938)				187 (Est. Samples=478188)				104 (Est. Samples=323729)				84 (Est. Samples=426777)																			
Associations (N=3079)	705				783				425				388																			
LD Regions (N=1830)	417				476				286				228																			
LD Region Genes (N=4293)	1306				1466				997				670																			
Druggable Genes (N=727)	256				219				170				135																			
Druggable Gene Priority (N=727)	Tier 1 105		Tier >1 151		Tier 1 79		Tier >1 140		Tier 1 67		Tier >1 103		Tier 1 48		Tier >1 87																	
Distance Rank (N=727)	<= 2 57	>= 3 65	<= 2 76	>= 3 96	<= 2 46	>= 3 45	<= 2 72	>= 3 77	<= 2 40	>= 3 35	<= 2 48	>= 3 64	<= 2 29	>= 3 22	<= 2 49	>= 3 42																
All Compounds (N=198980)	16747	9303	4157	2168	32763	85817	7228	1592	83599	98334	867	1258	10802	5404	1995	2551																
USAN/INN Compounds (N=2047)	351	204	17	19	519	729	71	24	808	1057	30	18	359	216	31	20																
Drugs (N=498)	87	55	3	3	154	28	18	4	113	74	2	0	133	27	2	6																
Drug I/Disease P concordant[C]/discordant[D] Drugs (N=108, N=241)	C 10	D 45	C 2	D 42	C 0	D 2	C 0	D 2	C 24	D 69	C 1	D 17	C 2	D 8	C 0	D 2	C 12	D 35	C 9	D 42	C 0	D 1	C 0	D 0	C 4	D 60	C 10	D 11	C 0	D 1	C 0	D 3
Targets (N=27, N=86)	3	12	2	9	0	2	0	1	6	8	1	6	1	3	0	3	2	12	3	8	0	1	0	0	4	12	4	4	0	2	0	2
Diseases (N=184)	Respiratory Tract Diseases				Skin and Connective Tissue Diseases				Immune System Diseases				Mental Disorders																			
Studies (N=609)	47 (Est. Samples=188565)				107 (Est. Samples=195185)				130 (Est. Samples=268725)				85 (Est. Samples=320019)																			
Associations (N=3079)	184				628				764				355																			
LD Regions (N=1830)	112				392				491				258																			
LD Region Genes (N=4293)	469				1059				1099				993																			
Druggable Genes (N=727)	91				181				211				158																			
Druggable Gene Priority (N=727)	Tier 1 32		Tier >1 59		Tier 1 71		Tier >1 110		Tier 1 81		Tier >1 130		Tier 1 48		Tier >1 110																	
Distance Rank (N=727)	<= 2 17	>= 3 23	<= 2 22	>= 3 44	<= 2 39	>= 3 38	<= 2 56	>= 3 69	<= 2 55	>= 3 41	<= 2 73	>= 3 72	<= 2 24	>= 3 28	<= 2 44	>= 3 77																
All Compounds (N=198980)	75362	72913	868	297	14601	81285	5701	4465	44208	8527	3284	1381	8171	10264	955	548																
USAN/INN Compounds (N=2047)	460	446	16	5	225	510	50	31	688	165	19	22	279	418	30	19																
Drugs (N=498)	18	11	0	2	80	46	5	7	76	57	2	7	101	31	6	2																
Drug I/Disease P concordant[C]/discordant[D] Drugs (N=108, N=241)	C 6	D 4	C 0	D 8	C 0	D 0	C 0	D 1	C 21	D 18	C 6	D 30	C 0	D 4	C 1	D 3	C 8	D 40	C 5	D 42	C 0	D 2	C 1	D 4	C 35	D 30	C 2	D 10	C 0	D 1	C 0	D 1
Targets (N=27, N=86)	2	2	0	3	0	0	0	1	6	8	2	11	0	2	1	3	4	13	1	13	0	1	1	3	2	8	2	3	0	1	0	2

Diseases (N=116)	Male Urogenital Diseases				Musculoskeletal Diseases				Endocrine System Diseases				Nutritional and Metabolic Diseases																			
Studies (N=326)	52 (Est. Samples=184027)				57 (Est. Samples=139636)				77 (Est. Samples=224472)				83 (Est. Samples=562768)																			
Associations (N=1572)	283				322				394				455																			
LD Regions (N=952)	192				184				240				265																			
LD Region Genes (N=2380)	722				585				823				795																			
Druggable Genes (N=399)	109				108				128				134																			
Druggable Gene Priority (N=399)	Tier 1 33		Tier >1 76		Tier 1 43		Tier >1 65		Tier 1 41		Tier >1 87		Tier 1 45		Tier >1 89																	
Distance Rank (N=399)	<= 2 15	>= 3 22	<= 2 37	>= 3 44	<= 2 26	>= 3 21	<= 2 28	>= 3 41	<= 2 24	>= 3 22	<= 2 45	>= 3 46	<= 2 28	>= 3 22	<= 2 45	>= 3 54																
All Compounds (N=128023)	3436	13033	1926	468	5185	3633	1623	1050	22890	73483	1701	4681	8848	4104	2199	4008																
USAN/INN Compounds (N=1276)	116	390	31	14	84	137	14	9	435	424	12	63	129	71	9	59																
Drugs (N=288)	25	19	12	7	15	55	4	2	73	16	2	7	33	41	2	5																
Drug I/Disease P concordant[C]/discordant[D] Drugs (N=30, N=128)	C 0	D 4	C 0	D 13	C 2	D 5	C 0	D 4	C 2	D 8	C 5	D 35	C 0	D 3	C 1	D 0	C 17	D 40	C 9	D 3	C 0	D 1	C 0	D 5	C 12	D 10	C 9	D 26	C 0	D 1	C 0	D 4
Targets (N=14, N=41)	0	2	0	3	1	1	0	3	2	5	1	7	0	2	1	0	5	6	2	3	0	1	0	3	2	5	2	5	0	1	0	2
Diseases (N=116)	Female Urogenital Diseases and Pregnancy Complications				Eye Diseases				Hemic and Lymphatic Diseases				Congenital, hereditary, and Neonatal Diseases and Abnormalities																			
Studies (N=326)	41 (Est. Samples=110979)				50 (Est. Samples=155095)				43 (Est. Samples=40283)				29 (Est. Samples=53101)																			
Associations (N=1572)	168				246				156				98																			
LD Regions (N=952)	127				157				105				76																			
LD Region Genes (N=2380)	546				436				356				262																			
Druggable Genes (N=399)	89				96				70				52																			
Druggable Gene Priority (N=399)	Tier 1 30		Tier >1 59		Tier 1 26		Tier >1 70		Tier 1 34		Tier >1 36		Tier 1 21		Tier >1 31																	
Distance Rank (N=399)	<= 2 11	>= 3 22	<= 2 24	>= 3 42	<= 2 22	>= 3 7	<= 2 42	>= 3 34	<= 2 17	>= 3 22	<= 2 13	>= 3 26	<= 2 9	>= 3 12	<= 2 15	>= 3 16																
All Compounds (N=128023)	2700	80230	390	359	83197	1908	1498	195	5779	867	527	1899	1334	122	169	388																
USAN/INN Compounds (N=1276)	64	695	12	10	703	30	4	4	151	62	7	11	111	12	7	9																
Drugs (N=288)	42	20	2	7	48	16	2	2	45	18	0	0	54	1	2	3																
Drug I/Disease P concordant[C]/discordant[D] Drugs (N=30, N=128)	C 4	D 31	C 0	D 14	C 0	D 1	C 0	D 4	C 1	D 19	C 0	D 1	C 0	D 1	C 1	D 1	C 0	D 27	C 0	D 14	C 0	D 0	C 0	D 0	C 2	D 3	C 0	D 1	C 0	D 1	C 0	D 2
Targets (N=14, N=41)	2	2	0	4	0	1	0	3	1	5	0	1	0	1	1	1	0	3	0	3	0	0	0	0	2	4	0	1	0	1	0	1

