



- (51) International Patent Classification:
C12Q 1/68 (2006.01)
- (21) International Application Number:
PCT/US2014/041617
- (22) International Filing Date:
10 June 2014 (10.06.2014)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
61/833,257 10 June 2013 (10.06.2013) US
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- (81) Designated States (*unless otherwise indicated, for every kind of national protection available*): AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

- (84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LR, LS, MW, MZ, NA, RW, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Published:

- *without international search report and to be republished upon receipt of that report (Rule 48.2(g))*

(54) Title: GENETIC MARKERS OF ANTIPSYCHOTIC RESPONSE

(57) Abstract: Provided herein are genetic markers for predicting response to antipsychotic treatment. Identification of the disclosed SNPs can be used to predict response to antipsychotic drugs in patients suffering from schizophrenia.



WO 2014/200952 A2

DESCRIPTION

GENETIC MARKERS OF ANTIPSYCHOTIC RESPONSE

[0001] This application claims the benefit of United States Provisional Patent Application No. 61/833,257, filed June 10, 2013, the entirety of which is incorporated herein
5 by reference.

[0002] This invention was made with government support under Grant No. MH078437 awarded by the National Institutes of Health. The government has certain rights in the invention.

BACKGROUND OF THE INVENTION

10 **1. Field of the Invention**

[0003] The present invention relates generally to the fields of medicine, genetics, and psychiatry. More particularly, it concerns genetic markers that are associated with response to antipsychotic treatments.

2. Description of Related Art

15 [0004] The schizophrenia spectrum disorders (SSDs) include schizophrenia (SZ), schizotypal personality disorder (SPD), and/or schizoaffective disorder (SD). Schizophrenia (SZ) is considered a clinical syndrome, and is probably a constellation of several pathologies. Substantial heterogeneity is seen between cases, which is thought to reflect multiple overlapping etiologic factors, including both genetic and environmental contributions. SD is
20 characterized by the presence of affective (depressive or manic) symptoms and schizophrenic symptoms within the same, uninterrupted episode of illness. SPD is characterized by a pervasive pattern of social and interpersonal deficits marked by acute discomfort with, and reduced capacity for, close relationships as well as by cognitive or perceptual distortions and eccentricities of behavior, beginning by early adulthood and present in a variety of contexts.

25 [0005] Various genes and chromosomes have been implicated in etiology of SZ. Many studies have suggested the presence of one or more important genes relating to SZ on most or all of the autosomes (Williams *et al.*, 1999; Fallin *et al.*, 2005; Badner *et al.*, 2002; Cooper-Casey *et al.*, 2005; Devlin *et al.*, 2002; Fallin *et al.*, 2003; Jablensky, 2006; Kirov *et al.*, 2005; Norton *et al.*, 2006; Owen *et al.*, 2004). However, none of these prior studies have
30 used high resolution genetic association methods to systematically compare genes involved in

response to treatments for SSD, *e.g.*, using anti-psychotics. Neither have any of these studies demonstrated that genetic polymorphisms in the genes defined herein are important in response to anti-psychotics.

[0006] Due to the severity of these disorders, especially the negative impact of a psychotic episode on a patient, and the diminishing recovery after each psychotic episode, there is a need to more conclusively identify individuals who will respond best to specific therapies, and/or who is likely to suffer the most severe side effects, to determine appropriate therapies based on genotypic subtype.

SUMMARY OF THE INVENTION

[0007] Results detailed in the instant application identify over 6,000 SNPs in genes impacting disease risk, disease presentation, and, particularly, response to antipsychotics drug treatment. Thus, in some embodiments methods are provided for detecting the presence of a polymorphism in and administering a treatment to a human subject, comprising (a) obtaining a genomic sample from a human subject having or at risk of developing SZ; (b) detecting the haplotype tagged by an allele selected from those provided in the tables herein; (c) identifying the subject having the haplotype tagged by the allele as likely (or unlikely) to have an improved response to a therapeutic as compared to a control subject; and (d) administering an appropriate treatment to the subject based on this identification.

[0008] In one embodiment is provided a method of detecting the presence of a polymorphism in and administering a treatment to a human subject, the method comprising (a) obtaining a genomic sample from a human subject having or at risk of developing SZ; (b) detecting the haplotype tagged by an allele selected from those provided in Table 1A in the genomic sample; (c) identifying the subject having the haplotype tagged by the allele provided in Table 1A in the genomic sample as likely to have an improved response to olanzapine as compared to control subject; and (d) administering a treatment comprising olanzapine to the subject with the haplotype tagged by the allele provided in Table 1A. In certain aspects, the method further comprises detecting the haplotype tagged by two or more alleles (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9 or more alleles) selected from those provided in Table 1A. In one aspect, said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 6.

[0009] In a further embodiment, there is provided a method of detecting the presence of a polymorphism in and administering a treatment to a human subject, the method comprising (a) obtaining a genomic sample from a human subject having or at risk of developing SZ; (b) detecting the haplotype tagged by an allele selected from those provided in Table 1B in the genomic sample; (c) identifying the subject having the haplotype tagged by the allele provided in Table 1B in the genomic sample as likely to have a poor response to olanzapine as compared to control subject; and (d) administering an antipsychotic treatment other than olanzapine to the subject with the haplotype tagged by the allele provided in Table 1B. In certain aspects, the method further comprises detecting the haplotype tagged by two or more alleles (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9 or more alleles) selected from those provided in Table 1B. In one aspect, said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 6. In certain aspects, the method comprises administering perphenazine, quetiapine, risperidone or ziprasidone to the subject.

[0010] Thus, in some aspects a method is provided for detecting the presence of a polymorphism in the CSMD1 or PTPRN2 gene and administering a treatment to a human subject, the method comprising (a) obtaining a genomic sample from a human subject having or at risk of developing SZ; (b) detecting the haplotype tagged by the “A” allele of rs17070785 or the haplotype tagged by the “C” allele of rs221253 in the genomic sample; (c) identifying the subject having the haplotype tagged by the “A” allele of rs17070785 or the haplotype tagged by the “C” allele of rs221253 in the genomic sample as likely to have an improved response to olanzapine as compared to control subject; and (d) administering a treatment comprising olanzapine to the subject with the haplotype tagged by the “A” allele of rs17070785 or the haplotype tagged by the “C” allele of rs221253.

[0011] In a further aspect there is provided a method of detecting the presence of a polymorphism in the PLAGL1 gene and administering an antipsychotic treatment to a human subject, the method comprising (a) obtaining a genomic sample from a human subject having or at risk of developing SZ; (b) detecting the haplotype tagged by the “C” allele of rs2247408 or the haplotype tagged by the “A” allele of rs3819811 in the genomic sample; (c) identifying the subject having the haplotype tagged by the “C” allele of rs2247408 or the haplotype tagged by the “A” allele of rs3819811 in the genomic sample as likely to have a poor response to olanzapine as compared to control subject; and (d) administering an antipsychotic treatment other than olanzapine to the subject with the haplotype tagged by the “C” allele of

rs2247408 or the haplotype tagged by the “A” allele of rs3819811. In certain aspects, the method comprises administering perphenazine, quetiapine, risperidone or ziprasidone to the subject.

[0012] In a further embodiment, the present invention provides a method of detecting
5 the presence of a polymorphism in and administering a treatment to a human subject, the method comprising (a) obtaining a genomic sample from a human subject having or at risk of developing SZ; (b) detecting the haplotype tagged by an allele selected from those provided in Table 2A in the genomic sample; (c) identifying the subject having the haplotype tagged by the allele provided in Table 2A in the genomic sample as likely to have an improved
10 response to perphenazine as compared to control subject; and (d) administering a treatment comprising perphenazine to the subject with the haplotype tagged by the allele provided in Table 2A. In certain aspects, the method further comprises detecting the haplotype tagged by two or more alleles (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9 or more alleles) selected from those provided in Table 2A. In one aspect, said two or more alleles are alleles from two or more different
15 correlated clusters selected from those provided in Table 7.

[0013] In still a further embodiment, a method is provided for detecting the presence of a polymorphism in and administering a treatment to a human subject, the method comprising (a) obtaining a genomic sample from a human subject having or at risk of developing SZ; (b) detecting the haplotype tagged by an allele selected from those provided
20 in Table 2B in the genomic sample; (c) identifying the subject having the haplotype tagged by the allele provided in Table 2B in the genomic sample as likely to have a poor response to perphenazine as compared to control subject; and (d) administering an antipsychotic treatment other than perphenazine to the subject with the haplotype tagged by the allele provided in Table 2B. In certain aspects, the method further comprises detecting the
25 haplotype tagged by two or more alleles (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9 or more alleles) selected from those provided in Table 2B. In one aspect, said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 7. In certain aspects, the method comprises administering olanzapine, quetiapine, risperidone or ziprasidone to the subject.

30 [0014] Thus, in some aspects, a method is provided for detecting the presence of a polymorphism in the MCPH1, PRKCE, CDH13, or SKOR2 gene and administering a treatment to a human subject, the method comprising (a) obtaining a genomic sample

from a human subject having or at risk of developing SZ; (b) detecting the haplotype tagged by the “C” allele of rs11774231, the haplotype tagged by the “C” allele of rs2278773, the haplotype tagged by the “A” allele of rs17570753, the haplotype tagged by the “C” allele of rs2116971, or the haplotype tagged by the “G” allele of rs9952628 in the genomic sample; (c) 5 identifying the subject having the haplotype tagged by the “C” allele of rs11774231, the haplotype tagged by the “C” allele of rs2278773, the haplotype tagged by the “A” allele of rs17570753, the haplotype tagged by the “C” allele of rs2116971, or the haplotype tagged by the “G” allele of rs9952628 in the genomic sample as likely to have an improved response to perphenazine as compared to control subject; and (d) administering a treatment comprising 10 perphenazine to the subject with the haplotype tagged by the “C” allele of rs11774231, the haplotype tagged by the “C” allele of rs2278773, the haplotype tagged by the “A” allele of rs17570753, the haplotype tagged by the “C” allele of rs2116971, or the haplotype tagged by the “G” allele of rs9952628.

[0015] In further aspects, a method is provided for detecting the presence of a 15 polymorphism in the MAML3 gene and administering a treatment to a human subject, the method comprising (a) obtaining a genomic sample from a human subject having or at risk of developing SZ; (b) detecting the haplotype tagged by the “A” allele of rs11100483 in the genomic sample; (c) identifying the subject having the haplotype tagged by the “A” allele of rs11100483 in the genomic sample as likely to have a poor response to perphenazine as 20 compared to control subject; and (d) administering an antipsychotic treatment other than perphenazine to the subject with the haplotype tagged by the “A” allele of rs11100483. In certain aspects, the method comprises administering olanzapine, quetiapine, risperidone or ziprasidone to the subject.

[0016] In a further embodiment, the present invention provides a method of detecting 25 the presence of a polymorphism in and administering a treatment to a human subject, the method comprising (a) obtaining a genomic sample from a human subject having or at risk of developing SZ; (b) detecting the haplotype tagged by an allele selected from those provided in Table 3A in the genomic sample; (c) identifying the subject having the haplotype tagged by the allele provided in Table 3A in the genomic sample as likely to have an improved 30 response to quetiapine as compared to control subject; and (d) administering a treatment comprising quetiapine to the subject with the haplotype tagged by the allele provided in Table 3A. In certain aspects, the method further comprises detecting the haplotype tagged by two

or more alleles (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9 or more alleles) selected from those provided in Table 3A. In one aspect, said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 8.

[0017] In yet a further embodiment, the present invention provides a method of
5 detecting the presence of a polymorphism in and administering a treatment to a human subject, the method comprising (a) obtaining a genomic sample from a human subject having or at risk of developing SZ; (b) detecting the haplotype tagged by an allele selected from those provided in Table 3B in the genomic sample; (c) identifying the subject having the haplotype tagged by the allele provided in Table 3B in the genomic sample as likely to have a
10 poor response to quetiapine as compared to control subject; and (d) administering an antipsychotic treatment other than quetiapine to the subject with the haplotype tagged by the allele provided in Table 3B. In certain aspects, the method further comprises detecting the haplotype tagged by two or more alleles (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9 or more alleles) selected from those provided in Table 3B. In one aspect, said two or more alleles are alleles from two
15 or more different correlated clusters selected from those provided in Table 8. In certain aspects, the method comprises administering olanzapine, perphenazine, risperidone or ziprasidone to the subject.

[0018] In some aspects a method is provided for detecting the presence of a polymorphism in the KCNMA1 gene and administering a treatment to a human subject, the
20 method comprising (a) obtaining a genomic sample from a human subject having or at risk of developing SZ; (b) detecting the haplotype tagged by the “C” allele of rs35793; (c) identifying the subject having the haplotype tagged by the “C” allele of rs35793 in the genomic sample as likely to have a poor response to quetiapine as compared to control subject; and (d) administering an antipsychotic treatment other than quetiapine to the subject
25 with the haplotype tagged by the “C” allele of rs35793. In certain aspects, the method comprises administering olanzapine, perphenazine, risperidone or ziprasidone to the subject.

[0019] In a further embodiment, the present invention provides a method of detecting the presence of a polymorphism in and administering a treatment to a human subject, the method comprising (a) obtaining a genomic sample from a human subject having or at risk of
30 developing SZ; (b) detecting the haplotype tagged by an allele selected from those provided in Table 4A in the genomic sample; (c) identifying the subject having the haplotype tagged by the allele provided in Table 4A in the genomic sample as likely to have an improved

response to risperidone as compared to control subject; and (d) administering a treatment comprising risperidone to the subject with the haplotype tagged by the allele provided in Table 4A. In certain aspects, the method further comprises detecting the haplotype tagged by two or more alleles (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9 or more alleles) selected from those provided
5 in Table 4A. In one aspect, said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 9.

[0020] In still a further embodiment, the present invention provides a method of detecting the presence of a polymorphism in and administering a treatment to a human subject, the method comprising (a) obtaining a genomic sample from a human subject having
10 or at risk of developing SZ; (b) detecting the haplotype tagged by an allele selected from those provided in Table 4B in the genomic sample; (c) identifying the subject having the haplotype tagged by the allele provided in Table 4B in the genomic sample as likely to have a poor response to risperidone as compared to control subject; and (d) administering an antipsychotic treatment other than risperidone to the subject with the haplotype tagged by the
15 allele provided in Table 4B. In certain aspects, the method further comprises detecting the haplotype tagged by two or more alleles (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9 or more alleles) selected from those provided in Table 4B. In one aspect, said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 9. In certain aspects, the method comprises administering olanzapine, perphenazine, quetiapine or
20 ziprasidone to the subject.

[0021] Thus, in some aspects a method is provided for detecting the presence of a polymorphism in the PSMD14, LRP1B, or TMEFF2 gene and administering a treatment to a human subject, the method comprising (a) obtaining a genomic sample from a human subject having or at risk of developing SZ; (b) detecting the haplotype tagged by the “A” allele of
25 rs9713, the haplotype tagged by the “C” allele of rs874295, or the haplotype tagged by the “C” allele of rs3738883 in the genomic sample; (c) identifying the subject having the haplotype tagged by the “A” allele of rs9713, the haplotype tagged by the “C” allele of rs874295, or the haplotype tagged by the “C” allele of rs3738883 in the genomic sample as likely to have an improved response to risperidone as compared to control subject; and (d)
30 administering a treatment comprising risperidone to the subject with the haplotype tagged by the “A” allele of rs9713, the haplotype tagged by the “C” allele of rs874295, or the haplotype tagged by the “C” allele of rs3738883.

