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Supplementary Material

Article Title: Candidate Gene Analysis Identifies a Polymorphism in HLA-DQB1 Associated With Clozapine-Induced Agranulocytosis

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eTable 1. Candidate Gene List

Gene Symbol	Gene Name
ADRA2C	adrenergic, alpha-2C-, receptor
ADRB1	adrenergic, beta 1 receptor
ADRB2	adrenergic, beta 2 receptor
ALB	Albumin
ARHGDIB	Rho GDP dissociation inhibitor (GDI) beta
ATP2A2	ATPase, Ca++ transporting, cardiac muscle, slow twitch 2
BAX	BCL2-associated X protein
BCL2L1	BCL2-like 1
BIK	BCL2-interacting killer (apoptosis-inducing)
CHRM3	cholinergic receptor, muscarinic 3
CHRM4	cholinergic receptor, muscarinic 4
CHRM5	cholinergic receptor, muscarinic 5
CSF2	colony stimulating factor 2 (granulocyte-macrophage)
CSF2RA	colony stimulating factor 2 receptor, alpha
CSF2RB	colony stimulating factor 2 receptor, beta
CSF3	colony stimulating factor 3
CSF3R	colony stimulating factor 3 receptor
CYBA	cytochrome b-245, alpha polypeptide
CYBB	cytochrome b-245, beta polypeptide
CYP1A2	cytochrome P450, family 1, subfamily A, polypeptide 2

CYP2C19	cytochrome P450, family 2, subfamily C, polypeptide 19
CYP2C9	cytochrome P450, family 2, subfamily C, polypeptide 9
CYP2D6	cytochrome P450, family 2, subfamily D, polypeptide 6
CYP3A4	cytochrome P450, family 3, subfamily A, polypeptide 4
CYR61	cysteine-rich, angiogenic inducer, 61
DRD1	dopamine receptor D1
DRD2	dopamine receptor D2
DRD3	dopamine receptor D3
DRD4	dopamine receptor D4
DRD5	dopamine receptor D5
FKBP1	FK506 binding protein 1A
FPR1	formyl peptide receptor 1
HGF	hepatocyte growth factor
HLA-C	major histocompatibility complex, class I, C
HLA-DQB1	major histocompatibility complex, class II, DQ beta 1
HLA-DRA	major histocompatibility complex, class II, DR alpha
HRH1	histamine receptor 1
HRH2	histamine receptor 2
HRH4	histamine receptor 4
HSPA1A	heat shock 70kDa protein 1A
HSPA1B	heat shock 70kDa protein 1B
HSPA1L	heat shock 70kDa protein 1-like
HTR2A	serotonin receptor 2A

HTR7	serotonin receptor 7
IL1R1	interleukin 1 receptor, type I
IL2	interleukin 2
IL2RA	interleukin 2 receptor, alpha
IL3	interleukin 3
IL3RA	interleukin 3 receptor, alpha
ITGAL	integrin, alpha L
ITGB2	integrin, beta 2
LAMR1	ribosomal protein SA (RPSA)
LEP	Leptin
LEPR	leptin receptor
MCL1	myeloid cell leukemia sequence 1
MET	met proto-oncogene; hepatocyte growth factor receptor
MPO	Myeloperoxidase
MTATP6	mitochondrially encoded ATP synthase 6
NCF2	neutrophil cytosolic factor 2
NCF4	neutrophil cytosolic factor 4
NFKB1	nuclear factor of kappa light polypeptide gene enhancer in B-cells 1
NQO2	NAD(P)H dehydrogenase, quinone 2
NTSR1	neutotensin receptor 1
P2RX1	purinergic receptor P2X, ligand-gated ion channel, 1
P2RX7	purinergic receptor P2X, ligand-gated ion channel, 7
P2RY2	purinergic receptor P2y, G-protein coupled, 2

PLAB	growth differentiation factor 15 (GDF15)
RAC2	ras-related C3 botulinum toxin substrate 2
SKI	v-ski sarcoma viral oncogene homolog (avian)
TACR1	tachykinin receptor 1
TNF	tumor necrosis factor
TNFRSF1A	tumor necrosis factor receptor superfamily, member 1A
TNFRSF1B	tumor necrosis factor receptor superfamily, member 1B
TXNIP	thioredoxin interacting protein