Diseases (N=3)	Wounds and Injuries				Psychological Phenomena and Processes				Occupational Diseases			
Studies (N=3)	1 (Est. Samples=288)				1 (Est. Samples=5888)				1 (Est. Samples=NA)			
Associations (N=3)	1				1				1			
LD Regions (N=3)	1				1				1			
LD Region Genes (N=7)	1				5				1			
Druggable Genes (N=0)	0				0				0			
Druggable Gene Priority (N=0)	Tier 1		Tier >1		Tier 1		Tier >1		Tier 1		Tier >1	
	0		0		0		0		0		0	
Distance Rank (N=0)	<= 2	>= 3	<= 2	>= 3	<= 2	>= 3	<= 2	>= 3	<= 2	>= 3	<= 2	>= 3
	0	0	0	0	0	0	0	0	0	0	0	0
All Compounds (N=0)	0	0	0	0	0	0	0	0	0	0	0	0
USAN/INN Compounds (N=0)	0	0	0	0	0	0	0	0	0	0	0	0
Drugs (N=0)	0	0	0	0	0	0	0	0	0	0	0	0
Drug I/Disease P concordant[C]/discordant[D] Drugs (N=0, N=0)	C	D	C	D	C	D	C	D	C	D	C	D
	0	0	0	0	0	0	0	0	0	0	0	0
Targets (N=0, N=0)	0	0	0	0	0	0	0	0	0	0	0	0

Fig. S3: Translational potential of GWAS disease associations across all MeSH root disease areas and mental disorders. The figure illustrates the results from GWAS studies, including LD regions, druggable genes in those regions, and compounds/drugs that have activity against the product of the druggable genes. In the penultimate row, the numbers of drugs that have an indication that is concordant (C) or discordant (D) with the GWAS phenotype are displayed. In the final row, the number of cognate targets for the concordant or discordant drugs is shown. Note that for the purposes of the figure, a drug target is a single gene even if it is part of a complex that is targeted by the drug. Within each cell the values represent the number of unique entities. For example, the cells in the Associations row represent the number of unique rsids. However, some values can be replicated across the figure because a GWAS study may have researched several of the disease areas. Additionally, there is some non-additivity between consecutive rows, namely Druggable Gene Priority - Distance Rank and Drugs - Drug indication/Disease Phenotypes. In the case of the former, this is due to the same gene being further away from the associated variant in different studies, such that it falls into a different partition. For the later, this is due to missing indications for some of the drugs, such that concordance or discordance could not be assigned. The values in the row labels represent the unique number of items across the row. The estimated number of samples is the sum of all the cases involved in the respective studies.

Diseases (N=78)	Digestive System Diseases				Neoplasms				Nervous System Diseases				Cardiovascular Diseases																			
Studies (N=253)	13 (Est. Samples=43443)				22 (Est. Samples=109650)				29 (Est. Samples=188951)				150 (Est. Samples=2383087)																			
Associations (N=1867)	48				100				125				1486																			
LD Regions (N=941)	35				68				86				692																			
LD Region Genes (N=2518)	246				212				206				1951																			
Druggable Genes (N=489)	57				34				68				371																			
Druggable Gene Priority (N=489)	Tier 1 17		Tier >1 40		Tier 1 14		Tier >1 20		Tier 1 31		Tier >1 37		Tier 1 133		Tier >1 238																	
Distance Rank (N=489)	<= 2 6	>= 3 13	<= 2 9	>= 3 33	<= 2 8	>= 3 9	<= 2 12	>= 3 12	<= 2 26	>= 3 13	<= 2 22	>= 3 26	<= 2 75	>= 3 78	<= 2 129	>= 3 145																
All Compounds (N=98267)	535	852	45	184	4780	2795	149	18	13108	8850	23188	24169	35958	30031	26556	26364																
USAN/INN Compounds (N=1265)	24	30	2	3	76	28	0	0	196	41	88	93	676	608	143	109																
Drugs (N=322)	0	8	0	2	26	19	0	0	51	11	0	2	196	67	17	2																
Drug I/Disease P concordant[C]/discordant[D] Drugs (N=160, N=84)	C 0	D 0	C 5	D 2	C 0	D 0	C 0	D 1	C 14	D 2	C 0	D 11	C 0	D 0	C 0	D 0	C 21	D 14	C 9	D 0	C 0	D 0	C 0	D 1	C 127	D 20	C 23	D 35	C 4	D 0	C 0	D 1
Targets (N=31, N=48)	0	0	1	2	0	0	0	1	1	1	0	3	0	0	0	0	5	7	2	0	0	0	1	20	12	7	16	2	0	0	1	

Diseases (N=78)	Respiratory Tract Diseases				Skin and Connective Tissue Diseases				Immune System Diseases				Mental Disorders																			
Studies (N=253)	17 (Est. Samples=182096)				19 (Est. Samples=94510)				16 (Est. Samples=54075)				39 (Est. Samples=329989)																			
Associations (N=1867)	117				68				66				107																			
LD Regions (N=941)	71				47				53				80																			
LD Region Genes (N=2518)	300				159				259				246																			
Druggable Genes (N=489)	62				34				65				61																			
Druggable Gene Priority (N=489)	Tier 1 23		Tier >1 39		Tier 1 15		Tier >1 19		Tier 1 21		Tier >1 44		Tier 1 27		Tier >1 34																	
Distance Rank (N=489)	<= 2 12	>= 3 15	<= 2 14	>= 3 31	<= 2 8	>= 3 12	<= 2 10	>= 3 12	<= 2 13	>= 3 14	<= 2 14	>= 3 32	<= 2 17	>= 3 11	<= 2 18	>= 3 19																
All Compounds (N=98267)	3924	947	224	240	4653	2980	460	21	1390	742	1057	731	6937	2730	166	1465																
USAN/INN Compounds (N=1265)	47	27	11	6	64	43	19	2	45	32	19	9	140	24	5	6																
Drugs (N=322)	11	8	0	2	26	21	2	0	9	5	2	3	45	5	3	2																
Drug I/Disease P concordant[C]/discordant[D] Drugs (N=160, N=84)	C 1	D 7	C 0	D 5	C 0	D 0	C 0	D 1	C 14	D 2	C 0	D 12	C 0	D 1	C 0	D 0	C 1	D 3	C 0	D 4	C 0	D 1	C 0	D 2	C 13	D 14	C 2	D 0	C 0	D 1	C 0	D 1
Targets (N=31, N=48)	2	2	0	1	0	0	0	1	1	1	0	4	0	1	0	0	1	2	0	4	0	1	0	1	4	7	2	0	0	1	0	2