[0022] In further aspects a method is provided for detecting the presence of a polymorphism in the AGAP1 or NPAS3 gene and administering a treatment to a human subject, the method comprising (a) obtaining a genomic sample from a human subject having or at risk of developing SZ; (b) detecting the haplotype tagged by the “C” allele of rs1869295 or the haplotype tagged by the “C” allele of rs1315115 in the genomic sample; (c) identifying the subject having the haplotype tagged by the “C” allele of rs1869295 or the haplotype tagged by the “C” allele of rs1315115 in the genomic sample as likely to have a poor response to risperidone as compared to control subject; and (d) administering an antipsychotic treatment other than risperidone to the subject with the haplotype tagged by the “C” allele of rs1869295 or the haplotype tagged by the “C” allele of rs1315115. In certain aspects, the method comprises administering olanzapine, perphenazine, quetiapine or ziprasidone to the subject.

[0023] In still a further embodiment, the present invention provides a method of detecting the presence of a polymorphism in and administering a treatment to a human subject, the method comprising (a) obtaining a genomic sample from a human subject having or at risk of developing SZ; (b) detecting the haplotype tagged by an allele selected from those provided in Table 5A in the genomic sample; (c) identifying the subject having the haplotype tagged by the allele provided in Table 5A in the genomic sample as likely to have an improved response to ziprasidone as compared to control subject; and (d) administering a treatment comprising ziprasidone to the subject with the haplotype tagged by the allele provided in Table 5A. In certain aspect, the method further comprises detecting the haplotype tagged by two or more alleles (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9 or more alleles) selected from those provided in Table 5A. In one aspect, said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 10.

[0024] In yet a further embodiment, the present invention provides a method of detecting the presence of a polymorphism in and administering a treatment to a human subject, the method comprising (a) obtaining a genomic sample from a human subject having or at risk of developing SZ; (b) detecting the haplotype tagged by an allele selected from those provided in Table 5B in the genomic sample; (c) identifying the subject having the haplotype tagged by the allele provided in Table 5B in the genomic sample as likely to have a poor response to ziprasidone as compared to control subject; and (d) administering an antipsychotic treatment other than ziprasidone to the subject with the haplotype tagged by the

allele provided in Table 5B. In certain aspects, the method further comprises detecting the haplotype tagged by two or more alleles (*e.g.*, 1, 2, 3, 4, 5, 6, 7, 8, 9 or more alleles) selected from those provided in Table 5B. In one aspect, said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 10. In certain
5 aspects, the method comprises administering olanzapine, perphenazine, quetiapine or risperidone to the subject.

[0025] Thus, in some aspects, a method is provided for detecting the presence of a polymorphism in the CDH4, LYN, or CNTN4 gene and administering a treatment to a human subject, the method comprising (a) obtaining a genomic sample from a human subject having
10 or at risk of developing SZ; (b) detecting the haplotype tagged by the “A” allele of rs4925300, the haplotype tagged by the “C” allele of rs1546519, or the haplotype tagged by the “A” allele of rs17194378 in the genomic sample; (c) identifying the subject having the haplotype tagged by the “A” allele of rs4925300, the haplotype tagged by the “C” allele of rs1546519, or the haplotype tagged by the “A” allele of rs17194378 in the genomic sample as
15 likely to have an improved response to ziprasidone as compared to control subject; and (d) administering a treatment comprising ziprasidone to the subject with the haplotype tagged by the “A” allele of rs4925300, the haplotype tagged by the “C” allele of rs1546519, or the haplotype tagged by the “A” allele of rs17194378.

[0026] In some aspects, the present invention provides a method of detecting the
20 presence of a polymorphism in the NALCN gene and administering a treatment to a human subject, the method comprising (a) obtaining a genomic sample from a human subject having or at risk of developing SZ; (b) detecting the haplotype tagged by the “C” allele of rs9585618 in the genomic sample; (c) identifying the subject having the haplotype tagged by the “C” allele of rs9585618 in the genomic sample as likely to have a poor response to ziprasidone as
25 compared to control subject; and (d) administering an antipsychotic treatment other than ziprasidone to the subject with the haplotype tagged by the “C” allele of rs9585618. In certain aspects, the method comprises administering olanzapine, perphenazine, quetiapine or risperidone to the subject.

[0027] In certain aspects of the present embodiments, the subject may have early,
30 intermediate, or aggressive SZ. In certain aspects of the present embodiments, the subject may have one or more risk factors associated with SZ. In certain aspects of the present embodiments, the subject may have a relative afflicted with SZ or a genetically-based

phenotypic trait associated with risk for SZ. In certain aspects of the present embodiments, the subject may be Caucasian or comprise European ancestry. In certain aspects of the present embodiments, determining the haplotype tagged by an allele may comprise determining the number of alleles tagging the haplotype in the subject.

5 [0028] In still a further embodiment, the present invention provides a method of identifying and administering a treatment to a human subject, the method comprising (a) obtaining a genomic sample from a human subject having or at risk of developing SZ; (b) detecting two or more haplotypes tagged by an allele selected from those provided in Table 1 for olanzapine, Table 2, for perphenazine, Table 3 for quetiapine, Table 4 for risperidone, or
10 Table 5 for ziprasidone in the genomic sample; (c) calculating a predicted treatment efficacy for at least two drugs selected from the group consisting of olanzapine, perphenazine, quetiapine, risperidone, and ziprasidone; (d) ranking the predicted efficacy of the at least two drugs; and (e) administering a treatment to the subject based on said ranking. In one aspect, detecting two or more haplotypes tagged by an allele comprises determining the number of
15 alleles tagging the two or more haplotypes in the subject. In further aspects, calculating a predicted treatment efficacy for a given drug comprises assigning a weighted value to each haplotype and multiplying the weighted value by the number of alleles tagging the haplotype in the subject. In another aspect, calculating a predicted treatment efficacy comprises using the equation:

$$P = C + \sum_i \beta_i N_i$$

wherein P is the predicted treatment efficacy measured in change in PANSS-T; C is the change in PANSS-T for individuals carrying zero alleles of any response-predicting haplotype for the drug, β is the weighted value for at least a first haplotype measured in PANSS-T; N is the number of alleles tagging at least the first haplotype; and i is the number of haplotypes detected. In one aspect, the method comprises determining a predicted treatment efficacy for three, four or five drugs selected from the group consisting of olanzapine, perphenazine, quetiapine, risperidone, and ziprasidone. In certain aspects, the subject may have early, intermediate, or aggressive SZ. In certain aspects, the subject may have one or more risk factors associated with SZ. In certain aspects, the subject may have a relative afflicted with SZ or a genetically-based phenotypic trait associated with risk for SZ. In certain aspects, the subject may be Caucasian or comprise European ancestry.

[0029] In aspect of the invention involving determining whether genetic material of the subject comprises a haplotype, the need transfer and store genetic information will be preferably met by recording and maintaining the information in a tangible medium, such as a computer-readable disk, a solid state memory device, an optical storage device or the like, more specifically, a storage device such as a hard drive, a Compact Disk (CD) drive, a floppy disk drive, a tape drive, a random access memory (RAM), etc.

[0030] One preferred manner of obtaining the haplotype information involves analyzing the genetic material of the subject to determine the presence or absence of the haplotype. This can be accomplished, for example, by testing the subject's genetic material through the use of a biological sample. In certain embodiments, the methods set forth will thus involve obtaining a biological sample from the subject and testing the biological sample to identify whether an haplotype is present. The biological sample may be any biological material that contains DNA or RNA of the subject, such as a nucleated cell source. Non-limiting examples of cell sources available in clinical practice include hair, skin, nucleated blood cells, buccal cells, any cells present in tissue obtained by biopsy or any other cell collection method. The biological sample may also be obtained from body fluids, including without limitation blood, saliva, sweat, urine, amniotic fluid (the fluid that surrounds a fetus during pregnancy), cerebrospinal fluid, feces, and tissue exudates at the site of infection or inflammation. DNA may be extracted from the biologic sample such as the cell source or body fluid using any of the numerous methods that are standard in the art.

[0031] Determining whether the genetic material exhibits an haplotype can be by any method known to those of ordinary skill in the art, such as genotyping (e.g., SNP genotyping) or sequencing. Techniques that may be involved in this determination are well-known to those of ordinary skill in the art. Examples of such techniques include allele specific oligonucleotide hybridization, size analysis, sequencing, hybridization, 5' nuclease digestion, single-stranded conformation polymorphism analysis, allele specific hybridization, primer specific extension, and oligonucleotide ligation assays. Additional information regarding these techniques is discussed in the specification below.

[0032] For haplotype determinations, the sequence of the extracted nucleic acid of the subject may be determined by any means known in the art, including but not limited to direct sequencing, hybridization with allele-specific oligonucleotides, allele-specific PCR, ligase-PCR, HOT cleavage, denaturing gradient gel electrophoresis (DDGE), and single-stranded

conformational polymorphism (SSCP) analysis. Direct sequencing may be accomplished by any method, including without limitation chemical sequencing, using the Maxam-Gilbert method, by enzymatic sequencing, using the Sanger method; mass spectrometry sequencing; and sequencing using a chip-based technology. In particular embodiments, DNA from a
5 subject is first subjected to amplification by polymerase chain reaction (PCR) using specific amplification primers. In some embodiments, the method further involves amplification of a nucleic acid from the biological sample. The amplification may or may not involve PCR. In some embodiments, the primers are located on a chip.

[0033] Moreover, the inventors contemplate that the genetic structure and sequence,
10 including SNP profiles, of individual subjects will at some point be widely or generally available, or will have been developed by an unrelated third party. In such instances, there will be no need to test or analyze the subject's biological material again. Instead, the genetic information will in such cases be obtained simply by analyzing the sequencing or genotyping outcome of the subject, for example, a SNP profile, a whole or partial genome sequence, etc.
15 These outcomes can then be obtained from or reported by a sequencing or a genotyping service, a laboratory, a scientist, or any genetic test platforms.

[0034] In some further aspects, the method may further comprise reporting the determination to the subject, a health care payer, an attending clinician, a pharmacist, a pharmacy benefits manager, or any person that the determination may be of interest.

20 [0035] Any of the SNPs listed in Tables 1-10 can be readily mapped on to the publically available human genome sequence (*e.g.*, NCBI Human Genome Build 37.3). For each of the SNPs listed herein the reference SNP (rs) number is provided, which provides the known sequence context for the given SNP (see, *e.g.*, National Center for Biotechnology Information (NCBI) SNP database available on the world wide web at ncbi.nlm.nih.gov/snp).

25 [0036] As used herein the specification, “a” or “an” may mean one or more. As used herein in the claim(s), when used in conjunction with the word “comprising”, the words “a” or “an” may mean one or more than one.

[0037] The use of the term “or” in the claims is used to mean “and/or” unless
30 explicitly indicated to refer to alternatives only or the alternatives are mutually exclusive, although the disclosure supports a definition that refers to only alternatives and “and/or.” As used herein “another” may mean at least a second or more.

[0038] Throughout this application, the term “about” is used to indicate that a value includes the inherent variation of error for the device, the method being employed to determine the value, or the variation that exists among the study subjects.

[0039] Other objects, features and advantages of the present invention will become
5 apparent from the following detailed description. It should be understood, however, that the detailed description and the specific examples, while indicating preferred embodiments of the invention, are given by way of illustration only, since various changes and modifications within the spirit and scope of the invention will become apparent to those skilled in the art from this detailed description.

10 **BRIEF DESCRIPTION OF THE DRAWINGS**

[0040] The following drawings form part of the present specification and are included to further demonstrate certain aspects of the present invention. The invention may be better understood by reference to one or more of these drawings in combination with the detailed description of specific embodiments presented herein.

15 [0041] **FIG. 1:** Summary of functional categories of newly evaluated SNPs on the custom BeadChip, based on NCBI resources.

[0042] **FIG. 2:** Q-Q (quantile-quantile) plots for $\log_{10}$ transformed observed P values from the association tests using the MMRM-predicted change in PANSS-T for olanzapine, perphenazine, quetiapine, risperidone, and ziprasidone. This analysis is limited to SNPs with
20 minor allele frequencies ≥ 0.03 in the particular drug arm. Gray areas represent 95% confidence intervals. If the slope for observed P values (blue circles) is steeper than the baseline assumption (red line, $y = x$), overall the observed P values are more significant than P values expected based on a theoretical distribution.

DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

25 [0043] Studies detailed herein identify over 6,000 SNPs in genes impacting disease risk, disease presentation, and, particularly, response to antipsychotics drug treatment. Most of the SNPs tag regions of linkage disequilibrium or represent functional variants that could not have been detected using the original genotypes provided by the CATIE consortium. Association analyses using the mixed model repeated measures approach of van den Oord

and coworkers (van den Oord *et al.*, 2009; McClay *et al.*, 2011) identified numerous SNPs predicting response to olanzapine, perphenazine, quetiapine, risperidone, and ziprasidone.

[0044] The targeted genotyping approach described here resulted in numerous associations for SNPs impacting response to antipsychotic medications for treatment of schizophrenia. The association results are not biased by post hoc selection of a response variable, due to the fact that a previously published MMRM-based approach was used to measure treatment response (van den Oord *et al.*, 2009). Tables 1-5 provide association results for all 6,789 newly genotyped SNPs with nominal P values ≤ 0.05 . Included in these tables are numerous examples of individual SNPs that impact response to one or more antipsychotic drugs.

[0045] Of the genes with the most significant SNP associations, only NPAS3 has been reported previously to contain common genetic variation that impacts response to antipsychotic treatment of schizophrenia. In the present study, rs1315115, located in an intron of NPAS3, was associated with response to risperidone. Lavedan and coworkers reported the association of SNPs in NPAS3 with response to the structurally related drug iloperidone (Lavedan *et al.*, 2009).

[0046] In the present studies, analysis was limited to the Caucasian patients to minimize effects of population stratification, in contrast to most previous studies, which combined subpopulations and used principal component adjustment for population stratification to increase sample size (McClay *et al.*, 2011; Sullivan *et al.*, 2008). Further, chromosomal regions not previously evaluated for the CATIE sample were targeted to generate results that would complement rather than replicate previous findings for CATIE. The findings of these studies follow the pattern seen by others in that no single SNP was associated strongly with response to more than one drug (McClay *et al.*, 2011; Need *et al.*, 2009). This is not surprising considering the diverse mechanisms of action for the various antipsychotic drugs evaluated in the CATIE study (Meltzer *et al.*, 2008).

[0047] The custom Illumina iSelect BeadChip was designed to capture common genetic variation, including functional variation, in genes suspected of having an impact on disease presentation or response to antipsychotics. As expected based on the linkage disequilibrium (LD) information available at the time the BeadChip was designed, most of

the SNPs defined, as well as tagged, haplotype blocks that could not have been detected using only SNP genotypes provided by the CATIE group.

I. Definitions

[0048] As used herein, an “allele” is one of a pair or series of genetic variants of a polymorphism at a specific genomic location. A “response allele” is an allele that is associated with altered response to a treatment. Where a SNP is biallelic, both alleles will be response alleles (*e.g.*, one will be associated with a positive response, while the other allele is associated with no or a negative response, or some variation thereof).

[0049] As used herein, “genotype” refers to the diploid combination of alleles for a given genetic polymorphism. A homozygous subject carries two copies of the same allele and a heterozygous subject carries two different alleles.

[0050] As used herein, a “haplotype” is one or a set of signature genetic changes (polymorphisms) that are normally grouped closely together on the DNA strand, and are inherited as a group; the polymorphisms are also referred to herein as “markers.” A “haplotype” as used herein is information regarding the presence or absence of one or more genetic markers in a given chromosomal region in a subject. A haplotype can consist of a variety of genetic markers, including indels (insertions or deletions of the DNA at particular locations on the chromosome); single nucleotide polymorphisms (SNPs) in which a particular nucleotide is changed; microsatellites; and minisatellites.

[0051] Microsatellites (sometimes referred to as a variable number of tandem repeats or VNTRs) are short segments of DNA that have a repeated sequence, usually about 2 to 5 nucleotides long (*e.g.*, a CA nucleotide pair repeated three times), that tend to occur in non-coding DNA. Changes in the microsatellites sometimes occur during the genetic recombination of sexual reproduction, increasing or decreasing the number of repeats found at an allele, changing the length of the allele. Microsatellite markers are stable, polymorphic, easily analyzed and occur regularly throughout the genome, making them especially suitable for genetic analysis.