eTable 2. Markers Selected for Evaluation in Cohort II

GENE	MARKER[a]
CSF2RB	REC 4 11T, 46G, 50G, 87G
	REC 4 11T, 46G, 50G, 86G
	REC 3 11T, 46G, 50G
	REC 4 11T, 44G, 46G, 86G
	REC 4 11T, 44G, 46G, 87G
	REC 3 11T, 44G, 46G
DRD1	REC 3 5C, 19C, 21G
	REC 3 21G, 22G, 50C
	REC 2 18G, 21G
	REC 2 21G, 50C
	REC 4 4T, 21G, 22G, 50C
	REC 3 18G, 21G, 49C
	REC 4 8T, 21G, 22G, 50C
HLA-DQB1	REC 4 5C, 21G, 22G, 50C
	REC 3 8T, 18G, 21G
	REC 3 10C, 18G, 21G
	REC 2 21G, 49C
	REC 4 19C, 21G, 22G, 50C
	REC 4 9G, 21G, 22G, 50C
	REC 3 4T, 21G, 50C

	REC 4 5C, 8T, 18G, 21G
	REC 3 9G, 18G, 21G
	REC 3 5C, 18G, 21G
	REC 3 4T, 21G, 42C
	REC 4 10C, 18G, 21G, 45I
	REC 4 5C, 18G, 21G, 49C
	REC 3 18G, 19C, 21G
NTSR1	REC 3 8C, 17C, 25A

[a] Marker nomenclature: 1) model ("REC" for recessive, "DOM" for dominant); 2) the number of variants that comprise the haplotype; and 3) an identifier and allele for each polymorphism in the marker (eg, polymorphic site #5 in *HLA-DQB1* is nucleotide C)

eTable 3. Primer Sequences, Cohort II

GENE	DIRECTION	TAIL [a,b]	SPECIFIC SEQUENCE [b]	SIZE OF PRODUCT (bp)
CSF2RB	Forward	TGTAAAACGACGGCCAGT	TCTCTCTCTCTCGGAGCTGTTGG	533
	Reverse	AGGAAACAGCTATGACCAT	GCACTGGGGAGCACTCTTCC	
	Forward	TGTAAAACGACGGCCAGT	CCTGGCACATAAGAGACCTCAGC	575
	Reverse	AGGAAACAGCTATGACCAT	AACAGGGAAACTGAGTCACAGAACC	
DRD1	Forward	TGTAAAACGACGGCCAGT	CTGACCTTTGGGGTTCATACGG	464
	Reverse	AGGAAACAGCTATGACCAT	CCTTAAAGTCCATCCTCCTTCAGC	
	Forward	TGTAAAACGACGGCCAGT	TTTGAGCAGGCCCCACTACC	461
	Reverse	AGGAAACAGCTATGACCAT	CAACCTCACTCACAAGGGTTCC	
	Forward	TGTAAAACGACGGCCAGT	CCACTTCCCTGGCTGAGACC	546
	Reverse	AGGAAACAGCTATGACCAT	CTAAGAGGGTTGAAAATGCCTTCC	
	Forward	TGTAAAACGACGGCCAGT	CCTTCTGCATTGATTCCAACACC	504

	Reverse	AGGAAACAGCTATGACCAT	CTTTTGGGATGAGCATGTGTGG	
HLA-DQB1	Forward	TGTAAAACGACGGCCAGT	GCATCAAGCTGAAGTTCTGTG	529
	Reverse	AGGAAACAGCTATGACCAT	GCTTCTCTTGAGCAGTCTGAGG	
	Forward	TGTAAAACGACGGCCAGT	AACCACGGGTTCTGGAGCTAGG	571
	Reverse	AGGAAACAGCTATGACCAT	AGGCTCTGCAGCGACTTCTTCC	
	Forward	TGTAAAACGACGGCCAGT	CTCCTGAACTTGTGTTGACTGAGC	549
NTSR1	Reverse	AGGAAACAGCTATGACCAT	GAGGGATGGAGTGCAGAATGG	
	Forward	TGTAAAACGACGGCCAGT	TCCCCAAACAACCATTCTCAAGG	530
	Reverse	AGGAAACAGCTATGACCAT	CTGCCTGACCCCCATCAAGG	

[a] For sequencing, used tail primer. [b] For PCR Amplification, used specific + tail primer. M13F and M13R tail sequences used for sequencing.

eTable 4. PCR Conditions, Cohort II

PCR STEP	TIME (min)	TEMP. (°C)
1	2:00	97
2	0:15	97
3	0:45	70
4	0:45	72
5	Repeat Steps 2-4: 23x. [a]	
6	0:15	97
7	0:45	55
8	0:45	72
9	Repeat Steps 6-8 22x.	
10	5:00	72

[a] Decrease annealing temp 0.7°C per cycle.