Diseases (N=61)	Male Urogenital Diseases				Musculoskeletal Diseases				Endocrine System Diseases				Nutritional and Metabolic Diseases																			
Studies (N=247)	18 (Est. Samples=373808)				37 (Est. Samples=403652)				63 (Est. Samples=730637)				133 (Est. Samples=2279389)																			
Associations (N=1831)	107				272				354				828																			
LD Regions (N=1010)	75				158				210				435																			
LD Region Genes (N=2445)	305				330				594				1278																			
Druggable Genes (N=424)	56				59				105				236																			
Druggable Gene Priority (N=424)	Tier 1 21		Tier >1 35		Tier 1 19		Tier >1 40		Tier 1 31		Tier >1 74		Tier 1 78		Tier >1 158																	
Distance Rank (N=424)	<= 2 6	>= 3 16	<= 2 12	>= 3 24	<= 2 13	>= 3 8	<= 2 24	>= 3 18	<= 2 24	>= 3 11	<= 2 36	>= 3 43	<= 2 50	>= 3 39	<= 2 66	>= 3 109																
All Compounds (N=148910)	925	3576	83	852	73049	6072	155	828	4806	983	4636	1842	17930	6800	5999	4294																
USAN/INN Compounds (N=1322)	60	69	0	7	476	52	3	9	111	56	28	17	323	162	37	36																
Drugs (N=266)	2	12	0	4	30	12	2	0	48	4	1	5	47	40	3	7																
Drug I/Disease P concordant[C]/discordant[D] Drugs (N=81, N=119)	C 0	D 2	C 0	D 10	C 0	D 0	C 0	D 2	C 20	D 0	C 2	D 6	C 0	D 1	C 0	D 0	C 4	D 37	C 1	D 2	C 0	D 0	C 0	D 4	C 19	D 15	C 3	D 24	C 0	D 1	C 0	D 5
Targets (N=24, N=38)	0	2	0	4	0	0	0	1	4	0	2	3	0	1	0	0	4	5	1	2	0	0	0	2	10	8	3	7	0	1	0	3
Diseases (N=61)	Female Urogenital Diseases and Pregnancy Complications				Eye Diseases				Hemic and Lymphatic Diseases				Congenital, hereditary, and Neonatal Diseases and Abnormalities																			
Studies (N=247)	14 (Est. Samples=367135)				17 (Est. Samples=138545)				45 (Est. Samples=495172)				47 (Est. Samples=442374)																			
Associations (N=1831)	99				98				488				283																			
LD Regions (N=1010)	65				71				265				178																			
LD Region Genes (N=2445)	304				254				812				462																			
Druggable Genes (N=424)	58				37				136				86																			
Druggable Gene Priority (N=424)	Tier 1 23		Tier >1 35		Tier 1 12		Tier >1 25		Tier 1 41		Tier >1 95		Tier 1 25		Tier >1 61																	
Distance Rank (N=424)	<= 2 7	>= 3 17	<= 2 11	>= 3 25	<= 2 10	>= 3 2	<= 2 15	>= 3 11	<= 2 21	>= 3 25	<= 2 39	>= 3 64	<= 2 15	>= 3 13	<= 2 28	>= 3 39																
All Compounds (N=148910)	1699	3700	651	852	3516	53	72	574	11610	4672	1489	1829	8407	246	827	696																
USAN/INN Compounds (N=1322)	65	74	1	7	175	1	4	3	253	111	12	32	271	15	23	10																
Drugs (N=266)	4	12	0	4	17	1	2	0	42	45	0	3	61	2	4	0																
Drug I/Disease P concordant[C]/discordant[D] Drugs (N=81, N=119)	C 0	D 2	C 1	D 10	C 0	D 0	C 0	D 2	C 1	D 9	C 0	D 1	C 0	D 1	C 0	D 0	C 8	D 25	C 4	D 28	C 0	D 0	C 0	D 2	C 35	D 0	C 2	D 0	C 0	D 0	C 0	D 0
Targets (N=24, N=38)	0	2	1	4	0	0	0	1	1	2	0	1	0	2	0	0	4	3	2	6	0	0	0	1	6	0	2	0	0	0	0	

	Wounds and Injuries				Psychological Phenomena and Processes				Occupational Diseases			
Diseases (N=4)												
Studies (N=3)	2 (Est. Samples=30716)				0 (Est. Samples=0)				0 (Est. Samples=0)			
Associations (N=3)	3				0				0			
LD Regions (N=3)	3				0				0			
LD Region Genes (N=14)	14				0				0			
Druggable Genes (N=0)	0				0				0			
Druggable Gene Priority (N=0)	Tier 1		Tier >1		Tier 1		Tier >1		Tier 1		Tier >1	
	0	0	0	0	0	0	0	0	0	0	0	
Distance Rank (N=0)	<= 2	>= 3	<= 2	>= 3	<= 2	>= 3	<= 2	>= 3	<= 2	>= 3	<= 2	>= 3
	0	0	0	0	0	0	0	0	0	0	0	0
All Compounds (N=0)	0	0	0	0	0	0	0	0	0	0	0	0
USAN/INN Compounds (N=0)	0	0	0	0	0	0	0	0	0	0	0	0
Drugs (N=0)	0	0	0	0	0	0	0	0	0	0	0	0
Drug I/Disease P concordant[C]/discordant[D] Drugs (N=0, N=0)	C	D	C	D	C	D	C	D	C	D	C	D
	0	0	0	0	0	0	0	0	0	0	0	0
Targets (N=0, N=0)	0	0	0	0	0	0	0	0	0	0	0	0

Fig. S4. Translational potential of GWAS biomarker associations with relevance to disease across the all MeSH root disease areas and mental disorders. The figure illustrates the results from GWAS studies, including LD regions, druggable genes in those regions, and compounds/drugs that have activity against the product of the druggable genes. In the penultimate row, the numbers of drugs that have an indication that is concordant (C) or discordant (D) with the GWAS phenotype are displayed. In the final row, the number of cognate targets for the concordant or discordant drugs is shown. Note that for the purposes of the figure, a drug target is a single gene even if it is part of a complex that is targeted by the drug. Within each cell, the values represent the number of unique entities. For example, the cells in the Associations row represent the number of unique rsids. However, some values can be replicated across the figure because a GWAS study may have researched several of the disease areas. Additionally, there is some non-additivity between consecutive rows, namely Druggable Gene Priority - Distance Rank and Drugs - Drug indication/Disease Phenotypes. In the case of the former, this is due to the same gene being further away from the associated variant in different studies, such that it falls into a different partition. For the later, this is due to missing indications for some of the drugs, such that concordance or discordance could not be assigned. The values in the row labels represent the unique number of items across the row. The estimated number of samples is the sum of all the cases involved in the respective studies.