[0052] “Copy number variation” (CNV), as used herein, refers to variation from the normal diploid condition for a gene or polymorphism. Individual segments of human chromosomes can be deleted or duplicated such that the subject's two chromosomes carry

fewer than two copies of the gene or polymorphism (a deletion or deficiency) or two or more copies (a duplication).

[0053] “Linkage disequilibrium” (LD) refers to when the observed frequencies of haplotypes in a population does not agree with haplotype frequencies predicted by multiplying together the frequency of individual genetic markers in each haplotype. When SNPs and other variations that comprise a given haplotype are in LD with one another, alleles at the different markers correlate with one another.

[0054] The term “chromosome” as used herein refers to a gene carrier of a cell that is derived from chromatin and comprises DNA and protein components (*e.g.*, histones). The conventional internationally recognized individual human genome chromosome numbering identification system is employed herein. The size of an individual chromosome can vary from one type to another with a given multi-chromosomal genome and from one genome to another. In the case of the human genome, the entire DNA mass of a given chromosome is usually greater than about 100,000,000 base pairs. For example, the size of the entire human genome is about 3×10^9 base pairs.

[0055] The term “gene” refers to a DNA sequence in a chromosome that codes for a product (either RNA or its translation product, a polypeptide). A gene contains a coding region and includes regions preceding and following the coding region (termed respectively “leader” and “trailer”). The coding region is comprised of a plurality of coding segments (“exons”) and intervening sequences (“introns”) between individual coding segments.

[0056] The term “probe” refers to an oligonucleotide. A probe can be single stranded at the time of hybridization to a target. As used herein, probes include primers, *i.e.*, oligonucleotides that can be used to prime a reaction, *e.g.*, a PCR reaction.

[0057] The term “label” or “label containing moiety” refers in a moiety capable of detection, such as a radioactive isotope or group containing the same, and nonisotopic labels, such as enzymes, biotin, avidin, streptavidin, digoxigenin, luminescent agents, dyes, haptens, and the like. Luminescent agents, depending upon the source of exciting energy, can be classified as radioluminescent, chemiluminescent, bioluminescent, and photoluminescent (including fluorescent and phosphorescent). A probe described herein can be bound, *e.g.*, chemically bound to label-containing moieties or can be suitable to be so bound. The probe can be directly or indirectly labeled.

[0058] The term “direct label probe” (or “directly labeled probe”) refers to a nucleic acid probe whose label after hybrid formation with a target is detectable without further reactive processing of the hybrid. The term “indirect label probe” (or “indirectly labeled probe”) refers to a nucleic acid probe whose label after hybrid formation with a target is further reacted in subsequent processing with one or more reagents to associate therewith one or more moieties that finally result in a detectable entity.

[0059] The terms “target,” “DNA target,” or “DNA target region” refers to a nucleotide sequence that occurs at a specific chromosomal location. Each such sequence or portion is preferably, at least partially, single stranded (*e.g.*, denatured) at the time of hybridization. When the target nucleotide sequences are located only in a single region or fraction of a given chromosome, the term “target region” is sometimes used. Targets for hybridization can be derived from specimens that include, but are not limited to, chromosomes or regions of chromosomes in normal, diseased or malignant human cells, either interphase or at any state of meiosis or mitosis, and either extracted or derived from living or postmortem tissues, organs or fluids; germinal cells including sperm and egg cells, or cells from zygotes, fetuses, or embryos, or chorionic or amniotic cells, or cells from any other germinating body; cells grown in vitro, from either long-term or short-term culture, and either normal, immortalized or transformed; inter- or intraspecific hybrids of different types of cells or differentiation states of these cells; individual chromosomes or portions of chromosomes, or translocated, deleted or other damaged chromosomes, isolated by any of a number of means known to those with skill in the art, including libraries of such chromosomes cloned and propagated in prokaryotic or other cloning vectors, or amplified in vitro by means well known to those with skill; or any forensic material, including but not limited to blood, or other samples.

[0060] The term “hybrid” refers to the product of a hybridization procedure between a probe and a target.

[0061] The term “hybridizing conditions” has general reference to the combinations of conditions that are employable in a given hybridization procedure to produce hybrids, such conditions typically involving controlled temperature, liquid phase, and contact between a probe (or probe composition) and a target. Conveniently and preferably, at least one denaturation step precedes a step wherein a probe or probe composition is contacted with a target. Guidance for performing hybridization reactions can be found in Ausubel et al.,

Current Protocols in Molecular Biology, John Wiley & Sons, N.Y. (2003), 6.3.1-6.3.6. Aqueous and nonaqueous methods are described in that reference and either can be used. Hybridization conditions referred to herein are a 50% formamide, 2× SSC wash for 10 minutes at 45°C followed by a 2× SSC wash for 10 minutes at 37°C.

5 **[0062]** Calculations of “identity” between two sequences can be performed as follows. The sequences are aligned for optimal comparison purposes (*e.g.*, gaps can be introduced in one or both of a first and a second nucleic acid sequence for optimal alignment and non-identical sequences can be disregarded for comparison purposes). The length of a sequence aligned for comparison purposes is at least 30% (*e.g.*, at least 40%, 50%, 60%,
10 70%, 80%, 90% or 100%) of the length of the reference sequence. The nucleotides at corresponding nucleotide positions are then compared. When a position in the first sequence is occupied by the same nucleotide as the corresponding position in the second sequence, then the molecules are identical at that position. The percent identity between the two sequences is a function of the number of identical positions shared by the sequences, taking
15 into account the number of gaps, and the length of each gap, which need to be introduced for optimal alignment of the two sequences.

[0063] The comparison of sequences and determination of percent identity between two sequences can be accomplished using a mathematical algorithm. In some embodiments, the percent identity between two nucleotide sequences is determined using the GAP program
20 in the GCG software package, using a Blossum 62 scoring matrix with a gap penalty of 12, a gap extend penalty of 4, and a frameshift gap penalty of 5.

[0064] As used herein, the term “substantially identical” is used to refer to a first nucleotide sequence that contains a sufficient number of identical nucleotides to a second nucleotide sequence such that the first and second nucleotide sequences have similar
25 activities. Nucleotide sequences that are substantially identical are at least 80% (*e.g.*, 85%, 90%, 95%, 97% or more) identical.

[0065] The term “nonspecific binding DNA” refers to DNA that is complementary to DNA segments of a probe, which DNA occurs in at least one other position in a genome, outside of a selected chromosomal target region within that genome. An example of
30 nonspecific binding DNA comprises a class of DNA repeated segments whose members commonly occur in more than one chromosome or chromosome region. Such common

repetitive segments tend to hybridize to a greater extent than other DNA segments that are present in probe composition.

[0066] As used herein, the term “stratification” refers to the creation of a distinction between subjects on the basis of a characteristic or characteristics of the subjects. Generally, in the context of clinical trials, the distinction is used to distinguish responses or effects in different sets of patients distinguished according to the stratification parameters. In some embodiments, stratification includes distinction of subject groups based on the presence or absence of particular markers or alleles described herein. The stratification can be performed, *e.g.*, in the course of analysis, or can be used in creation of distinct groups or in other ways.

10 II. Methods of Predicting Response and Selecting Optimal Treatment

[0067] Described herein are a variety of methods for predicting a subject's response, or selecting and optimizing (and optionally administering) a treatment for a subject having an SSD (*e.g.*, SZ) based on the presence or absence of a response allele.

[0068] As used herein, “determining the identity of an allele” includes obtaining information regarding the identity (*i.e.*, of a specific nucleotide), presence or absence of one or more specific alleles in a subject. Determining the identity of an allele can, but need not, include obtaining a sample comprising DNA from a subject, and/or assessing the identity, presence or absence of one or more genetic markers in the sample. The individual or organization who determines the identity of the allele need not actually carry out the physical analysis of a sample from a subject; the methods can include using information obtained by analysis of the sample by a third party. Thus the methods can include steps that occur at more than one site. For example, a sample can be obtained from a subject at a first site, such as at a health care provider, or at the subject's home in the case of a self-testing kit. The sample can be analyzed at the same or a second site, *e.g.*, at a laboratory or other testing facility.

[0069] Determining the identity of an allele can also include or consist of reviewing a subject's medical history, where the medical history includes information regarding the identity, presence or absence of one or more response alleles in the subject, *e.g.*, results of a genetic test.

[0070] In some embodiments, to determine the identity of an allele described herein, a biological sample that includes nucleated cells (such as blood, a cheek swab or mouthwash)

is prepared and analyzed for the presence or absence of preselected markers. Such diagnoses may be performed by diagnostic laboratories, or, alternatively, diagnostic kits can be manufactured and sold to health care providers or to private individuals for self-diagnosis. Diagnostic or prognostic tests can be performed as described herein or using well known techniques, such as described in U.S. Pat. No. 5,800,998.

[0071] Results of these tests, and optionally interpretive information, can be returned to the subject, the health care provider or to a third party payor. The results can be used in a number of ways. The information can be, *e.g.*, communicated to the tested subject, *e.g.*, with a prognosis and optionally interpretive materials that help the subject understand the test results and prognosis. The information can be used, *e.g.*, by a health care provider, to determine whether to administer a specific drug, or whether a subject should be assigned to a specific category, *e.g.*, a category associated with a specific disease endophenotype, or with drug response or non-response. The information can be used, *e.g.*, by a third party payor such as a healthcare payer (*e.g.*, insurance company or HMO) or other agency, to determine whether or not to reimburse a health care provider for services to the subject, or whether to approve the provision of services to the subject. For example, the healthcare payer may decide to reimburse a health care provider for treatments for an SSD if the subject has a particular response allele. As another example, a drug or treatment may be indicated for individuals with a certain allele, and the insurance company would only reimburse the health care provider (or the insured individual) for prescription or purchase of the drug if the insured individual has that response allele. The presence or absence of the response allele in a patient may be ascertained by using any of the methods described herein.

A. Response Alleles

[0072] This document provides methods for predicting response and selecting an optimal treatment based on evaluation of one or more single nucleotide polymorphisms (SNPs) associated with specific treatment responses in subjects having SZ or SZ-spectrum disorders including SZ, SPD, or SD. Table A and Tables 1-5 list specific SNPs, variation of which is associated with altered response to treatment. One of skill in the art will appreciate that other variants can be identified and verified by Case/Control comparisons using the SNP markers presented herein. Using SNP markers that are identical to or in linkage disequilibrium with the exemplary SNPs, one can determine additional alleles of the genes, such as haplotypes, relating to response to treatment of an SSD (*e.g.*, SZ). The allelic variants

thus identified can be used, *e.g.*, to select optimal treatments (*e.g.*, pharmaceutical and/or psychosocial intervention) for patients.

TABLE A: Summary of SNPs (NCBI Human Genome Build 37.3)

Gene	Chr	Position (BP)	Gene	Chr	Position (BP)
CSMD1	8	4,467,528	PLAGL1 ; LOC100652728	6	144,278,262
PLAGL1 ; LOC100652728	6	144,280,529	PTPRN2	7	157,332,172
KIAA0182	16	85,700,360	FREM1	9	14,801,738
CNTNAP2	7	147,750,195	ZNF71	19	57,105,726
PCDH15	10	55,629,421	DGKD	2	234,296,650
PDGFD ; DDI1	11	103,908,968	SEMA5A	5	9,445,434
ROBO2	3	77,103,671	CNTN4	3	2,287,920
CNTN4	3	2,294,001	NAB1	2	191,520,845
GRIN3A	9	104,470,105	GPC6	13	94,021,687
DLG2	11	84,529,337	DLG2	11	84,434,238
PARK2	6	161,981,577	DLG2	11	84,467,936
SCN3A	2	165,996,327	SEMA5A	5	9,034,674
IL17RD	3	57,125,380	TPH2	12	72,430,314
RAP1GAP2	17	2,940,720	GRIK3	1	37,186,174
SEMA3F	3	50,222,926	RBFOX1	16	6,029,562
PCDH15	10	56,309,093	CA10	17	49,868,887
NPAS3	14	33,608,871	CSMD1	8	4,493,580
MAGI2	7	77,917,038	AK5	1	77,828,321
SLC16A9	10	61,431,755	FAM19A1	3	68,197,782
CSMD1	8	4,812,290	PKNOX2	11	125,301,805
PSD3	8	18,933,166	PPA2	4	106,364,129
CLIC5	6	45,916,999	PTGER3	1	71,476,872
CNTNAP2	7	146,198,525	NELL1	11	21,418,874
DLG2	11	84,457,943	KITLG	12	88,890,521
FBN3	19	8,130,420	LIMCH1	4	41,658,985
CNTNAP2	7	147,725,495	DENND5B	12	31,536,772
DLGAP2	8	1,649,938	UNC13C	15	54,891,716
COL22A1	8	139,666,447	HPS4	22	26,877,463
SYN3	22	32,908,723	ERBB4	2	212,946,149
WNT5B	12	1,753,844	ANO2	12	5,940,753
ADTRP	6	11,774,792	PCLO	7	82,730,446
PCDH15	10	55,747,770	CNTNAP2	7	146,202,073
PPARG	3	12,500,651	LOC100129345	14	98,112,541
CNTNAP2	7	147,607,367	JPH2	20	42,805,719
CNTNAP2	7	147,958,959	CHN2	7	29,212,051
CSMD1	8	4,493,912	PLD1	3	171,324,666
CDH23	10	73,457,735	ANK3	10	61,800,837
NOS1AP	1	162,339,754	ANK3	10	62,088,266
ANK3	10	62,105,916	GALNTL4	11	11,521,053

TABLE A: Summary of SNPs (NCBI Human Genome Build 37.3)

Gene	Chr	Position (BP)	Gene	Chr	Position (BP)
NAB1	2	191,510,532	NALCN	13	101,801,061
VDAC1	5	133,326,423	CNTNAP2	7	146,848,333
ELOVL7	5	60,049,577	DLG2	11	83,166,720
CACNA2D3	3	54,949,461	MTIF3	13	28,022,617
INS-IGF2 ; IGF2	11	2,157,044	LYN	8	56,808,662
CDH20	18	59,218,968	CGNL1	15	57,806,751
TSNAX-DISC1	1	232,177,487	CNTNAP2	7	146,833,030
DGKD	2	234,296,444	CPNE4	3	131,659,901
NTNG2	9	135,110,456	SCD5	4	83,722,608
ZNF804A	2	185,524,642	TMC8	17	76,137,337
CSMD1	8	2,809,544	KCNJ2	17	69,089,167
OPCML	11	133,055,664	DLG2	11	84,456,685
GRIN3A	9	104,469,267	SLC1A3	5	36,648,442
WDR48	3	39,137,883	HPCAL1	2	10,502,982
KLHL32	6	97,374,850	WWC1	5	167,872,381
KCNN2	5	113,832,673	IFT74	9	26,953,102
IFT74	9	26,955,661	FMN2	1	240,301,487
ARVCF	22	19,996,878	FBN3	19	8,203,113
KCNQ1	11	2,473,131	MAGI2	7	78,890,598
BRE ; LOC100505716	2	28,531,903	CNTN4	3	2,342,825
GRIA1	5	152,908,929	CSMD1	8	3,513,875
NALCN	13	101,843,483	CSMD3	8	113,235,729
CNTN4	3	2,152,057	GPSM1	9	139,251,945
SLC25A18	22	18,073,592	KIAA1797	9	20,740,671
CTNNA3	10	67,679,568	ITPR1	3	4,685,191
CDH13	16	82,778,559	FAM46C	1	118,167,653
SYNPR	3	63,437,186	TRPM3	9	73,564,717
IGF2R	6	160,448,324	GRB10	7	50,675,930
PRICKLE2	3	64,106,014	SLC35F3	1	234,166,807
SLIT1	10	98,875,408	PLCB1	20	8,317,335
C9orf84	9	114,454,544	CACNA2D3	3	54,948,993
PHACTR3	20	58,160,628	NCAM2	21	22,571,465
FKTN	9	108,366,734	CTBP2	10	126,717,714
DOK6	18	67,190,086	CDH13	16	83,177,332
XPR1	1	180,853,719	GFRA1	10	117,967,808
LOC100130887	10	123,688,152	ATXN3	14	92,573,993
SRRM4	12	119,559,044	RGS6	14	72,415,017
ERC2	3	55,586,738	FAM186A	12	50,727,811
PACRG	6	163,721,073	KCNIP1	5	169,816,977
CNTNAP2	7	146,193,534	PARD3B	2	205,875,785
CNTNAP2	7	147,654,425	9-Sep	17	75,398,498
IGF1R	15	99,449,683	ITGA1	5	52,249,612
ITGA1	5	52,248,873	ASAP1	8	131,076,710