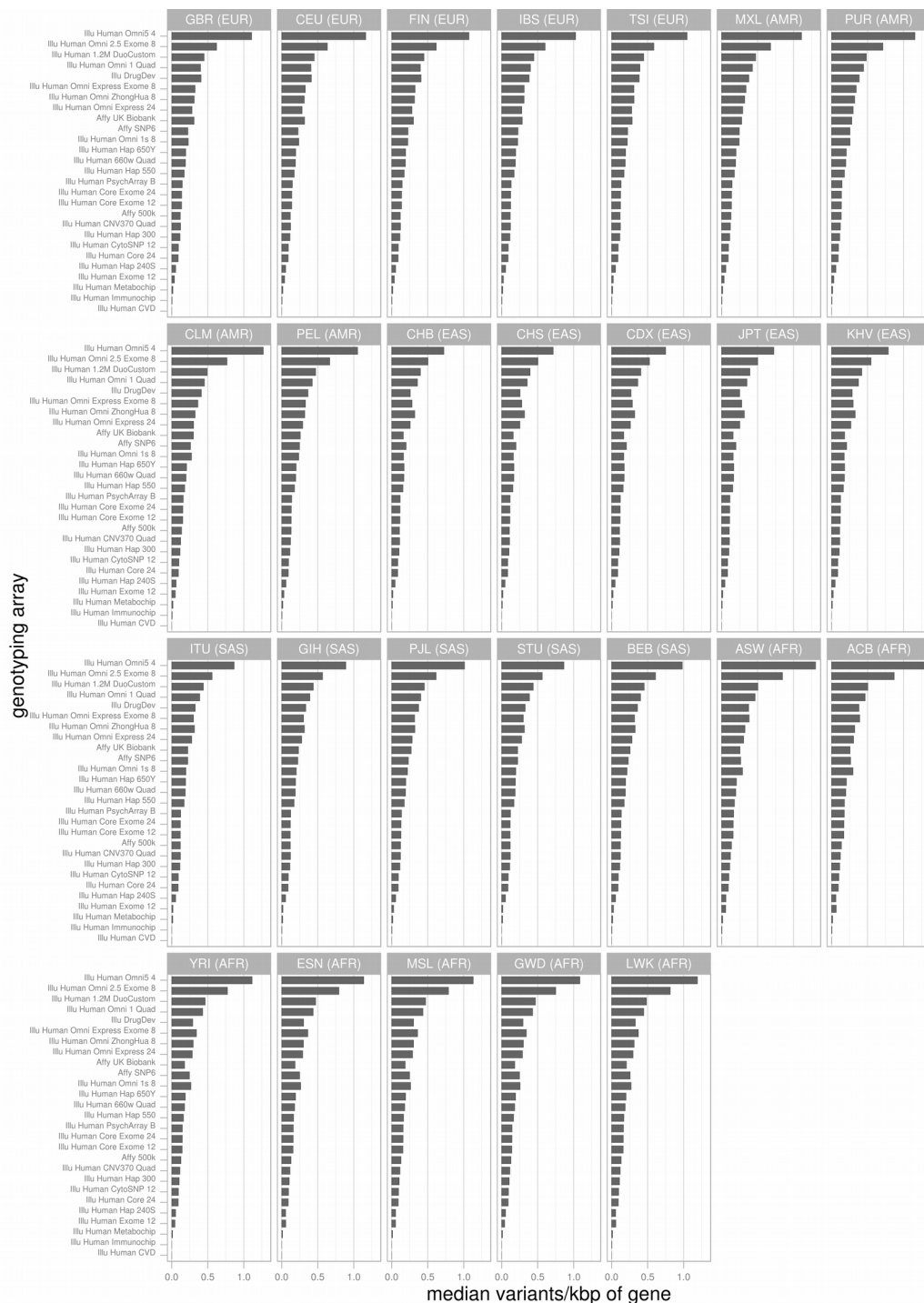


Fig. S5. Density of variant coverage across the druggable genome. Data are shown for directly typed variants in major commercial arrays including the DrugDev array introduced in this manuscript and for all the 1000 genomes phase 3 sub-populations (indicated at the top of each plot) with the super population group in brackets. EUR – European populations (GBR – British in England and Scotland, CEU – Utah Residents (CEPH) with Northern and Western Ancestry, FIN – Finnish in Finland, IBS – Iberian Population in Spain, TSI – Toscani in Italy). AMR – American populations (MXL – Mexican Ancestry from Los Angeles USA, PUR – Puerto Ricans from Puerto Rico, CLM – Colombians from Medellin, Colombia, PEL – Peruvians from Lima, Peru). EAS – East Asians (CHB – Han Chinese in Beijing, China, CHS – Southern Han Chinese, CDX – Chinese Dai in Xishuangbanna, China, JPT – Japanese in Tokyo, Japan, KHV – Kinh in Ho Chi Minh City, Vietnam). SAS – South Asians (ITU – Indian Telugu from the UK, GIH – Gujarati Indian from Houston, Texas, PJI – Punjabi from Lahore, Pakistan, STU – Sri Lankan Tamil from the UK, BEB – Bengali from Bangladesh). AFR – Africans (ASW – Americans of African Ancestry in SW USA, ACB – African Caribbeans in Barbados, YRI – Yoruba in Ibadan, Nigeria, ESN – Esan in Nigeria, MSL – Mende in Sierra Leone, GWD – Gambian in Western Divisions in the Gambia, LWK – Luhya in Webuye, Kenya)



Fig. S6. Density of variant coverage across the druggable genome. Data are shown for directly typed and tagged variants (at $r^2 \geq 0.8$) in major commercial arrays including the DrugDev array introduced in this manuscript and for all the 1000 genomes phase 3 sub-populations (indicated at the top of each plot) with the super population group in brackets. EUR – European populations (GBR –British in England and Scotland, CEU – Utah Residents (CEPH) with Northern and Western Ancestry, FIN - Finnish in Finland, IBS - Iberian Population in Spain, TSI - Toscani in Italy). AMR – American populations (MXL - Mexican Ancestry from Los Angeles USA, PUR - Puerto Ricans from Puerto Rico, CLM - Colombians from Medellin, Colombia, PEL - Peruvians from Lima, Peru). EAS – East Asians (CHB - Han Chinese in Beijing, China, CHS - Southern Han Chinese, CDX - Chinese Dai in Xishuangbanna, China, JPT - Japanese in Tokyo, Japan, KHV - Kinh in Ho Chi Minh City, Vietnam). SAS – South Asians (ITU - Indian Telugu from the UK, GIH - Gujarati Indian from Houston, Texas, PJJ - Punjabi from Lahore, Pakistan, STU - Sri Lankan Tamil from the UK, BEB - Bengali from Bangladesh). AFR – Africans (ASW - Americans of African Ancestry in SW USA, ACB - African Caribbeans in Barbados, YRI - Yoruba in Ibadan, Nigeria, ESN - Esan in Nigeria, MSL - Mende in Sierra Leone, GWD - Gambian in Western Divisions in the Gambia, LWK - Luhya in Webuye, Kenya)

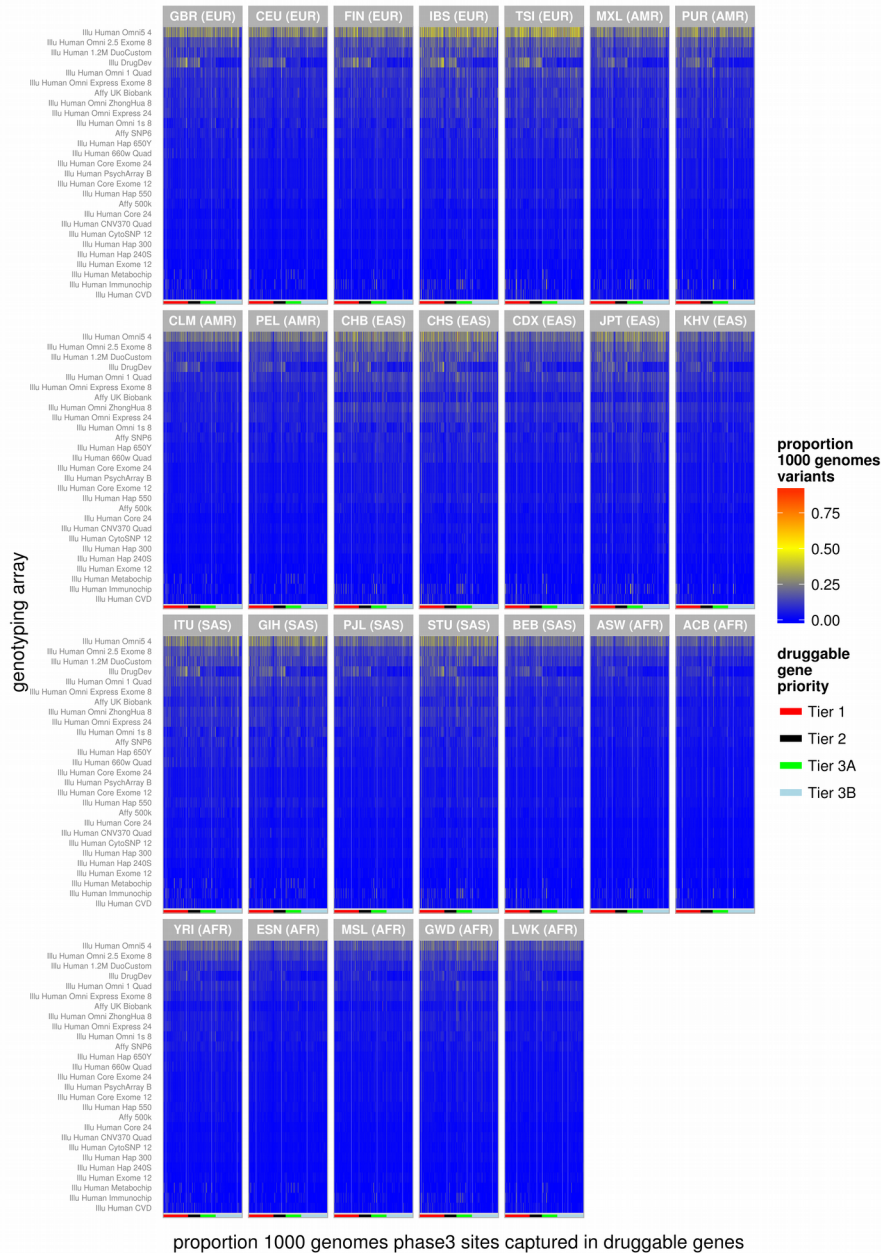


Fig. S7. Directly typed variant coverage of druggable genes in the 1000 genomes subpopulations. Coverage of the druggable gene set is represented as a proportion of 1000 genomes phase 3 variants (bi-allelic with $\text{maf} \geq 0.005$) that are directly typed. Within each plot, a column represents a druggable gene and each row a genotyping array. The druggable genes are grouped according to their druggability tier, which is indicated by the color bar at the base of each plot. To aid visualization, the druggable genes are further sorted within each tier on their median coverage across all the arrays, and the genotyping arrays are sorted based on their median coverage of the druggable genome across all the 1000 genomes subpopulations, with the super population group in parentheses at the top of each section. EUR – European populations (GBR – British in England and Scotland, CEU – Utah Residents (CEPH) with Northern and Western Ancestry, FIN – Finnish in Finland, IBS – Iberian Population in Spain, TSI – Toscani in Italy). AMR – American populations (MXL – Mexican Ancestry from Los Angeles USA, PUR – Puerto Ricans from Puerto Rico, CLM – Colombians from Medellin, Colombia, PEL – Peruvians from Lima, Peru). EAS – East Asians (CHB – Han Chinese in Beijing, China, CHS – Southern Han Chinese, CDX – Chinese Dai in Xishuangbanna, China, JPT – Japanese in Tokyo, Japan, KHV – Kinh in Ho Chi Minh City, Vietnam). SAS – South Asians (ITU – Indian Telugu from the UK, GIH – Gujarati Indian from Houston, Texas, PJI – Punjabi from Lahore, Pakistan, STU – Sri Lankan Tamil from the UK, BEB – Bengali from Bangladesh). AFR – Africans (ASW – Americans of African Ancestry in SW USA, ACB – African Caribbeans in Barbados, YRI – Yoruba in Ibadan, Nigeria, ESN – Esan in Nigeria, MSL – Mende in Sierra Leone, GWD – Gambian in Western Divisions in the Gambia, LWK – Luhya in Webuye, Kenya). Note that all of the arrays contained content that could not be mapped to the 1000 genomes phase 3 (see fig. S10).

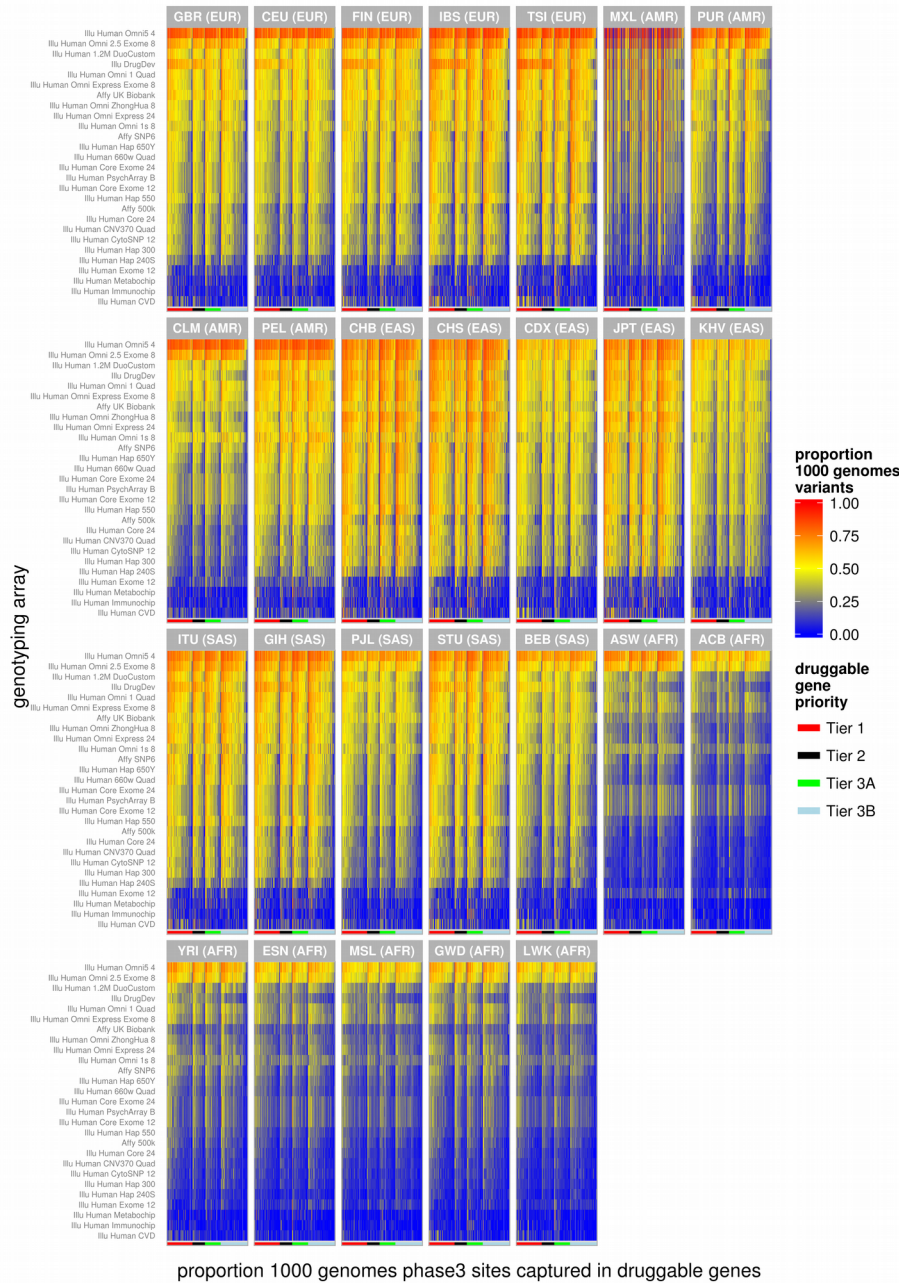


Fig. S8. Directly typed variant coverage of druggable genes in the 1000 genomes subpopulations. Coverage of the druggable gene set is represented as a proportion of 1000 genomes phase 3 variants (bi-allelic with $\text{maf} \geq 0.005$) that are directly typed or tagged (at $r^2 \geq 0.8$). Within each plot, a column represents a druggable gene and each row a genotyping array. The druggable genes are grouped according to their druggability tier, which is indicated by the color bar at the base of each plot. To aid visualization, the druggable genes are further sorted within each tier on their median coverage across all the arrays, and the genotyping arrays are sorted based on their median coverage of the druggable genome across all the 1000 genomes subpopulations, with the super population group in parentheses at the top of each section. EUR – European populations (GBR – British in England and Scotland, CEU – Utah Residents (CEPH) with Northern and Western Ancestry, FIN - Finnish in Finland, IBS - Iberian Population in Spain, TSI - Toscani in Italy). AMR – American populations (MXL - Mexican Ancestry from Los Angeles USA, PUR - Puerto Ricans from Puerto Rico, CLM - Colombians from Medellin, Colombia, PEL - Peruvians from Lima, Peru). EAS – East Asians (CHB - Han Chinese in Beijing, China, CHS - Southern Han Chinese, CDX - Chinese Dai in Xishuangbanna, China, JPT - Japanese in Tokyo, Japan, KHV - Kinh in Ho Chi Minh City, Vietnam). SAS – South Asians (ITU - Indian Telugu from the UK, GIH - Gujarati Indian from Houston, Texas, PJI - Punjabi from Lahore, Pakistan, STU - Sri Lankan Tamil from the UK, BEB - Bengali from Bangladesh). AFR – Africans (ASW - Americans of African Ancestry in SW USA, ACB - African Caribbeans in Barbados, YRI - Yoruba in Ibadan, Nigeria, ESN - Esan in Nigeria, MSL - Mende in Sierra Leone, GWD - Gambian in Western Divisions in the Gambia,

LWK - Luhya in Webuye, Kenya). Note that all of the arrays contained content that could not be mapped to the 1000 genomes phase 3 (see fig. S10).