TABLE A: Summary of SNPs (NCBI Human Genome Build 37.3)

Gene	Chr	Position (BP)	Gene	Chr	Position (BP)
ARVCF	22	19,973,205	F13A1	6	6,152,140
ANK3	10	61,822,622	PCDH15	10	56,266,165
DLG2	11	84,540,424	CYP4V2	4	187,133,031
ALS2	2	202,587,653	ERBB4	2	213,275,113
LOC100505973	21	20,933,344	SAMD12	8	119,611,476
CSMD1	8	4,492,162	ZNF169	9	97,064,989
SGCZ	8	14,975,143	XPR1	1	180,853,815
SGCZ	8	14,982,457	ASPHD2	22	26,830,285
DENND5B	12	31,539,303	FMNL2	2	153,371,471
CNTNAP2	7	146,584,080	CGNL1	15	57,882,297
SLC25A21	14	37,261,482	GPC6	13	94,702,014
CAMK2D	4	114,393,744	APCDD1	18	10,488,091
MICAL2	11	12,147,395	PRUNE2	9	79,229,024
ARVCF	22	19,969,106	SAMD4A	14	55,055,645
MBP	18	74,782,653	RORA	15	61,127,206
NALCN	13	101,855,309	MACROD2	20	15,572,198
CSMD1	8	3,154,726	ITPR1	3	4,801,017
GAS7	17	9,902,914	TRPC4	13	38,227,229
PARD3B	2	205,929,857	MEPE	4	88,767,942
RIMS1	6	73,112,922	RARB	3	25,513,209
SORCS3	10	106,591,813	LRP1B	2	142,795,322
TMC5	16	19,499,993	RBFOX2	22	36,444,188
LOC100505501	8	60,032,541	BIK	22	43,498,114
CDH13	16	82,831,642	BLZF1	1	169,337,515
NEDD4L	18	55,783,683	CSMD1	8	4,812,593
DAOA-AS1	13	106,115,591	PCP4L1	1	161,219,555
ATP2B2	3	10,449,459	PI4KA ; SERPIND1	22	21,141,434
MTIF3	13	28,024,694	SLC35F3	1	234,119,810
FMNL2	2	153,371,042	DLGAP1	18	3,569,937
DLG2	11	84,529,252	FHIT	3	60,379,450
PPP1R9A	7	94,722,785	FAM173B	5	10,073,549
CDH13	16	83,829,129	KCNIP1	5	170,134,498
RASGEF1C	5	179,528,067	MAGI2	7	78,846,556
CACNA1B	9	140,866,826	SEMA5A	5	9,036,790
GRM8	7	126,884,788	GRM8	7	126,884,478
DLG2	11	84,465,866	SEC16B	1	177,898,579
KLHL29	2	23,802,390	PCDH17	13	58,252,801
IL15	4	142,557,279	KCND2	7	120,039,538
KCND2	7	120,019,161	MCPH1	8	6,302,183
HTR1B	6	78,173,382	DLG2	11	84,434,573
CTNNA2	2	80,234,384	ERCC6	10	50,678,369
PARK2	6	161,971,076	SLC6A5	11	20,622,975
ZNF638	2	71,558,924	ARHGAP31	3	119,096,594

TABLE A: Summary of SNPs (NCBI Human Genome Build 37.3)

Gene	Chr	Position (BP)	Gene	Chr	Position (BP)
ANGPT1	8	108,263,134	LRP1B	2	142,261,821
EML1	14	100,375,707	CERK	22	47,082,159
PTPRN2	7	157,748,524	SGCZ	8	14,832,287
PTPRT	20	40,872,429	SPOCK1	5	136,314,013
GPM6A ; LOC100506176	4	176,655,003	KCNH1	1	210,990,713
QRFPR	4	122,303,714	FSTL5	4	162,876,015
NTRK2	9	87,621,188	SDK1	7	4,189,075
CNTNAP2	7	148,090,584	ASAP1	8	131,414,632
GPSM1	9	139,252,879	CSMD1	8	2,832,139
C8orf34	8	69,350,425	CNTNAP2	7	147,704,874
NRXN1	2	50,147,171	KLHL29	2	23,929,979
RNF144A	2	7,181,486	NAV3	12	78,446,057
PCLO	7	82,720,226	ERBB4	2	213,040,853
CNTNAP2	7	146,226,654	KDM4C	9	7,013,909
ERBB4	2	213,388,276	FHIT	3	60,534,147
SULT4A1	22	44,232,887	PSD3	8	18,615,974
GAN	16	81,411,793	PPP1R9A	7	94,550,361
QRFPR	4	122,303,941	RNF144A	2	7,209,885
ATP10A	15	25,958,797	ANK3	10	61,800,984
SLC35F3	1	234,133,139	SLC16A4	1	110,936,383
CTNNA2	2	80,242,693	CREB5	7	28,805,889
NTSR2	2	11,810,488	KIAA0182	16	85,689,653
GPC6	13	94,028,022	WDR90	16	712,867
FAM170A	5	118,964,967	AGAP1	2	236,846,042
PKP4	2	159,321,822	JPH2	20	42,806,429
LINC00114	21	40,122,021	MACROD2	20	14,399,511
CSMD1	8	3,512,965	ARVCF	22	19,998,618
KAZN	1	15,346,531	EXOC2	6	654,985
PDE10A	6	165,927,101	ARNT2	15	80,719,387
ANK3	10	61,796,546	IL1RAP	3	190,344,900
ATP2B2	3	10,455,784	CACNG4	17	64,992,951
IL1RAP	3	190,348,298	IL1RAP	3	190,348,515
FMN2	1	240,308,147	ITPR1	3	4,802,573
NTRK2	9	87,638,506	NRXN3	14	79,174,840
WBSCR17	7	70,601,065	GNG2	14	52,404,912
CTNNA2	2	80,236,036	LDB2	4	16,504,184
PID1	2	229,889,268	FGF14	13	102,791,267
ATP2B2	3	10,447,146	PRDM2	1	14,028,493
ZNF169	9	97,065,439	MAGI2	7	78,536,207
ERG	21	40,017,446	MAGI1	3	65,537,584
SGCZ	8	14,852,684	FBXO4	5	41,934,957
EHD4	15	42,192,040	EHD4	15	42,191,909
GOT2	16	58,741,215	TMEM132B	12	126,140,791

TABLE A: Summary of SNPs (NCBI Human Genome Build 37.3)

Gene	Chr	Position (BP)	Gene	Chr	Position (BP)
CREB5	7	28,796,955	CACNA2D1	7	81,724,466
CPNE5	6	36,705,200	KCND2	7	120,131,749
PEBP4	8	22,577,263	NTRK2	9	87,622,324
LRP1B	2	142,572,840	ARNTL	11	13,318,566
CSMD1	8	2,808,520	ADAMTS9-AS2	3	64,852,147
IFT74	9	27,063,175	DLGAP1	18	3,681,185
MCPH1	8	6,504,316	ARNTL	11	13,297,789
PRKCE	2	46,412,422	MCPH1	8	6,502,359
CDH13	16	82,666,139	SKOR2	18	44,754,651
MAML3	4	141,022,317	SKOR2	18	44,746,997
GABBR2	9	101,339,947	CACNA2D3	3	54,597,829
MACROD2	20	16,034,051	NAALADL2	3	175,473,047
CSMD1	8	4,309,952	ETV1	7	14,000,421
KATNAL2	18	44,526,582	CDH13	16	82,861,704
PIP5K1B	9	71,363,249	AMPH	7	38,433,726
CSMD1	8	4,321,410	SAMD12	8	119,568,066
GABBR2	9	101,341,893	SPINK1	5	147,211,393
FERD3L	7	19,185,757	UNC13C	15	54,694,399
CLSTN2	3	139,694,900	PLCXD2	3	111,423,413
ROBO1	3	78,801,897	SDK1	7	4,246,412
MACROD2	20	15,974,988	CACNA2D1	7	81,617,702
DYNC1I1	7	95,612,737	ITGAD	16	31,420,134
STK31	7	23,748,048	SAMD12	8	119,580,949
NPAS3	14	33,814,728	PLCXD2	3	111,423,342
CCDC165	18	8,797,189	CACNB2	10	18,680,963
HSPA12A	10	118,431,297	NBAS	2	15,402,016
COL4A3 ; LOC654841	2	228,133,001	CLSTN2	3	139,674,735
CDH10	5	24,603,661	FER1L6 ; FER1L6-AS1	8	125,046,232
DNAH17	17	76,422,473	CADPS2	7	122,147,037
FSTL5	4	162,321,420	ROBO1	3	78,805,282
CLSTN2	3	139,660,269	RIBC2	22	45,828,594
OPCML	11	132,697,265	ERBB4	2	212,783,175
OPCML	11	132,696,752	TRIO	5	14,508,971
EPHB2	1	23,142,871	CDH13	16	82,828,582
NPY	7	24,322,659	NPY	7	24,321,827
NKAIN3	8	63,159,013	NRXN3	14	80,001,533
KCNK10	14	88,715,733	PSMD14	2	162,165,008
OPCML	11	132,661,587	KCNA10	1	111,060,752
KLHL32	6	97,371,823	PLCB1	20	8,865,718
CCDC93	2	118,676,429	RNF144B	6	18,424,430
PLCB1	20	8,865,783	CA10	17	50,171,183
SCLT1	4	129,961,179	CSMD3	8	113,288,576

TABLE A: Summary of SNPs (NCBI Human Genome Build 37.3)

Gene	Chr	Position (BP)	Gene	Chr	Position (BP)
PARK2	6	162,874,150	NBAS	2	15,385,364
GFRA2	8	21,557,285	FHIT	3	60,066,991
CDH13	16	83,091,529	FGF14	13	102,477,248
PTDSS1	8	97,384,315	TSPAN13	7	16,792,096
RBFOX3	17	77,276,546	MTSS1	8	125,686,010
PHIP	6	79,675,701	ATXN1	6	16,306,204
CA10	17	50,174,076	LYPD6	2	150,329,726
NAB1	2	191,515,442	NPAS3	14	33,551,543
KCNQ1 ; KCNQ1OT1	11	2,702,513	CTNND2	5	11,368,864
FLJ35024	9	2,495,694	NEBL	10	21,387,376
NEDD4L	18	55,893,217	BAALC ; LOC100499183	8	104,178,381
NKAIN3	8	63,275,763	SLC18A2	10	119,014,948
SLC18A2	10	119,014,931	HTR1B	6	78,176,538
GNAS	20	57,444,146	RIBC2	22	45,821,956
FSTL5	4	162,517,943	MAGI1	3	65,757,246
RAB6B	3	133,575,865	BLZF1	1	169,337,376
SYNRG	17	35,883,586	NPAS3	14	33,811,253
MMP27	11	102,576,382	DLGAP2	8	1,656,318
MCPH1 ; ANGPT2	8	6,357,611	ZFPM2	8	106,814,656
ACCN1	17	31,340,390	CNTN4	3	2,286,504
INADL	1	62,257,036	DYNCH1	7	95,613,449
KCNQ3	8	133,363,129	PCDH10	4	132,506,771
PCDH10	4	132,505,315	KCNB2	8	73,454,767
PCLO	7	82,764,425	MYT1L	2	1,794,410
GNG2	14	52,385,962	DOK5	20	53,267,576
NECAB1	8	91,969,669	SHROOM3	4	77,484,202
CA10	17	50,067,262	NBEA	13	36,080,730
PACRG	6	163,613,335	SMARCA2	9	2,082,671
LINC00299	2	8,446,735	NBEA	13	36,147,469
AGL	1	100,327,026	SLC7A14	3	170,179,582
NPAS3	14	34,044,752	GABBR2	9	101,233,069
PPARGC1A	4	23,893,017	RASGRP1	15	38,786,114
KCNMA1	10	78,934,838	COL4A3 ; LOC654841	2	228,130,088
KCNQ1	11	2,537,751	CAST	5	96,078,337
CAST	5	96,077,968	WWOX	16	78,905,235
PCSK6	15	101,847,800	MACROD2	20	15,339,430
FERMT1	20	6,104,673	FLJ35024	9	2,564,179
SYNE1	6	152,487,926	IKZF2	2	213,870,678
SDK1	7	3,529,504	FAM186A	12	50,724,444
NRXN3	14	79,631,747	ATF6	1	161,761,312
LOC100505806	5	9,546,995	LOC100505806	5	9,547,941

TABLE A: Summary of SNPs (NCBI Human Genome Build 37.3)

Gene	Chr	Position (BP)	Gene	Chr	Position (BP)
MAP1B	5	71,445,991	CNOT2	12	70,645,867
PDE4D	5	58,782,554	CSMD1	8	3,015,710
LOC100129434	2	56,410,666	CA10	17	50,155,850
KCNB1	20	47,988,601	SGCZ	8	14,149,802
ELMOD1	11	107,474,795	NEDD9	6	11,234,164
CDH13	16	82,681,884	CCDC165	18	8,814,140
NKAIN3	8	63,903,178	RORA	15	61,130,792
CLSTN2	3	140,266,593	CA10	17	50,172,676
ACCS	11	44,085,369	ATRN	20	3,628,312
KCNIP4	4	21,333,470	PTPRN2	7	158,151,977
NRXN3	14	79,983,905	ST8SIA1	12	22,347,663
FMN2	1	240,463,718	DGKB	7	14,234,314
KCNB2	8	73,519,816	CERS5	12	50,526,814
SKOR2	18	44,751,856	NRXN3	14	80,078,238
MAGI2	7	78,316,880	ATP2B2	3	10,454,880
RBFOX3	17	77,270,593	AKAP9	7	91,712,698
GNG2	14	52,389,257	GABRR2	6	89,996,405
PACRG	6	163,623,169	MACROD2	20	15,323,521
FBLN7	2	112,940,578	FBLN7	2	112,939,548
KCNMA1	10	78,951,780	PDE1C	7	31,881,291
EMID2	7	101,202,565	CSMD1	8	4,305,023
CSMD1	8	3,788,431	EPHB2	1	23,141,653
DLG2	11	83,479,572	LOC100505985	6	50,294,443
RYR2	1	237,427,945	DGKI	7	137,130,197
CD247	1	167,400,074	KCNQ1	11	2,639,712
SPINK1	5	147,234,756	GRB10	7	50,673,363
SVEP1	9	113,199,768	SLC22A16	6	110,745,977
EPAS1	2	46,523,934	COMMD1	2	62,153,717
NRCAM	7	108,074,766	MGAT2	14	50,089,696
TSPAN9	12	3,256,711	MAGI2	7	78,265,298
PARK2	6	162,877,216	PRKG1	10	53,425,550
NKAIN3	8	63,883,904	TRPM3	9	73,163,235
NCS1	9	132,998,557	PIK3C2G	12	18,634,528
TSPAN9	12	3,251,901	ROBO1	3	79,013,878
VCAN	5	82,848,642	PREX1	20	47,320,829
ARHGAP21	10	24,929,560	NRG3	10	83,090,548
LOC100506689	8	102,503,717	ATP2B2	3	10,454,406
ZNF536	19	31,137,357	ZNF536	19	31,118,591
FHIT	3	60,217,330	RGS7	1	241,070,371
CA10	17	50,067,961	NALCN	13	102,024,360
NAV2	11	19,885,338	RYR2	1	237,416,049
EXOC2	6	514,721	FERD3L	7	19,184,059
NBEA	13	36,185,434	GPC6	13	93,999,944
CCDC50	3	191,112,226	GABBR2	9	101,339,629