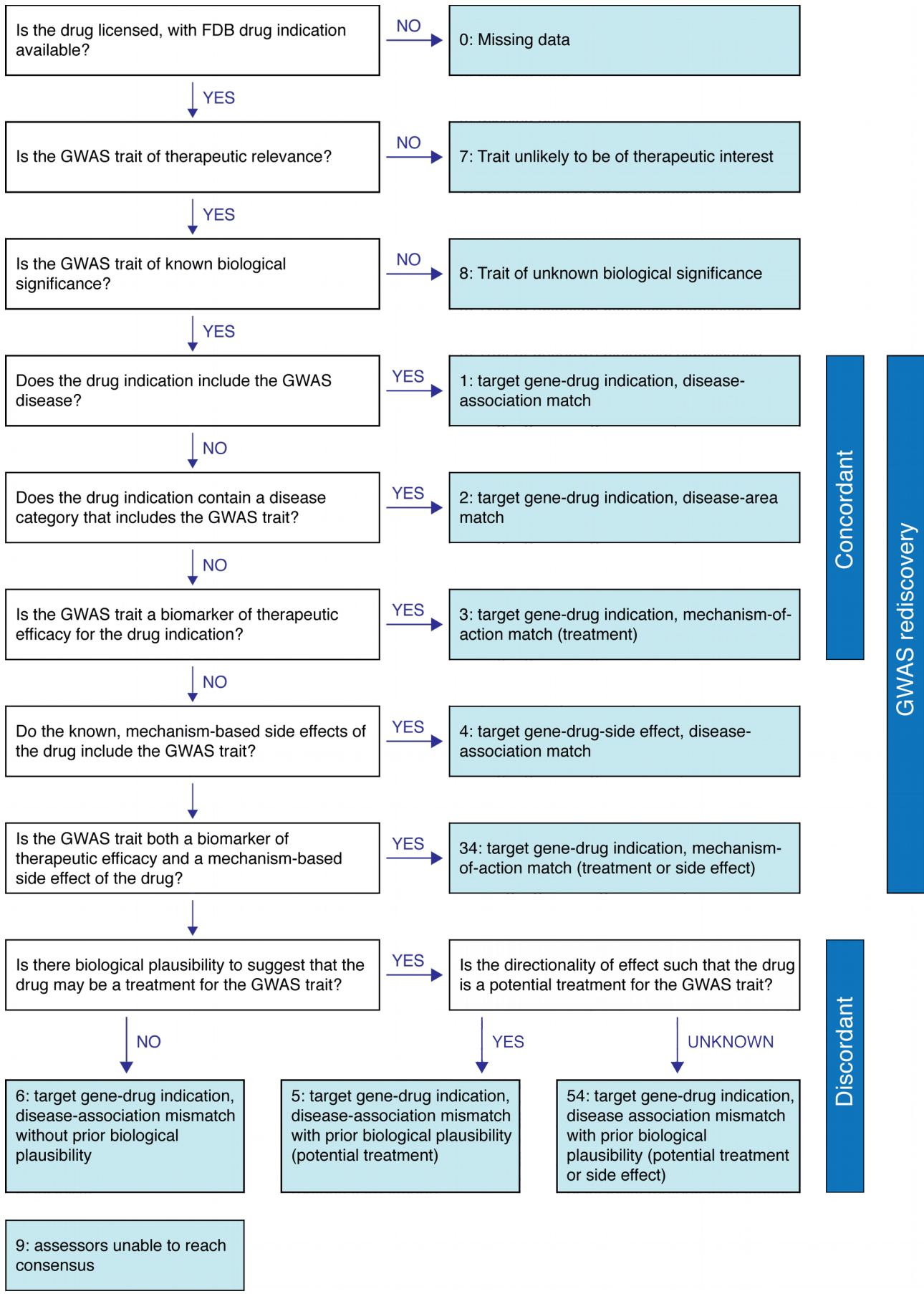


Fig. S9. Criteria for manual evaluation of the concordance/discordance of GWAS phenotypes and drug indications and side effects.

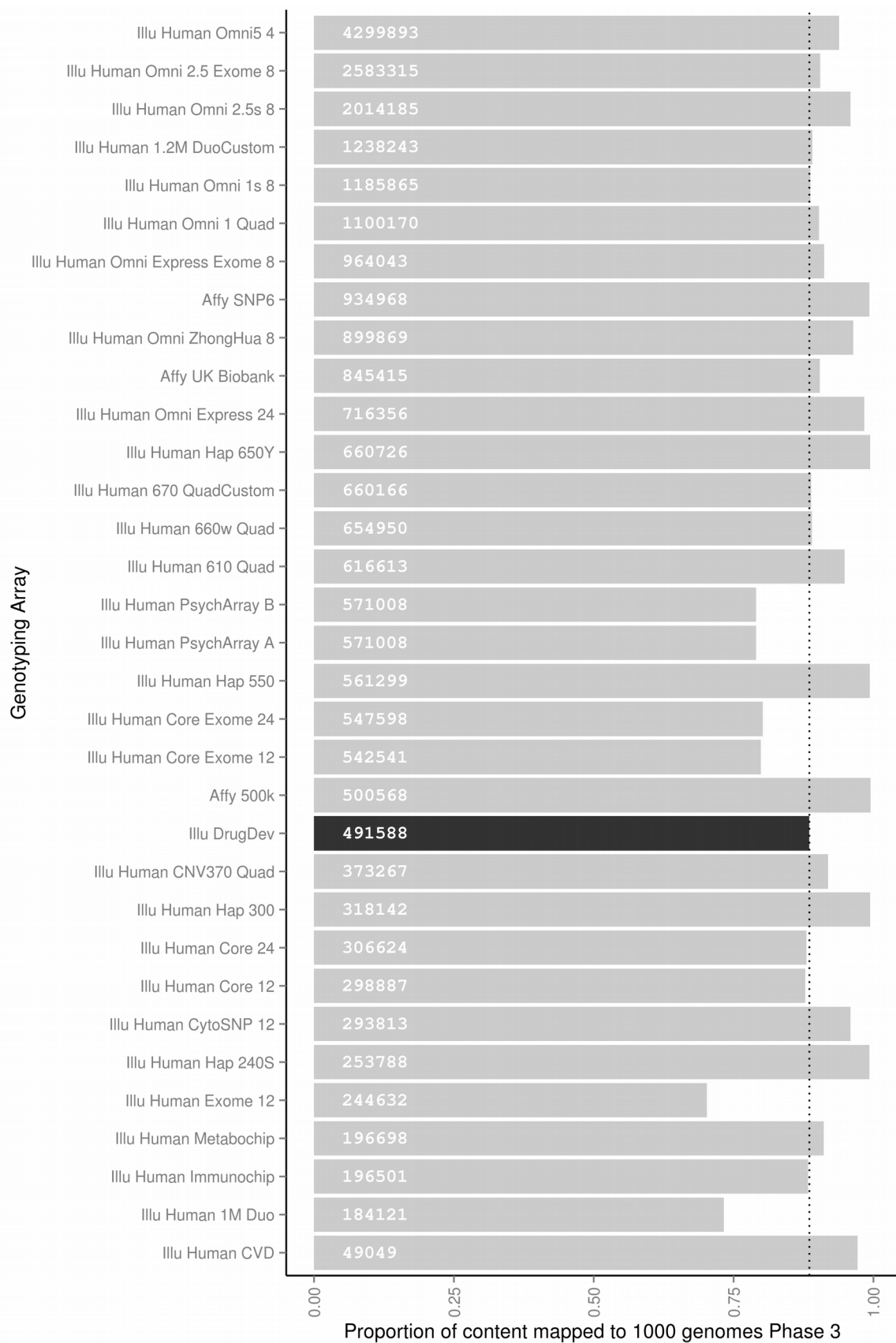


Fig. S10. Proportion of content in various commercial arrays mapped to the 1000 genomes phase 3 set of variants. The numbers in the bars show the total content on the array. The black bar is the DrugDev array introduced in this manuscript. The numbers after some of the array names indicate version numbers. The dashed line is to aid comparison of the Drug Dev array with the other arrays on the plot

Table S1: The druggable genome. Druggable genes, their locations and druggability priority, as well as the number of times each gene has overlapped an LD region surrounding a significant GWAS association ($P \leq 5 \times 10^{-8}$) are indicated along with the type of molecule that binds to each of the druggable genes. Provided as an Excel file.

Tier 1		Tier 2		Tier 3	
Pfam-A	#	Pfam-A	#	Pfam-A	#
Pkinase *	194	Pkinase *	81	7tm_1 *	113
7tm_1 *	119	7tm_1 *	41	V-set	74
Pkinase_Tyr *	100	Trypsin *	16	Collagen	61
p450 *	47	Ion_trans *	13	Ion_trans *	61
fn3	32	Y_phosphatase *	11	LRR_8	59
Ion_trans *	30	PI3_PI4_kinase *	9	Pkinase *	55
Neur_chan_LBD *	28	Hormone_recep *	9	Ig_2	55
Neur_chan_memb	28	zf-C4	9	Trypsin *	52
SH2 *	25	Pro_isomerase *	9	I-set	50
Hormone_recep *	25	Neur_chan_LBD *	8	EGF_CA	49
zf-C4	25	SH2 *	8	Ig_3	44
ig	23	Pkinase_C	8	EGF	42
ABC_tran *	23	Neur_chan_memb	8	7tm_4	41
ANF_receptor *	22	Bromodomain *	7	Kelch_1	40
Pkinase_C	21	Pkinase_Tyr *	6	Lectin_C	39

Table S2. Pfam-A domain content in three tiers of druggable genes. Summarized are counts of the 15 most frequent Pfam-A domains in genes assigned to each of the three tiers. Pfam domains with measured small molecule interactions are marked with asterisks. Tiers 1 and 2 incorporated domain types belonging to well-studied drug target classes, such as GPCRs, kinases, and ligand-gated ion channels. The domain composition of Tier 3 reflects enrichment for secreted and extracellular proteins, including constituents of the extracellular matrix, immunoglobulins, and leucine-rich repeats found on membrane-bound toll-like receptors.

Gene	Drug	Drug type	Curati on code	GWAS EFO term	Drug Indication (FDB)	Variant	Pubmed ID	Min. dist. from drug gene (bp)	Dist. rank of drug gene	Genes in LD region	Drug genes in LD region
ALDH2	Disulfiram	Small molecule	1	alcohol drinking drinking behavior	Alcoholism (adjunctive treatment)	rs11066280 rs12229654 rs2074356 rs671	21270382 21372407 23364009 24277619	6016 - 790230	1 -18	22 - 33	2 - 4
PDE4D	Aminophylline	Small molecule	1	asthma	Acute asthma Acute exacerbation of chronic obstructive airways disease Bronchial asthma Chronic obstructive pulmonary disease Left ventricular failure - cardiac failure - cardiac asthma Reversible airways obstruction Routine maintenance therapy in chronic bronchitis and asthma	rs1588265	19426955	448153	1	2	1
IGF1R	Mecasermin	Protein	1	body height	Growth failure due to primary IGF-1 deficiency	rs2871865	20881960 25429064	2696	1	2	1
TNFSF11	Denosumab	Antibody	1	bone density	Prevention of skeletal related events in advanced malignancy involving bone Treatment of bone loss associated with hormone ablation in prostate cancer Treatment of osteoporosis in postmenopausal women to prevent fractures	rs17536328 rs9525638	24945404	6157 - 8295	1	1	1
ESR1	Tamoxifen Citrate	Small molecule	1	breast carcinoma	Carcinoma of breast Infertility - female - anovulatory	rs140068132 rs3757318 rs9383938	22976474 23535729 25327703	9531 - 63713	1 - 2	2	1
PLG	Alteplase	Enzyme	1	coronary heart disease large artery stroke stroke	Acute ischaemic stroke: fibrinolytic treatment Thrombolysis in acute myocardial infarction Thrombolysis of occluded central venous access devices Thrombolytic treatment in acute massive pulmonary embolism	rs10455872	24262325	113152	3	3	2
TNF	Adalimumab	Antibody	1	Crohn's disease	Active polyarticular juvenile chronic arthritis-inadequate response to MTX Active progressive rheumatoid arthritis Moderate to severe plaque	rs1799964	21102463	1036	2	13	4

					psoriasis: when other treatment is inappropriate Moderate/severe ulcerative colitis: when other treatment is inappropriate Rheumatoid arthritis when inadequate response to DMARDs incl. methotrexate Severe active rheumatoid arthritis Severe ankylosing spondylitis in adults if conventional therapy inadequate Treatment of active & progressive psoriatic arthritis when DMARD inadequate Treatment of active Crohn's disease						
CACNA1D	Amlodipine	Small molecule	1	diastolic blood pressure	Essential hypertension when stabilised on same ingreds.in same proportions Hypertension-not adequately controlled by individual components Prinzmetal's angina Prophylaxis of chronic stable angina pectoris Treatment of essential hypertension	rs9810888	25249183	106912	1	1	1
GUCY1A3	Isosorbide Dinitrate	Small molecule	1	diastolic blood pressure	Angina Angina pectoris - prophylaxis of acute attacks Angina pectoris - treatment of acute attacks Congestive heart failure (adjunct) Intracoronary use during angioplasty and to prevent/relieve coronary spasm Left ventricular failure Prophylaxis of angina pectoris Treatment of angina pectoris Treatment of unresponsive LVF, either post MI or of various aetiology Treatment severe/unstable angina	rs13139571	21909115	7988	1	2	1
NPC1L1	Ezetimibe	Small molecule	1	LDL cholesterol low density lipoprotein cholesterol measurement total cholesterol measurement	Combined hyperlipidaemia: lipid lowering therapy adjunct to diet Homozygous familial hypercholesterolaemia (adjunct to statin therapy) Homozygous familial hypercholesterolaemia: Adjunct to diet	rs2072183	20686565 24097068	1734	1	1	1

					Homozygous sitosterolaemia (phytosterolaemia) Primary hypercholesterolaemia (hyperlipidaemia type IIa): Adjunct to diet Primary hypercholesterolaemia: lipid lowering therapy adjunct to diet						
PPARA	Gemfibrozil	Small molecule	1	LDL cholesterol low density lipoprotein cholesterol measurement total cholesterol measurement	Mixed hyperlipidaemia when statin is contraindicated or not tolerated Primary hypercholesterolaemia: lipid lowering therapy adjunct to diet Reduction of cardiac events in hypercholesterolaemia Severe hypertriglyceridaemia with or without low HDL cholesterol	rs4253772	24097068	12050	1	7	2
CASR	Cinacalcet Hcl	Small molecule	1	calcium measurement	Homoeopathic Hypercalcaemia due to malignant disease Hypercalcaemia in primary HPT when parathyroidectomy contraindicated Secondary hyperparathyroidism in end stage renal disease: treatment	rs17251221 rs1801725	20661308 20705733 24068962	1585 - 12095	1	5	1
IL6R	Tocilizumab	Antibody	1	rheumatoid arthritis	Active juvenile idiopathic arthritis (unresp to NSAIDs) in comb with MTX Active juvenile idiopathic arthritis when inadequate response to NSAIDs Rheumatoid arthritis (unresp to DMARD/TNF inhib.) in comb with methotrexate Rheumatoid arthritis when inadequate response to DMARDs incl. methotrexate	rs2228145	24390342	14956	1	1	1
TNF	Adalimumab	Antibody	1	rheumatoid arthritis	Active polyarticular juvenile chronic arthritis-inadequate response to MTX Active progressive rheumatoid arthritis Moderate to severe plaque psoriasis: when other treatment is inappropriate Moderate/severe ulcerative colitis: when other treatment is	rs2596565	24532677	190015	24	145	27