TABLE A: Summary of SNPs (NCBI Human Genome Build 37.3)

Gene	Chr	Position (BP)	Gene	Chr	Position (BP)
PTPRT	20	41,421,036	ITPR1	3	4,781,815
ATRN	20	3,629,254	ATRN	20	3,631,881
MTUS2	13	30,079,826	ELOVL7	5	60,049,119
CHMP6	17	78,973,474	NBAS	2	15,310,606
GABRR2	6	90,021,541	DCAF11	14	24,583,846
PON1	7	94,955,221	MACROD2	20	15,312,488
C19orf45	19	7,573,098	CDH13	16	83,814,659
KCNB2	8	73,455,936	SLC1A1	9	4,516,768
FAM104A	17	71,205,036	LEPREL1	3	189,842,190
NBEA	13	36,119,563	RYR2	1	237,487,678
ASTN2	9	119,262,849	MACROD2	20	16,034,339
KCNQ3	8	133,413,386	PTPN5	11	18,815,270
ITPR1	3	4,622,318	ITPR1	3	4,619,381
DPP10	2	116,503,671	CELF2	10	11,139,698
MUC7	4	71,346,701	TRPC4	13	38,216,068
CCDC165	18	8,787,857	IGSF22	11	18,747,959
SGCZ	8	14,675,294	LINC00308	21	24,062,292
NCAM2	21	22,910,051	CA10	17	50,067,848
CSMD1	8	3,518,993	SGCZ	8	14,746,634
SLC17A8	12	100,813,976	ACYP2	2	54,509,549
GRHL2	8	102,586,388	CNTNAP2	7	148,117,730
SHC3	9	91,675,560	ESRRG	1	216,676,445
PDE1C	7	32,111,306	CTNNA2	2	80,513,925
GRID2	4	94,295,669	DLC1	8	13,057,273
PTGER3	1	71,477,539	SLC4A1AP	2	27,887,034
ERC2	3	56,012,933	MYO5B	18	47,352,134
STXBP5L	3	120,658,659	PTPRG	3	61,728,839
PCDH7	4	30,863,804	MAGI2	7	78,246,671
DNAH9	17	11,814,378	DNAH9	17	11,811,666
ATRN1	10	117,445,235	RYR3	15	33,732,098
ROBO2	3	77,565,844	ITPR1	3	4,625,437
NRXN3	14	79,633,990	FHIT	3	60,216,250
CHMP6	17	78,973,901	PACRG	6	163,618,100
TBC1D2B	15	78,303,748	SGCZ	8	14,737,262
WWOX	16	78,933,487	ELFN2	22	37,766,196
PCSK6	15	101,854,583	PLCG2	16	81,849,382
OPCML	11	132,651,586	NPAS3	14	33,948,400
PIKFYVE	2	209,206,633	PARK2	6	162,144,016
KCNMA1	10	79,183,038	SORBS1	10	97,271,827
NLGN1	3	173,335,268	NPAS3	14	33,662,267
NRG3	10	83,933,250	CNTN4	3	2,913,017
GREM2	1	240,652,947	NPAS3	14	33,668,714
SORBS1	10	97,295,395	FHIT	3	60,082,619
ARSB	5	78,135,241	COL22A1	8	139,622,943

TABLE A: Summary of SNPs (NCBI Human Genome Build 37.3)

Gene	Chr	Position (BP)	Gene	Chr	Position (BP)
COL22A1	8	139,616,386	RGS7	1	241,258,422
ETV1	7	14,030,119	ROBO2	3	77,382,285
NAV2	11	19,868,759	GRID2	4	94,250,785
ETV1	7	13,976,258	COL4A4	2	227,867,385
NALCN	13	101,820,926	CNTNAP2	7	146,588,537
NAV2	11	19,902,266	NPFGR2	4	73,003,569
ETV1	7	14,029,772	ETV1	7	14,029,739
ETV1	7	14,030,093	LRP1B	2	141,644,560
MYO3B	2	171,260,797	CSMD1	8	3,031,069
TMEFF2	2	193,057,128	ARMC3	10	23,214,761
L3MBTL4	18	5,954,871	PLCG2	16	81,977,741
PSD3	8	18,385,538	PPP2R2B	5	146,460,691
LOC100289230	5	98,548,315	DCC	18	49,896,109
DOK6	18	67,279,176	CSMD1	8	3,351,147
TMEFF2	2	193,055,583	DGKB	7	14,665,239
DOK6	18	67,281,637	SLC6A1	3	11,055,705
ADAMTS9	3	64,546,459	NLGN1	3	173,310,633
FHIT	3	60,070,931	EPHA6	3	96,849,058
FHIT	3	60,438,854	LRP1B	2	141,639,645
PTPRT	20	41,179,698	DCTN4	5	150,097,883
MACROD2	20	14,747,025	ANK3	10	61,957,641
RGS7	1	241,242,460	SVEP1	9	113,150,431
KAZN	1	15,293,051	PTPRG	3	62,160,653
GPM6A	4	176,566,472	RORA	15	61,525,619
TRAPPC10	21	45,479,712	NRP2	2	206,545,421
DNAH5	5	13,755,378	BNIP2	15	59,955,668
NRG3	10	84,230,405	9-Sep	17	75,496,361
NLGN1	3	173,902,010	BTN3A1	6	26,420,425
BTN3A1	6	26,414,483	BTN3A1	6	26,415,798
KYNU	2	143,717,774	MSR1	8	15,967,438
MSR1	8	15,967,078	PLA2G2D	1	20,439,522
CDH7	18	63,530,016	NLGN1	3	173,936,752
TLN2	15	63,133,002	ZNF532	18	56,587,802
PRICKLE2	3	64,191,981	9-Sep	17	75,496,342
CCDC93	2	118,677,813	CSMD1	8	4,372,185
CNTN4	3	2,741,787	NCS1	9	132,963,115
LOC286094	8	136,070,005	CACNA2D1	7	81,669,017
KCNIP4	4	20,870,617	MAGI2	7	78,748,068
PCSK6	15	101,861,383	MYO10	5	16,706,766
OPCML	11	133,167,123	CLSTN2	3	139,710,833
MACROD2	20	15,684,293	GALNTL4	11	11,420,192
DGKB	7	14,204,193	DLG2	11	84,546,793
CRISPLD1	8	75,906,641	FHIT	3	59,871,049
TFB1M	6	155,637,025	EPHB1	3	134,655,266

TABLE A: Summary of SNPs (NCBI Human Genome Build 37.3)

Gene	Chr	Position (BP)	Gene	Chr	Position (BP)
PDE4D	5	58,333,097	NRG3	10	84,225,687
MSI2	17	55,749,233	RYR3	15	34,099,483
THADA	2	43,783,241	SLCO3A1	15	92,531,229
GPR97	16	57,722,833	DUOX2	15	45,383,446
ATXN1	6	16,514,083	PARK2	6	162,499,315
SMEK2	2	55,776,793	CNTNAP2	7	148,037,751
ERG	21	39,824,245	NELL1	11	20,698,929
CACNA2D1	7	81,942,310	SMARCA2	9	2,177,170
PIK3CG	7	106,546,087	GRM5	11	88,241,196
PRKCE	2	46,335,714	ZFPM2	8	106,589,247
PJA2	5	108,672,755	EMID2	7	101,005,926
KCNQ1	11	2,464,728	SFRP1	8	41,155,258
PARD3B	2	205,416,821	NALCN	13	101,815,002
NALCN	13	101,816,161	CSMD1	8	3,648,320
MAGI2	7	78,107,199	ARHGAP15	2	144,383,727
CDH7	18	63,475,059	CDH7	18	63,470,003
DOK6	18	67,284,044	LRP1B	2	141,641,929
GALNT9	12	132,689,052	TRIM9	14	51,495,398
SOBP	6	107,980,406	HAAO	2	42,995,840
CDH13	16	83,628,618	PTPRT	20	40,728,095
			INMT- FAM188B ; FAM188B	7	30,817,249
CACNA2D3	3	54,467,289	PLCG2	16	81,916,163
CTNNA2	2	79,760,772	C13orf35	13	113,288,426
MACROD2	20	14,734,270	MSR1	8	15,965,906
RIMBP2	12	130,888,767	RNF144B	6	18,389,833
CREB3L2	7	137,671,487	FMNL2	2	153,405,594
UNC13C	15	54,805,350			
LOC100128590 ; SLC8A1	2	40,455,984	SDK2	17	71,362,083
WWOX	16	78,590,925	CPLX2	5	175,223,616
MYO10	5	16,666,180	CNTN6	3	1,319,496
CTNNA2	2	80,657,752	OPCML	11	133,148,455
KCNK2	1	215,298,570	NAV3	12	78,319,532
NLGNI	3	173,921,634	KCNB1	20	47,989,624
TMC1	9	75,135,825	MCPH1	8	6,422,141
MACROD2	20	14,768,903	SHC3	9	91,637,142
MAGI2	7	78,692,139	PSD3	8	18,786,787
GALNTL4	11	11,319,245	MAGI2	7	78,764,223
NBEA	13	35,140,485	CDH13	16	83,023,920
ABCA4	1	94,476,467	OPCML	11	132,544,060
CADPS	3	62,788,035	RYR2	1	237,858,185
MUSK	9	113,579,789	NCEH1	3	172,350,135
KCNQ3	8	133,418,396	NLGNI	3	173,357,992

TABLE A: Summary of SNPs (NCBI Human Genome Build 37.3)

Gene	Chr	Position (BP)	Gene	Chr	Position (BP)
INMT- FAM188B ; FAM188B	7	30,842,257	DENND4C	9	19,343,291
LRP1B	2	141,242,918	KCNJ3	2	155,586,570
PRKG1	10	53,853,246	DGKB	7	14,305,589
ATXN1	6	16,497,883	SNTG1	8	50,822,736
CERK	22	47,093,846	C15orf41	15	36,931,320
MUSK	9	113,430,771	NRG3	10	84,231,385
EPHA7	6	93,950,764	CTNNA2	2	80,307,777
NAV2	11	19,770,927	GRID2	4	94,250,702
LRFN2	6	40,458,625	ATP2B2	3	10,448,426
NALCN	13	101,900,696	DOK6	18	67,286,267
OPCML	11	132,554,005	MYO3A	10	26,250,566
KCNIP4	4	20,856,597	STX11	6	144,508,698
STX11	6	144,512,989	IRF8	16	86,010,523
IRF8	16	86,009,519	SORBS1	10	97,272,652
RGS7	1	241,125,990	ST8SIA1	12	22,348,998
NPAS3	14	33,576,437	DLC1	8	13,000,629
NFIL3	9	94,187,265	SLC35F3	1	234,039,968
CSMD1	8	3,645,978	FOXP1	3	71,156,340
CCBE1	18	57,365,526	LOC100128590 ; SLC8A1	2	40,455,568
PLCG2	16	81,982,491	TMTC2	12	83,526,911
CHRM3	1	239,821,058	CNTN4	3	2,582,255
EPHB1	3	134,554,163	LOC100128590 ; SLC8A1	2	40,455,632
MAGI2	7	78,701,601	RGS7	1	241,442,019
JAG1	20	10,621,305	EXOC2	6	593,109
EMID2	7	101,159,950	SEMA5A	5	9,380,118
CLSTN2	3	139,700,967	SAMD4A	14	55,124,327
NLGN1	3	173,932,956	MUSK	9	113,580,133
NCAM2	21	22,511,763	NEDD4L	18	55,731,712
FOXP1	3	71,430,995	ITPR2	12	26,986,198
ERG	21	39,909,266	GPR116	6	46,827,239
FMN2	1	240,358,173	TMEM132E	17	32,966,065
TMEM132E	17	32,966,119	KCNMA1	10	79,294,680
CADPS	3	62,761,047	CA10	17	49,811,358
FLJ38109	5	153,815,054	KCNQ1	11	2,755,346
SELT	3	150,346,654	USP10	16	84,790,559
NRCAM	7	107,939,793	LRRK1	15	101,606,889
SGCZ	8	13,955,788	LDB2	4	16,508,781
PACRG	6	163,303,962	TGIF1	18	3,432,439
MIR3974	12	17,358,689	FREM1	9	14,816,829
MDGA2	14	47,812,311	ADAMTS9 ; ADAMTS9-AS2	3	64,672,474
NRCAM	7	107,938,376	FBXL2	3	33,428,373

TABLE A: Summary of SNPs (NCBI Human Genome Build 37.3)

Gene	Chr	Position (BP)	Gene	Chr	Position (BP)
PARD3B	2	205,775,783	CTNND2	5	11,161,237
PTPRT	20	41,138,259	SEC23B	20	18,488,065
PKP4	2	159,320,951	TSC1	9	135,767,943
PDE4D	5	58,293,664	GRID2	4	93,453,356
IYD	6	150,719,380	CNTN6	3	1,296,226
DOK6	18	67,282,973	MYO10	5	16,883,395
CLSTN2	3	139,931,872	RAB6B	3	133,615,546
RAB6B	3	133,616,135	CTNND2	5	11,291,983
RAB6B	3	133,615,263	RYR3	15	33,621,235
RPRD1A	18	33,571,268	SORBS1	10	97,083,979
GNG2	14	52,360,813	ARNTL	11	13,325,695
NCAM2	21	22,864,581	KIAA0182	16	85,683,171
SH2D4B	10	82,865,385	EXOC2	6	633,557
AKAP9	7	91,708,898	DOK6	18	67,264,134
ROBO2	3	77,604,690	INPP4A	2	99,133,611
CDH13	16	83,106,301	RGS7	1	241,115,683
DLG2	11	84,456,440	PLXDC2	10	20,105,936
PIKFYVE	2	209,214,407	CSMD1	8	4,493,225
CNTNAP2	7	147,935,699	OSBPL1A	18	21,828,835
NPY	7	24,324,759	CSMD1	8	3,807,943
CCDC85A	2	56,460,013	RYR2	1	237,383,271
CCDC85A	2	56,596,394	NAV3	12	78,301,608
HYDIN	16	70,926,334	CSMD1	8	4,493,493
NPY	7	24,320,646	MACROD2	20	15,503,398
RAB6B	3	133,616,371	FMN2	1	240,564,616
PSD3	8	18,792,419	MSI2	17	55,748,408
WBSCR17	7	70,738,028	CTNND2	5	11,166,899
TOX	8	60,018,743	NRG3	10	84,315,759
DPP6	7	153,896,243	SORBS1	10	97,123,793
SNCA	4	90,682,504	CACNG2	22	37,024,953
PLCB1	20	8,490,081	HAAO	2	42,997,614
KCNB2	8	73,736,766	ARHGAP21	10	24,929,141
PREX2	8	68,910,473	LRP1B	2	142,488,592
AGAP1	2	236,995,045	NPAS3	14	33,567,750
TMEFF2	2	192,922,256	C7orf58	7	120,876,835
CAMK2D	4	114,384,328	CACNB4	2	152,695,191
SLC35F3	1	234,121,873	DNAH17	17	76,491,309
EXOC2	6	538,063	FHIT	3	60,271,669
DENND4C	9	19,290,143	NRCAM	7	107,907,393
LRP1B	2	142,391,367	MAMDC2 ; LOC100507299	9	72,834,056
POLR2M	15	57,999,304	CTBP2	10	126,683,857
KCNB2	8	73,484,874	MAML3	4	141,035,921
EPHA4	2	222,283,000	NRXN3	14	79,651,600

TABLE A: Summary of SNPs (NCBI Human Genome Build 37.3)