					inappropriate Rheumatoid arthritis when inadequate response to DMARDs incl. methotrexate Severe active rheumatoid arthritis Severe ankylosing spondylitis in adults if conventional therapy inadequate Treatment of active & progressive psoriatic arthritis when DMARD inadequate Treatment of active Crohn's disease						
ABCC8	Glimepiride	Small molecule	1	type II diabetes mellitus	Type 2 diabetes (NIDDM) not controlled by diet,weight loss & exercise alone	rs5219	19056611	4860 - 5802	3	5	3
ABCC8	Glipizide	Small molecule	1	type II diabetes mellitus	Non insulin dependent diabetes mellitus when diet has failed	rs5219	19056611	4860 - 5802	3	5	3
ABCC8	Glyburide	Small molecule	1	type II diabetes mellitus	Type 2 diabetes (NIDDM) not controlled by diet,weight loss & exercise alone	rs5215 rs5219	17463248 17463249 19056611 24509480	4860 - 5802	3	5	3
ABCC8	Nateglinide	Small molecule	1	type II diabetes mellitus	Control of type-2 diabetes (NIDDM) with metformin if metformin inadequate	rs5219	19056611	4860 - 5802	3	5	3
ABCC8	Repaglinide	Small molecule	1	type II diabetes mellitus	Control of type-2 diabetes (NIDDM) with metformin if metformin inadequate Type 2 diabetes (NIDDM) not controlled by diet,weight loss & exercise alone	rs5219	19056611	4860 - 5802	3	5	3
KCNJ11	Glimepiride	Small molecule	1	type II diabetes mellitus	Type 2 diabetes (NIDDM) not controlled by diet,weight loss & exercise alone	rs5219	19056611	1224 - 1306	1	5	3
KCNJ11	Glipizide	Small molecule	1	type II diabetes mellitus	Non insulin dependent diabetes mellitus when diet has failed	rs5219	19056611	1224 - 1306	1	5	3
KCNJ11	Glyburide	Small molecule	1	type II diabetes mellitus	Type 2 diabetes (NIDDM) not controlled by diet,weight loss & exercise alone	rs5215 rs5219	17463248 17463249 19056611 24509480	1224 - 1306	1	5	3
KCNJ11	Nateglinide	Small molecule	1	type II diabetes mellitus	Control of type-2 diabetes (NIDDM) with metformin if metformin inadequate	rs5219	19056611	1224 - 1306	1	5	3

KCNJ11	Repaglinide	Small molecule	1	type II diabetes mellitus	Control of type-2 diabetes (NIDDM) with metformin if metformin inadequate Type 2 diabetes (NIDDM) not controlled by diet, weight loss & exercise alone	rs5219	19056611	1224 - 1306	1	5	3
PPARG	Pioglitazone Hcl	Small molecule	1	type II diabetes mellitus	Combination treatment of Type 2 diabetes with insulin Control of type-2 diabetes if metformin+sulphonylurea therapy is inadequate Monotherapy for type2 diabetes if overweight and metformin inappropriate Oral combination treatment of type 2 diabetes	rs1801282	24509480	64258	1	1	1
SCN1A	Oxcarbazepine	Small molecule	1	Mesial temporal lobe epilepsy with hippocampal sclerosis febrile seizures	Epilepsy - combination of both partial and tonic-clonic seizures Epilepsy - partial seizures	rs7587026	24014518	5773 - 52194	1	3	1
GRIN3B	Memantine Hcl	Small molecule	1	Alzheimer's disease	Moderate to severe Alzheimer's disease No information available	rs115550680	23571587	40689	8	8	2
SLC22A12	Sulfinpyrazone	Small molecule	1	urate measurement	Gout (prophylaxis) Gouty arthritis Hyperuricaemia	rs2078267 rs478607	20884846 23263486	23999 - 108243	2 -3	2 -3	2
SLC22A11	Probenecid	Small molecule	1	urate measurement uric acid measurement		rs17300741 rs2078267	19503597 20884846 23263486	6233 - 8364	1	1 - 2	1 - 2
PDE4D	Roflumilast	Small molecule	2	asthma	Chronic obstructive pulmonary disease	rs1588265	19426955	448153	1	2	1
SCN2A	Carbamazepine	Small molecule	2	febrile seizures	Epilepsy - grand mal Epilepsy - partial seizures Epilepsy - tonic-clonic seizures Prophylaxis of manic-depressive illness unresponsive to lithium Trigeminal neuralgia	rs3769955	25344690	14186	1	1	1
FSHR	Menotropins	Unknown	2	polycystic ovary syndrome	Anovulation unresponsive to clomifene citrate Ovarian stimulation before in vitro fertilisation Stimulation of spermatogenesis with concomitant hCG therapy in hypogonadism	rs2268361	22885925	12316	1	1	1

PLG	Alteplase	Enzyme	3	plasma plasminogen measurement	Acute ischaemic stroke: fibrinolytic treatment Thrombolysis in acute myocardial infarction Thrombolysis of occluded central venous access devices Thrombolytic treatment in acute massive pulmonary embolism	rs4252129	25208887	21442	1	1	1
DIO1	Propylthiouracil	Small molecule	3	thyroxine thyroxine measurement	Hyperthyroidism Thyrotoxic crisis Unlicensed product	rs2235544	23408906	1189	1	4	1
PDE4D	Dipyridamole	Small molecule	4	asthma	Alternative to exercise stress in thallium-201 myocardial imaging Ischemic stroke: Secondary prevention (with/without aspirin) Secondary prevention of ischaemic stroke Secondary prevention of transient ischaemic attacks Thromboembolism+prosthetic heart valve: prophylaxis (+oral anticoagulant) Transient ischemic attacks: Secondary prevention (with/without aspirin)	rs1588265	19426955	448153	1	2	1
ACHE	Rivastigmine	Small molecule	4	resting heart rate	Mild - moderate dementia in Alzheimer's disease Mild - moderate dementia in idiopathic Parkinson's disease	rs12666989 rs314370	20639392	861 - 34407	3 - 7	9	4
ACHE	Neostigmine Methylsulfate	Small molecule	4	heart rate	Myasthenia gravis Paralytic ileus Paroxysmal supra-ventricular tachyarrhythmias Post operative distention Post operative urinary retention Reversal of residual competitive neuromuscular block Unlicensed product	rs13245899	23583979	861 - 34407	1 - 71	9	4
CHRM2	Tolterodine Tartrate	Small molecule	4	heart rate	Symptomatic treatment of urinary urgency, frequency or urge incontinence	rs2350782	23583979	62368	1	3	1

Table S3. Illustrative examples of mapping SNPs curated in the GWAS catalog to LD intervals containing targets of licensed and clinically used drugs. The genes encoding the drug targets are listed using Human Genome Nomenclature Catalogue designation. Drug names and indications are from First Data bank. GWAS SNPs are listed according to Refseq number, and physical distances are in base pairs (bp). Curation code refers to the correspondence between the treatment indication and

GWAS disease or trait association. Some examples show treatment indication rediscoveries (curation codes 1 and 2). For many of these, the drug target gene is the sole occupant of the LD interval defined by the GWAS SNP. Examples come from a variety of disease areas and, for some diseases (such as type 2 diabetes and rheumatoid arthritis), multiple target rediscoveries are noted. Examples of rediscoveries of mechanism of action (curation code 3) and mechanism-based side effects (curation code 4) are also seen.

Group	N	SNP/gene distance (bp)	SNP/gene distance (rank)	LD region length (bp)	# genes in LD region	# druggable genes in LD region
Unassigned - 0	1348	29020 [9531-62570]	1 [1-3]	79320 [39740-217100]	2 [1-9]	1 [1-3]
Concordant 1-4,34	2100	29020 [9489-39160]	1 [1-1]	50260 [26440-75500]	1 [1-2]	1 [1-1]
Discordant 5-6	1523	72620 [22650-178900]	3 [1-7]	137900 [63490-5e+05]	5 [2-17]	1 [1-4]
Mixed 54	582	39260 [10760-52190]	1 [1-2]	116800 [59720-229300]	3 [1-4]	1 [1-2]
Remaining 7-9	797	18260 [8416-86080]	1 [1-6]	128700 [23860-320700]	5 [2-16]	2 [1-5]

Table S4. Summary of the physical properties of LD regions. The properties were stratified by the manually curated concordance/discordance group to which compounds targeting the druggable genes within them are assigned.