Gene	Chr	Position (BP)	Gene	Chr	Position (BP)
DLEU2	13	50,855,108	LRRK1	15	101,609,737
NRG3	10	84,606,682	ROBO1	3	78,685,024
CCDC50	3	191,087,740	TBC1D22A	22	47,310,557
LRP1B	2	142,876,051	CBLB	3	105,399,476
PLCG2	16	81,912,081	CHRM3	1	239,844,600
APBB2	4	40,812,669	DHODH	16	72,058,881
ALK	2	29,543,736	RORA	15	61,151,622
GBE1	3	81,812,406	GLDN	15	51,687,839
SNX21 ; ACOT8	20	44,471,340	MSI2	17	55,710,880
NALCN	13	101,747,265	BNC2	9	16,416,995
CHRM3	1	239,824,248	NRXN3	14	78,920,327
PTPRN2	7	157,642,767	CSMD1	8	4,641,941
CHN2	7	29,554,284	NBN	8	90,946,601
EXOC2	6	534,527	GAS7	17	9,999,817
SAG	2	234,229,320	SORCS2	4	7,743,283
TMX2-CTNND1	11	57,525,883	GRB10	7	50,801,117
GRB10	7	50,801,917	DTNBP1	6	15,628,102
DTNBP1	6	15,651,132	IQGAP2	5	75,964,507
DTNBP1	6	15,653,649	SERPINI1	3	167,455,005
GLP1R	6	39,054,589	CDH13	16	82,779,603
C14orf182	14	50,473,098	ATRNL1	10	116,875,810
ATXN3	14	92,525,145	PCSK5	9	78,778,550
NPAS3	14	34,116,992	PJA2	5	108,747,204
ARPP21	3	35,712,071	NCAM2	21	22,503,372
NPAS3	14	34,127,481	KIAA0947	5	5,818,164
CGNL1	15	57,712,536	NXPH2	2	139,428,096
CGNL1	15	57,817,191	NPAS3	14	33,806,438
ODZ3	4	183,240,892	PLA2G1B	12	120,760,911
SKAP1	17	46,262,171	WWOX	16	78,324,042
ITPR1	3	4,870,000	DGKB	7	14,596,054
ATF3	1	212,793,849	VPS41	7	38,949,424
AKAP13	15	86,291,013	ABI2	2	204,192,201
ROBO1	3	78,977,507	PTPRG	3	62,038,177
FLJ22447	14	62,120,575	RYR2	1	237,201,051
PKIA	8	78,951,278	ARPP21	3	35,715,712
PDE1C	7	31,961,538	CBLB	3	105,425,910
MYL12B	18	3,327,868	CSMD1	8	4,626,927
LOXL2	8	23,155,337	KAZN	1	15,275,515
LRP1B	2	142,179,858	VTI1A	10	114,575,767
SULT4A1	22	44,229,793	SULT4A1	22	44,236,864
KCNB2	8	73,777,863	UNC5C	4	96,390,341
ARPP21	3	35,728,881	LOC100506731	14	85,995,799
CBLB	3	105,432,459	PARD3B	2	206,215,828
TBC1D1	4	37,904,456	EVC	4	5,804,830

TABLE A: Summary of SNPs (NCBI Human Genome Build 37.3)

Gene	Chr	Position (BP)	Gene	Chr	Position (BP)
MR1	1	181,025,110	EPHB2	1	23,171,706
BAALC	8	104,229,824	ABT1	6	26,600,156
CLASP2	3	33,537,513	GLDN	15	51,648,597
TMEFF2	2	192,959,316	BAALC	8	104,238,747
GDA	9	74,863,887	CCBE1	18	57,365,344
NPAS3	14	34,115,818	ARFGAP3	22	43,192,480
			TMX2- CTNND1 ; CTNND1	11	57,550,785
PLA2G4D	15	42,391,075	NPAS3	14	33,439,678
TMEM163	2	135,288,375	COL22A1	8	139,758,550
RAB11FIP4	17	29,717,879	NALCN	13	101,744,417
NALCN	13	101,749,365	CNTNAP2	7	146,541,290
PLEKHH2	2	43,884,582	SAMD12	8	119,207,140
SAMD12	8	119,206,468	RORA	15	61,164,545
SAMD12	8	119,207,381	MICAL2	11	12,169,917
ZNF365	10	64,307,317	CARD11	7	3,012,242
PRKCE	2	46,344,717	GBE1	3	81,539,382
ST8SIA2	15	93,012,351	PARD3B	2	205,898,117
QRFP	9	133,769,786	IP6K1	3	49,762,662
CGNL1	15	57,843,391	GRID2	4	93,452,091
TBC1D22A	22	47,569,605	CGNL1	15	57,674,534
PAPPA	9	119,024,929			
LOC286190 ; LACTB2	8	71,549,614	PSD3	8	18,636,688
SLC2A9	4	9,828,745	NCAM2	21	22,503,145
CHN2	7	29,500,433	SAAL1	11	18,091,665
SLC41A1	1	205,759,195	DOK6	18	67,400,139
LOC728755	14	27,620,796	CSMD1	8	3,214,267
PDE1C	7	31,962,443	ANO2	12	5,698,059
DEAF1	11	674,259	TRIP12	2	230,657,496
PTPRT	20	40,821,926	MTSS1	8	125,587,871
HS1BP3	2	20,818,883	PRKCE	2	46,343,735
NTRK2	9	87,704,881	CLSTN2	3	139,714,321
FAM69A	1	93,308,853	BIRC6	2	32,822,957
EXOC4	7	133,424,668	EXOC2	6	531,483
ADAMTS19	5	129,074,369	ADAMTS19	5	129,074,560
ADAMTS19	5	129,072,943	CCDC165	18	8,817,778
SLC2A13	12	40,150,610	DLC1	8	12,943,065
DEAF1	11	644,325	PPM1H	12	63,038,698
LRP1B	2	141,883,206	FSTL5	4	162,823,690
SYNE1	6	152,521,714	ANO2	12	5,860,329
KCNN3	1	154,838,050	ERBB4	2	212,240,337
NCAM2	21	22,502,758	CAMKV	3	49,896,618
ARPP21	3	35,718,847	CDH13	16	83,426,932
CSMD1	8	3,135,844	FLJ45139	21	40,250,008

TABLE A: Summary of SNPs (NCBI Human Genome Build 37.3)

Gene	Chr	Position (BP)	Gene	Chr	Position (BP)
NPAS3	14	34,136,476	SORBS1	10	97,081,500
C15orf41	15	36,948,788	SLC2A13	12	40,151,546
SLC2A13	12	40,151,891	ARL13B ;		
HHAT	1	210,570,783	STX19	3	93,738,694
QPCT	2	37,600,427	FAM69A	1	93,307,908
PLD5	1	242,545,880	SYNE1	6	152,453,291
LPHN3	4	62,919,707	NAV2	11	19,787,053
PRKG1	10	53,615,000	RORA	15	61,155,328
DFNB31	9	117,167,192	DFNB31	9	117,169,935
RORA	15	61,154,619	PDE1C	7	32,021,399
GLDN	15	51,648,847	TOX	8	59,946,434
FSTL5	4	162,807,615	ST8SIA2	15	93,007,974
DGKB	7	14,284,617	SNCA	4	90,758,945
NRG3	10	84,724,221	MACROD2	20	15,975,305
GALNTL4	11	11,312,467	CAMKMT	2	44,999,709
IL17RD	3	57,203,398	KDM4C	9	7,322,335
ATP10A	15	25,925,094	CDH8	16	62,002,956
NRG3	10	84,565,851	CSMD1	8	4,657,295
SLIT2	4	20,251,518	DAB2IP	9	124,433,681
PLCB1	20	8,432,314	LRP1B	2	141,889,752
PCLO	7	82,462,834	RYSR2	1	237,944,814
UNC5C	4	96,393,071	FBXL17	5	107,240,149
PTCHD4	6	47,868,517	DOK6	18	67,393,698
HTR5A	7	154,876,342	NPAS3	14	33,920,194
CELF2	10	11,075,552	OTOG	11	17,580,175
ABCA1	9	107,665,978	EPAS1	2	46,565,091
SVEP1	9	113,127,180	FRMD1	6	168,462,765
DGKB	7	14,282,726	PCSK5	9	78,776,057
KCNIP1	5	170,038,936	PTPRM	18	7,564,653
CDH23	10	73,392,466	CACNA2D3	3	54,257,411
WWOX	16	78,691,132	NCAM2	21	22,505,742
RGS7	1	240,938,621	RGS7	1	240,938,417
ATRNL1	10	117,029,233	CSMD1	8	3,230,841
GPC6	13	94,084,293	GPC6	13	94,080,565
SULT4A1	22	44,241,285	SLC35F3	1	234,178,299
UNC5C	4	96,314,874	CACNA2D3	3	54,651,305
ANK3	10	61,789,753	TMEM106B	7	12,272,116
CERKL	2	182,403,387	KCNN3	1	154,833,978
HS6ST3	13	97,489,905	DGKB	7	14,276,741
MAGI2	7	78,658,175	PSD3	8	18,782,224
NAV3	12	78,240,316	DOK6	18	67,133,967
CAMKMT	2	44,728,418	PDE10A	6	165,800,773
RABGEF1	7	66,276,312	ATP2B2	3	10,370,486
			DOK6	18	67,141,451

TABLE A: Summary of SNPs (NCBI Human Genome Build 37.3)

Gene	Chr	Position (BP)	Gene	Chr	Position (BP)
CSMD1	8	3,485,004	CLASP2	3	33,760,037
DGKB	7	14,198,845	NKAIN2	6	124,912,456
GRIN3A	9	104,465,623	LOC100505806	5	9,547,958
LRP1B	2	142,878,897	SORBS1	10	97,118,644
MTSS1	8	125,668,599	THBS4	5	79,330,559
MAML3	4	140,694,319	MAGI2	7	78,843,289
SGCZ	8	14,143,813	NALCN	13	101,774,206
KLF12	13	74,268,928	KCNK10	14	88,795,203
LOC100506128	1	177,704,242	SORCS3	10	106,403,115
SVEP1	9	113,131,354	GPC5	13	93,279,684
NTM	11	131,778,518	EXOC2	6	647,406
VPS41	7	38,763,891	PLCB1	20	8,865,006
PLCB1	20	8,865,868	PPM1H	12	63,041,307
NRG3	10	84,415,305	DPP6	7	153,909,539
PRODH	22	18,912,678	RYSR2	1	237,825,673
GRB10	7	50,809,771	GRID2	4	94,259,545
BMPRI1B	4	96,076,465	UNC5C	4	96,089,692
CDH4	20	60,392,038	LYN	8	56,824,558
CNTN4	3	2,465,091	NALCN	13	101,724,041
SLIT2	4	20,286,220	CDH4	20	60,392,016
NALCN	13	101,726,145	ARHGAP31	3	119,137,912
GRIA1	5	152,919,794	HIATL1	9	97,223,294
PSD3	8	18,645,147	MACROD2	20	15,510,834
LOC100616530	8	96,775,900	BAG3	10	121,429,394
NALCN	13	101,737,731	FHIT	3	60,595,646
ODZ2	5	167,304,609	ODZ2	5	167,270,818
TRPM3	9	73,502,424	PARD3B	2	205,593,602
SGCZ	8	14,789,538	NEDD9	6	11,186,049
FMN2	1	240,466,440	ZNF169	9	97,064,273
PARD3B	2	205,619,609	ANK2	4	114,279,674
CDH4	20	60,308,635	C15orf41	15	37,010,246
S100PBP	1	33,324,088	BCL2L11	2	111,923,630
SGCZ	8	14,965,403	VSNL1	2	17,720,520
PTPRG	3	61,610,728	CDS1	4	85,572,374
CAPZB, LOC644083	1	19,727,062	CSMD1	8	4,501,890
PARD3B	2	205,606,092	KCNB2	8	73,815,971
ADAMTSL1	9	18,797,857	TMEM181	6	159,051,186
METTL21A	2	208,489,101	PTPRG	3	61,608,761
EPHB1	3	134,519,445	ATP10A	15	26,038,355
NPAS3	14	33,618,223	NALCN	13	101,706,716
EPHB1	3	134,509,337	DAPK1	9	90,292,625
SLC25A21	14	37,156,758	DAPK1	9	90,293,359
CNTNAP2	7	147,023,663	VSNL1	2	17,747,999

TABLE A: Summary of SNPs (NCBI Human Genome Build 37.3)

Gene	Chr	Position (BP)	Gene	Chr	Position (BP)
RGS7	1	241,241,733	SYCP2	20	58,476,841
CTNNA2	2	80,484,593	MAGI1	3	65,383,903
TRPM3	9	73,484,805	NALCN	13	101,732,146
GRID2	4	93,236,404	TSPAN9	12	3,394,098
RAB36	22	23,505,804	SCUBE1	22	43,703,729
ARNTL	11	13,297,925	ARNTL	11	13,298,485
ARNTL	11	13,298,519	ARNTL	11	13,298,687
ARNTL	11	13,298,750	RC3H1	1	174,188,285
DYNC1I1	7	95,725,936	NXPH1	7	8,582,476
ERC2	3	55,660,874	GLP1R	6	39,055,421
CNTN4	3	2,730,859	SYNE1	6	152,539,054
ARNTL	11	13,318,587	CDH7	18	63,491,797
RYR2	1	237,550,323	HYDIN	16	70,891,640
EYA4	6	133,678,974	RHOG	11	3,855,859
PES1	22	30,977,353	DPYSL5	2	27,152,874
PRKG1	10	53,295,318	DLGAP1	18	3,651,423
NKAIN2	6	124,196,534	DLGAP1	18	3,656,488
ADAMTS19	5	128,823,842	NBEA	13	35,827,215
UTRN	6	144,852,201	EXOC2	6	604,461
CTNNA3, LRRTM3	10	68,685,929	ZNF169	9	97,064,439
CAPZB, LOC644083	1	19,727,145	ODZ2	5	167,251,985
ADAMTSL1	9	18,789,128	MTSS1	8	125,742,166
LIMCH1	4	41,387,463	SRRM4	12	119,419,603
CACNA2D1	7	81,614,857	NALCN	13	101,720,300
DAPK1	9	90,297,750	PACRG	6	163,213,454
UTRN	6	144,817,792	KCNMA1	10	78,806,647
MAGI2	7	78,125,648	SDK1	7	3,726,122
SGCZ	8	14,846,341	SEMA3E	7	82,995,006
SDK1	7	3,344,401	ODZ2	5	167,236,746
DLG2	11	83,456,191	NCKAP5	2	133,694,153
PLCG2	16	81,906,377	FGF5	4	81,207,963
ADAMTSL1	9	18,799,412	INPP4A	2	99,207,180
DGKI	7	137,072,931	TBC1D1	4	38,007,099
TSPAN11	12	31,145,084	GABRP	5	170,207,363
FBXL17	5	107,352,294	GRM8	7	126,884,450
F5	1	169,511,878	FBXL17	5	107,349,711
GABBR2	9	101,052,858	ULK1	12	132,378,133
SHC3	9	91,640,058	PLD5	1	242,675,820
KLHL29	2	23,766,136	DOK6	18	67,513,581
MSI2	17	55,536,291	ODZ2	5	167,304,210
KCNMA1	10	78,726,699	PLA2R1	2	160,920,122
ODZ2	5	167,278,330	SLC35F3	1	234,424,751

TABLE A: Summary of SNPs (NCBI Human Genome Build 37.3)

Gene	Chr	Position (BP)	Gene	Chr	Position (BP)
CNTN5	11	99,690,286	UTRN	6	144,822,128
LIMCH1	4	41,376,680	INSC	11	15,243,059
KLHL29	2	23,769,972	KCNK9	8	140,632,384
SDK1	7	3,343,382	CDH13	16	83,719,772
RYR3	15	33,731,261	ODZ2	5	167,177,952
ODZ2	5	167,210,121	CDH13	16	83,727,444
LOC100289130, GPX1	3	49,395,757	CTNNA2	2	79,991,329
LIMCH1	4	41,380,276	PARK2	6	161,971,805
SCD5	4	83,595,238	RAB11FIP4	17	29,863,723
PDE4D	5	59,032,179	CDS1	4	85,571,339
ATF6	1	161,735,397	RORA	15	60,878,030
RARB	3	25,512,768	TPH2	12	72,355,179
ATP10A	15	26,094,520	MICAL2	11	12,190,617
LRP1B	2	142,878,411	KCNJ3	2	155,622,177
C12orf5	12	4,462,161	CDH13	16	83,492,421
SYT13	11	45,276,308	ARHGAP19- SLIT1	10	98,946,244
CDH13	16	83,621,093	NCAM2	21	22,381,606
DPYSL5	2	27,171,245	DPYSL5	2	27,172,069
PRUNE2	9	79,318,998	PRUNE2	9	79,320,640
CPLX2	5	175,309,540	C15orf41	15	36,989,469
CTNND2	5	11,168,613	MAGI1	3	65,376,512
FHIT	3	59,998,294	CDH13	16	82,697,593
TRPC4	13	38,444,350	OPCML	11	132,700,012
FSTL5	4	162,318,470	GIGYF2	2	233,641,924
DLG2	11	83,463,013	SYT13	11	45,309,171
SYT13	11	45,309,202	UBL3	13	30,343,129
UBL3	13	30,418,719	PTPRG	3	61,583,771
PTPRG	3	61,590,517	SPIB	19	50,931,964
NELL1	11	21,426,570	CDH23	10	73,199,595
VSNL1	2	17,754,316	CTBP2	10	126,715,154
NCKAP5	2	133,696,308	NAV3	12	78,519,147
NRXN3	14	79,890,456	NRXN3	14	79,681,303
KYNU	2	143,746,494	DENND5B	12	31,536,540
CACNA2D3	3	54,633,739	USH2A	1	216,597,759
PSD3	8	18,634,283	NLGN1	3	173,438,357
FMN2	1	240,496,759	CSMD1	8	4,492,255
MAGI2	7	79,081,703	KIAA1797	9	20,663,063
BMP7	20	55,745,485	PCLO	7	82,516,893
CDH4	20	60,512,369	GALNTL4	11	11,525,323
CACNB2	10	18,688,883	SDK1	7	3,336,778
NRXN3	14	79,657,049	NCKAP5	2	133,541,107
F5	1	169,481,950	CDH13	16	83,677,493

TABLE A: Summary of SNPs (NCBI Human Genome Build 37.3)

Gene	Chr	Position (BP)	Gene	Chr	Position (BP)
ROBO1	3	79,639,575	LRRC4C	11	40,181,102
NRXN3	14	80,247,360	MBP	18	74,691,225
MICAL2	11	12,191,487	MIER1	1	67,451,487
WVOX	16	79,091,392	PTGS2	1	186,650,321
SH3GL3	15	84,215,428	ABCA13	7	48,392,771
TBXAS1	7	139,681,804	RYS2	1	237,650,289
DLG2	11	83,577,954	SLC22A23	6	3,307,422
COL22A1	8	139,869,353	DOCK1	10	129,249,662
CDH23	10	73,163,995	ADCY8	8	132,053,412
MIR1270-1	19	20,506,989	AKAP6	14	33,293,531
ARHGEF10	8	1,906,630	SLCO3A1	15	92,529,323
CTBP2	10	126,741,854	CCDC88C	14	91,771,625
MTO1	6	74,171,467	PARK2	6	162,291,767
DLC1	8	12,942,342	CNTN4	3	2,876,258
MAGI1	3	65,554,067	DOK6	18	67,192,125
CACNA1E	1	181,768,985	SLC1A3	5	36,667,579
C10orf112	10	19,678,497	COL6A3	2	238,233,410
SNRNP27	2	70,131,791	FHIT	3	59,761,158
MBP	18	74,724,257	WVOX	16	78,327,521
PTPRT	20	40,791,519	FBXL2	3	33,348,480
PCSK6	15	102,024,136	PCSK6	15	102,028,088
FMN2	1	240,472,692	TPH2	12	72,412,572
COL6A3	2	238,262,021	LIMCH1	4	41,378,712
TRDN	6	123,776,326	CRISPLD2	16	84,942,638
CNTNAP2	7	147,809,195	MMP16	8	89,075,226
PDE1C	7	32,025,543	CTNND2	5	10,984,056
MIOX	22	50,928,340	MACROD2	20	15,438,981
PTPRN2	7	157,870,786	TMC8	17	76,137,589
COL4A4	2	228,014,602	GAS7	17	9,943,867
PCDH17	13	58,258,094	TRPM6	9	77,350,356
ZXDC	3	126,156,660	STK10	5	171,471,045
GRK5	10	121,161,798	KCNJ3	2	155,553,275
CELSR3	3	48,675,064	TSPAN5	4	99,550,164
GRID2	4	93,304,682	SH3GL3	15	84,178,640
TMEM132B	12	126,140,066	LRRC4C	11	40,227,380
SHROOM3	4	77,441,688	NAALADL2	3	175,521,611
CELSR3	3	48,697,654	LRP1B	2	142,835,731

B. Markers in Linkage Disequilibrium (LD)

[0073] Linkage disequilibrium (LD) is a measure of the degree of association between alleles in a population. One of skill in the art will appreciate that alleles involving

markers in LD with the polymorphisms described herein can also be used in a similar manner to those described herein. Methods of calculating LD are known in the art (see, *e.g.*, Morton *et al.*, 2001; Tapper *et al.*, 2005; Maniatis *et al.*, 2002). Thus, in some cases, the methods can include analysis of polymorphisms that are in LD with a polymorphism described herein.

5 Methods are known in the art for identifying such polymorphisms; for example, the International HapMap Project provides a public database that can be used, see hapmap.org, as well as The International HapMap Consortium (2003) and The International HapMap Consortium (2005). Generally, it will be desirable to use a HapMap constructed using data from individuals who share ethnicity with the subject. For example, a HapMap for
10 Caucasians would ideally be used to identify markers in LD with an exemplary marker described herein for use in genotyping a subject of Caucasian descent.

[0074] Alternatively, methods described herein can include analysis of polymorphisms that show a correlation coefficient (r^2) of value > 0.5 with the markers described herein. Results can be obtained from on line public resources such as HapMap.org
15 on the World Wide Web. The correlation coefficient is a measure of LD, and reflects the degree to which alleles at two loci (for example, two SNPs) occur together, such that an allele at one SNP position can predict the correlated allele at a second SNP position, in the case where r^2 is >0.5 .

C. Identifying Additional Genetic Markers

20 [0075] In general, genetic markers can be identified using any of a number of methods well known in the art. For example, numerous polymorphisms in the regions described herein are known to exist and are available in public databases, which can be searched using methods and algorithms known in the art. Alternately, polymorphisms can be identified by sequencing either genomic DNA or cDNA in the region in which it is desired to
25 find a polymorphism. According to one approach, primers are designed to amplify such a region, and DNA from a subject is obtained and amplified. The DNA is sequenced, and the sequence (referred to as a “subject sequence” or “test sequence”) is compared with a reference sequence, which can represent the “normal” or “wild type” sequence, or the “affected” sequence. In some embodiments, a reference sequence can be from, for example,
30 the human draft genome sequence, publicly available in various databases, or a sequence deposited in a database such as GenBank. In some embodiments, the reference sequence is a composite of ethnically diverse individuals.

[0076] In general, if sequencing reveals a difference between the sequenced region and the reference sequence, a polymorphism has been identified. The fact that a difference in nucleotide sequence is identified at a particular site is what determines that a polymorphism exists at that site.

5 [0077] In most instances, particularly in the case of SNPs, only two polymorphic variants will exist at any location. However, in the case of SNPs, up to four variants may exist since there are four naturally occurring nucleotides in DNA. Other polymorphisms, such as insertions and deletions, may have more than four alleles.

[0078] In some embodiments, the methods include determining the presence or
10 absence of one or more other markers that are or may be associated with treatment response, e.g., in one or more genes, e.g., as described in WO 2009/092032, WO 2009/089120, WO 2009/082743, US2006/0177851, or US2009/0012371, incorporated herein in their entirety. See also, e.g., OMIM entry no. 181500 (SCZD).

D. Methods of Determining the Identity of a Subject's Response Allele

15 [0079] The methods described herein include determining the identity, e.g., the specific nucleotide, presence or absence, of alleles associated with a predicted response to a treatment for an SSD, e.g., SZ. In some embodiments, a predicted response to a method of treating an SSD is determined by detecting the presence of an identical allele in both the subject and an individual with a known response to a method of treating an SSD, e.g., in an
20 unrelated reference subject or a first or second-degree relation of the subject, and, in some cases, the absence of the allele in an reference individual having a known but opposite response. Thus the methods can include obtaining and analyzing a sample from a suitable reference individual. Samples that are suitable for use in the methods described herein contain genetic material, e.g., genomic DNA (gDNA). Genomic DNA is typically extracted
25 from biological samples such as blood or mucosal scrapings of the lining of the mouth, but can be extracted from other biological samples including urine or expectorant. The sample itself will typically include nucleated cells (e.g., blood or buccal cells) or tissue removed from the subject. The subject can be an adult, child, fetus, or embryo. In some embodiments, the sample is obtained prenatally, either from a fetus or embryo or from the mother (e.g.,
30 from fetal or embryonic cells in the maternal circulation). Methods and reagents are known in the art for obtaining, processing, and analyzing samples. In some embodiments, the sample is

obtained with the assistance of a health care provider, *e.g.*, to draw blood. In some embodiments, the sample is obtained without the assistance of a health care provider, *e.g.*, where the sample is obtained non-invasively, such as a sample comprising buccal cells that is obtained using a buccal swab or brush, or a mouthwash sample.

5 **[0080]** In some cases, a biological sample may be processed for DNA isolation. For example, DNA in a cell or tissue sample can be separated from other components of the sample. Cells can be harvested from a biological sample using standard techniques known in the art. For example, cells can be harvested by centrifuging a cell sample and resuspending the pelleted cells. The cells can be resuspended in a buffered solution such as phosphate-
10 buffered saline (PBS). After centrifuging the cell suspension to obtain a cell pellet, the cells can be lysed to extract DNA, *e.g.*, gDNA. See, *e.g.*, Ausubel *et al.* (2003). The sample can be concentrated and/or purified to isolate DNA. All samples obtained from a subject, including those subjected to any sort of further processing, are considered to be obtained from the subject. Routine methods can be used to extract genomic DNA from a biological sample,
15 including, for example, phenol extraction. Alternatively, genomic DNA can be extracted with kits such as the QIAamp® Tissue Kit (Qiagen, Chatsworth, Calif.) and the Wizard® Genomic DNA purification kit (Promega). Non-limiting examples of sources of samples include urine, blood, and tissue.

[0081] The presence or absence of an allele or genotype associated with a predicted
20 response to treatment for an SPD (*e.g.*, SZ) as described herein can be determined using methods known in the art. For example, gel electrophoresis, capillary electrophoresis, size exclusion chromatography, sequencing, and/or arrays can be used to detect the presence or absence of specific response alleles. Amplification of nucleic acids, where desirable, can be accomplished using methods known in the art, *e.g.*, PCR. In one example, a sample (*e.g.*, a
25 sample comprising genomic DNA), is obtained from a subject. The DNA in the sample is then examined to determine the identity of an allele as described herein, *i.e.*, by determining the identity of one or more alleles associated with a selected response. The identity of an allele can be determined by any method described herein, *e.g.*, by sequencing or by hybridization of the gene in the genomic DNA, RNA, or cDNA to a nucleic acid probe, *e.g.*,
30 a DNA probe (which includes cDNA and oligonucleotide probes) or an RNA probe. The nucleic acid probe can be designed to specifically or preferentially hybridize with a particular polymorphic variant.

[0082] Other methods of nucleic acid analysis can include direct manual sequencing (Church and Gilbert, 1988; Sanger *et al.*, 1977; U.S. Pat. No. 5,288,644); automated fluorescent sequencing; single-stranded conformation polymorphism assays (SSCP) (Schafer *et al.*, 1995); clamped denaturing gel electrophoresis (CDGE); two-dimensional gel electrophoresis (2DGE or TDGE); conformational sensitive gel electrophoresis (CSGE); denaturing gradient gel electrophoresis (DGGE) (Sheffield *et al.*, 1989); denaturing high performance liquid chromatography (DHPLC, Underhill *et al.*, 1997); infrared matrix-assisted laser desorption/ionization (IR-MALDI) mass spectrometry (WO 99/57318); mobility shift analysis (Orita *et al.*, 1989); restriction enzyme analysis (Flavell *et al.*, 1978; Geever *et al.*, 1981); quantitative real-time PCR (Raca *et al.*, 2004); heteroduplex analysis; chemical mismatch cleavage (CMC) (Cotton *et al.*, 1985); RNase protection assays (Myers *et al.*, 1985); use of polypeptides that recognize nucleotide mismatches, *e.g.*, *E. coli* mutS protein; allele-specific PCR, and combinations of such methods. See, *e.g.*, U.S. Patent Publication No. 2004/0014095, which is incorporated herein by reference in its entirety.

[0083] Sequence analysis can also be used to detect specific polymorphic variants. For example, polymorphic variants can be detected by sequencing exons, introns, 5' untranslated sequences, or 3' untranslated sequences. A sample comprising DNA or RNA is obtained from the subject. PCR or other appropriate methods can be used to amplify a portion encompassing the polymorphic site, if desired. The sequence is then ascertained, using any standard method, and the presence of a polymorphic variant is determined. Real-time pyrophosphate DNA sequencing is yet another approach to detection of polymorphisms and polymorphic variants (Alderborn *et al.*, 2000). Additional methods include, for example, PCR amplification in combination with denaturing high performance liquid chromatography (DHPLC) (Underhill *et al.*, 1997).

[0084] In order to detect polymorphisms and/or polymorphic variants, it may be desirable to amplify a portion of genomic DNA (gDNA) encompassing the polymorphic site. Such regions can be amplified and isolated by PCR using oligonucleotide primers designed based on genomic and/or cDNA sequences that flank the site. PCR refers to procedures in which target nucleic acid (*e.g.*, genomic DNA) is amplified in a manner similar to that described in U.S. Pat. No. 4,683,195, and subsequent modifications of the procedure described therein. Generally, sequence information from the ends of the region of interest or beyond are used to design oligonucleotide primers that are identical or similar in sequence to

opposite strands of a potential template to be amplified. See *e.g.*, *PCR Primer: A Laboratory Manual*, Dieffenbach and Dveksler, (Eds.); McPherson *et al.*, 2000; Mattila *et al.*, 1991; Eckert *et al.*, 1991; *PCR* (eds. McPherson *et al.*, IRL Press, Oxford); and U.S. Pat. No. 4,683,202. Other amplification methods that may be employed include the ligase chain
5 reaction (LCR) (Wu and Wallace, 1989; Landegren *et al.*, 1988), transcription amplification (Kwoh *et al.*, 1989), self-sustained sequence replication (Guatelli *et al.*, 1990), and nucleic acid based sequence amplification (NASBA). Guidelines for selecting primers for PCR amplification are well known in the art. See, *e.g.*, McPherson *et al.* (2000). A variety of computer programs for designing primers are available, *e.g.*, 'Oligo' (National Biosciences,
10 Inc, Plymouth Minn.), MacVector (Kodak/IBI), and the GCG suite of sequence analysis programs (Genetics Computer Group, Madison, Wis. 53711).

[0085] In some cases, PCR conditions and primers can be developed that amplify a product only when the variant allele is present or only when the wild type allele is present (MSPCR or allele-specific PCR). For example, patient DNA and a control can be amplified
15 separately using either a wild type primer or a primer specific for the variant allele. Each set of reactions is then examined for the presence of amplification products using standard methods to visualize the DNA. For example, the reactions can be electrophoresed through an agarose gel and the DNA visualized by staining with ethidium bromide or other DNA intercalating dye. In DNA samples from heterozygous patients, reaction products would be
20 detected in each reaction.

[0086] Real-time quantitative PCR can also be used to determine copy number. Quantitative PCR permits both detection and quantification of specific DNA sequence in a sample as an absolute number of copies or as a relative amount when normalized to DNA input or other normalizing genes. A key feature of quantitative PCR is that the amplified
25 DNA product is quantified in real-time as it accumulates in the reaction after each amplification cycle. Methods of quantification can include the use of fluorescent dyes that intercalate with double-stranded DNA, and modified DNA oligonucleotide probes that fluoresce when hybridized with a complementary DNA. Methods of quantification can include determining the intensity of fluorescence for fluorescently tagged molecular probes
30 attached to a solid surface such as a microarray.

[0087] The first report of extensive copy number variation (CNV) in the human genome used intensity analysis of microarray data to document numerous examples of genes

that vary in copy number (Redon *et al.*, 2006). Subsequent studies have shown that certain copy number variants are associated with complex genetic diseases such as SZ (Walsh *et al.*, 2008; Stone *et al.*, 2008).

[0088] In some embodiments, a peptide nucleic acid (PNA) probe can be used instead of a nucleic acid probe in the hybridization methods described above. PNA is a DNA mimetic with a peptide-like, inorganic backbone, *e.g.*, N-(2-aminoethyl)glycine units, with an organic base (A, G, C, T or U) attached to the glycine nitrogen via a methylene carbonyl linker (see, *e.g.*, Nielsen *et al.*, 1994). The PNA probe can be designed to specifically hybridize to a nucleic acid comprising a polymorphic variant.

[0089] In some cases, allele-specific oligonucleotides can also be used to detect the presence of a polymorphic variant. For example, polymorphic variants can be detected by performing allele-specific hybridization or allele-specific restriction digests. Allele specific hybridization is an example of a method that can be used to detect sequence variants, including complete genotypes of a subject (*e.g.*, a mammal such as a human). See Stoneking *et al.*, 1991; Prince *et al.*, 2001. An “allele-specific oligonucleotide” (also referred to herein as an “allele-specific oligonucleotide probe”) is an oligonucleotide that is specific for particular a polymorphism can be prepared using standard methods (see, Ausubel *et al.*, 2003). Allele-specific oligonucleotide probes typically can be approximately 10-50 base pairs, preferably approximately 15-30 base pairs, that specifically hybridizes to a nucleic acid region that contains a polymorphism. Hybridization conditions are selected such that a nucleic acid probe can specifically bind to the sequence of interest, *e.g.*, the variant nucleic acid sequence. Such hybridizations typically are performed under high stringency as some sequence variants include only a single nucleotide difference. In some cases, dot-blot hybridization of amplified oligonucleotides with allele-specific oligonucleotide (ASO) probes can be performed. See, for example, Saiki *et al.*, 1986.

[0090] In some embodiments, allele-specific restriction digest analysis can be used to detect the existence of a polymorphic variant of a polymorphism, if alternate polymorphic variants of the polymorphism result in the creation or elimination of a restriction site. Allele-specific restriction digests can be performed in the following manner. A sample containing genomic DNA is obtained from the individual and genomic DNA is isolated for analysis. For nucleotide sequence variants that introduce a restriction site, restriction digest with the particular restriction enzyme can differentiate the alleles. In some cases, polymerase chain

reaction (PCR) can be used to amplify a region comprising the polymorphic site, and restriction fragment length polymorphism analysis is conducted (see, Ausubel *et al.*, 2003). The digestion pattern of the relevant DNA fragment indicates the presence or absence of a particular polymorphic variant of the polymorphism and is therefore indicative of the subject's response allele. For sequence variants that do not alter a common restriction site, mutagenic primers can be designed that introduce a restriction site when the variant allele is present or when the wild type allele is present. For example, a portion of a nucleic acid can be amplified using the mutagenic primer and a wild type primer, followed by digest with the appropriate restriction endonuclease.

[0091] In some embodiments, fluorescence polarization template-directed dye-terminator incorporation (FP-TDI) is used to determine which of multiple polymorphic variants of a polymorphism is present in a subject (Chen *et al.*, 1999). Rather than involving use of allele-specific probes or primers, this method employs primers that terminate adjacent to a polymorphic site, so that extension of the primer by a single nucleotide results in incorporation of a nucleotide complementary to the polymorphic variant at the polymorphic site.

[0092] In some cases, DNA containing an amplified portion may be dot-blotted, using standard methods (see Ausubel *et al.*, 2003), and the blot contacted with the oligonucleotide probe. The presence of specific hybridization of the probe to the DNA is then detected. Specific hybridization of an allele-specific oligonucleotide probe (specific for a polymorphic variant indicative of a predicted response to a method of treating an SSD) to DNA from the subject is indicative of a subject's response allele.

[0093] The methods can include determining the genotype of a subject with respect to both copies of the polymorphic site present in the genome (*i.e.*, both alleles). For example, the complete genotype may be characterized as $-/-$, as $-/+$, or as $+/+$, where a minus sign indicates the presence of the reference or wild type sequence at the polymorphic site, and the plus sign indicates the presence of a polymorphic variant other than the reference sequence. If multiple polymorphic variants exist at a site, this can be appropriately indicated by specifying which ones are present in the subject. Any of the detection means described herein can be used to determine the genotype of a subject with respect to one or both copies of the polymorphism present in the subject's genome.

[0094] Methods of nucleic acid analysis to detect polymorphisms and/or polymorphic variants can include, e.g., microarray analysis. Hybridization methods, such as Southern analysis, Northern analysis, or in situ hybridizations, can also be used (see, Ausubel *et al.*, 2003). To detect microdeletions, fluorescence in situ hybridization (FISH) using DNA probes
5 that are directed to a putatively deleted region in a chromosome can be used. For example, probes that detect all or a part of a microsatellite marker can be used to detect microdeletions in the region that contains that marker.

[0095] In some embodiments, it is desirable to employ methods that can detect the presence of multiple polymorphisms (e.g., polymorphic variants at a plurality of polymorphic
10 sites) in parallel or substantially simultaneously. Oligonucleotide arrays represent one suitable means for doing so. Other methods, including methods in which reactions (e.g., amplification, hybridization) are performed in individual vessels, e.g., within individual wells of a multi-well plate or other vessel may also be performed so as to detect the presence of multiple polymorphic variants (e.g., polymorphic variants at a plurality of polymorphic sites)
15 in parallel or substantially simultaneously according to the methods provided herein.

[0096] Nucleic acid probes can be used to detect and/or quantify the presence of a particular target nucleic acid sequence within a sample of nucleic acid sequences, e.g., as hybridization probes, or to amplify a particular target sequence within a sample, e.g., as a primer. Probes have a complimentary nucleic acid sequence that selectively hybridizes to the
20 target nucleic acid sequence. In order for a probe to hybridize to a target sequence, the hybridization probe must have sufficient identity with the target sequence, *i.e.*, at least 70% (e.g., 80%, 90%, 95%, 98% or more) identity to the target sequence. The probe sequence must also be sufficiently long so that the probe exhibits selectivity for the target sequence over non-target sequences. For example, the probe will be at least 20 (e.g., 25, 30, 35, 50,
25 100, 200, 300, 400, 500, 600, 700, 800, 900 or more) nucleotides in length. In some embodiments, the probes are not more than 30, 50, 100, 200, 300, 500, 750, or 1000 nucleotides in length. Probes are typically about 20 to about 1×10^6 nucleotides in length. Probes include primers, which generally refers to a single-stranded oligonucleotide probe that can act as a point of initiation of template-directed DNA synthesis using methods such as
30 PCR (polymerase chain reaction), LCR (ligase chain reaction), *etc.*, for amplification of a target sequence.

[0097] The probe can be a test probe such as a probe that can be used to detect polymorphisms in a region described herein (*e.g.*, an allele associated with treatment response as described herein). In some embodiments, the probe can bind to another marker sequence associated with SZ, SPD, or SD as described herein or known in the art.

5 [0098] Control probes can also be used. For example, a probe that binds a less variable sequence, *e.g.*, repetitive DNA associated with a centromere of a chromosome, can be used as a control. Probes that hybridize with various centromeric DNA and locus-specific DNA are available commercially, for example, from Vysis, Inc. (Downers Grove, Ill.), Molecular Probes, Inc. (Eugene, Oreg.), or from Cytocell (Oxfordshire, UK). Probe sets are
10 available commercially such from Applied Biosystems, *e.g.*, the Assays-on-Demand SNP kits. Alternatively, probes can be synthesized, *e.g.*, chemically or *in vitro*, or made from chromosomal or genomic DNA through standard techniques. For example, sources of DNA that can be used include genomic DNA, cloned DNA sequences, somatic cell hybrids that contain one, or a part of one, human chromosome along with the normal chromosome
15 complement of the host, and chromosomes purified by flow cytometry or microdissection. The region of interest can be isolated through cloning, or by site-specific amplification via the polymerase chain reaction (PCR). See, for example, Nath and Johnson, (1998); Wheelless *et al.*, (1994); U.S. Pat. No. 5,491,224.

 [0099] In some embodiments, the probes are labeled, *e.g.*, by direct labeling, with a
20 fluorophore, an organic molecule that fluoresces after absorbing light of lower wavelength/higher energy. A directly labeled fluorophore allows the probe to be visualized without a secondary detection molecule. After covalently attaching a fluorophore to a nucleotide, the nucleotide can be directly incorporated into the probe with standard techniques such as nick translation, random priming, and PCR labeling. Alternatively,
25 deoxycytidine nucleotides within the probe can be transaminated with a linker. The fluorophore then is covalently attached to the transaminated deoxycytidine nucleotides. See, *e.g.*, U.S. Pat. No. 5,491,224.

 [00100] Fluorophores of different colors can be chosen such that each probe in a set can be distinctly visualized. For example, a combination of the following fluorophores
30 can be used: 7-amino-4-methylcoumarin-3-acetic acid (AMCA), TEXAS RED™ (Molecular Probes, Inc., Eugene, Oreg.), 5-(and -6)-carboxy-X-rhodamine, lissamine rhodamine B, 5-(and -6)-carboxyfluorescein, fluorescein-5-isothiocyanate (FITC), 7-diethylaminocoumarin-

3-carboxylic acid, tetramethylrhodamine-5-(and -6)-isothiocyanate, 5-(and -6)-carboxytetramethylrhodamine, 7-hydroxycoumarin-3-carboxylic acid, 6-[fluorescein 5-(and -6)-carboxamido]hexanoic acid, N-(4,4-difluoro-5,7-dimethyl-4-bora-3a,4a diaza-3-indacenepropionic acid, eosin-5-isothiocyanate, erythrosin-5-isothiocyanate, and
5 CASCADE™ blue acetylazide (Molecular Probes, Inc., Eugene, Oreg.). Fluorescently labeled probes can be viewed with a fluorescence microscope and an appropriate filter for each fluorophore, or by using dual or triple band-pass filter sets to observe multiple fluorophores. See, for example, U.S. Pat. No. 5,776,688. Alternatively, techniques such as flow cytometry can be used to examine the hybridization pattern of the probes. Fluorescence-
10 based arrays are also known in the art.

[00101] In other embodiments, the probes can be indirectly labeled with, *e.g.*, biotin or digoxigenin, or labeled with radioactive isotopes such as ³²P and ³H. For example, a probe indirectly labeled with biotin can be detected by avidin conjugated to a detectable marker. For example, avidin can be conjugated to an enzymatic marker such as alkaline
15 phosphatase or horseradish peroxidase. Enzymatic markers can be detected in standard colorimetric reactions using a substrate and/or a catalyst for the enzyme. Catalysts for alkaline phosphatase include 5-bromo-4-chloro-3-indolylphosphate and nitro blue tetrazolium. Diaminobenzoate can be used as a catalyst for horseradish peroxidase.

[00102] In another aspect, this document features arrays that include a substrate
20 having a plurality of addressable areas, and methods of using them. At least one area of the plurality includes a nucleic acid probe that binds specifically to a sequence comprising a polymorphism listed in Table A (or Tables 1-10), and can be used to detect the absence or presence of said polymorphism, *e.g.*, one or more SNPs, microsatellites, minisatellites, or indels, as described herein, to determine a response allele. For example, the array can include
25 one or more nucleic acid probes that can be used to detect a polymorphism listed in Table A or Tables 1-10. In some embodiments, the array further includes at least one area that includes a nucleic acid probe that can be used to specifically detect another marker associated with a predicted response to a method of treating an SSD (*e.g.*, SZ), as described herein. In some embodiments, the probes are nucleic acid capture probes.

[00103] Generally, microarray hybridization is performed by hybridizing a
30 nucleic acid of interest (*e.g.*, a nucleic acid encompassing a polymorphic site) with the array and detecting hybridization using nucleic acid probes. In some cases, the nucleic acid of

interest is amplified prior to hybridization. Hybridization and detecting are generally carried out according to standard methods. See, *e.g.*, PCT Application Nos. WO 92/10092 and WO 95/11995, and U.S. Pat. No. 5,424,186. For example, the array can be scanned to determine the position on the array to which the nucleic acid hybridizes. The hybridization data
5 obtained from the scan is typically in the form of fluorescence intensities as a function of location on the array.

[00104] Arrays can be formed on substrates fabricated with materials such as paper, glass, plastic (*e.g.*, polypropylene, nylon, or polystyrene), polyacrylamide, nitrocellulose, silicon, optical fiber, or any other suitable solid or semisolid support, and can
10 be configured in a planar (*e.g.*, glass plates, silicon chips) or three dimensional (*e.g.*, pins, fibers, beads, particles, microtiter wells, capillaries) configuration. Methods for generating arrays are known in the art and include, *e.g.*, photolithographic methods (see, *e.g.*, U.S. Pat. Nos. 5,143,854; 5,510,270; and 5,527,681), mechanical methods (*e.g.*, directed-flow methods as described in U.S. Pat. No. 5,384,261), pin-based methods (*e.g.*, as described in U.S. Pat.
15 No. 5,288,514), and bead-based techniques (*e.g.*, as described in PCT US/93/04145). The array typically includes oligonucleotide hybridization probes capable of specifically hybridizing to different polymorphic variants. Oligonucleotide probes that exhibit differential or selective binding to polymorphic sites may readily be designed by one of ordinary skill in the art. For example, an oligonucleotide that is perfectly complementary to a sequence that
20 encompasses a polymorphic site (*i.e.*, a sequence that includes the polymorphic site, within it or at one end) will generally hybridize preferentially to a nucleic acid comprising that sequence, as opposed to a nucleic acid comprising an alternate polymorphic variant.

[00105] Oligonucleotide probes forming an array may be attached to a substrate by any number of techniques, including, without limitation, (i) *in situ* synthesis (*e.g.*, high-
25 density oligonucleotide arrays) using photolithographic techniques; (ii) spotting/printing at medium to low density on glass, nylon or nitrocellulose; (iii) by masking, and (iv) by dot-blotting on a nylon or nitrocellulose hybridization membrane. Oligonucleotides can be immobilized via a linker, including by covalent, ionic, or physical linkage. Linkers for immobilizing nucleic acids and polypeptides, including reversible or cleavable linkers, are
30 known in the art. See, for example, U.S. Pat. No. 5,451,683 and WO98/20019. Alternatively, oligonucleotides can be non-covalently immobilized on a substrate by hybridization to anchors, by means of magnetic beads, or in a fluid phase such as in microtiter wells or

capillaries. Immobilized oligonucleotide probes are typically about 20 nucleotides in length, but can vary from about 10 nucleotides to about 1000 nucleotides in length.

[00106] Arrays can include multiple detection blocks (*i.e.*, multiple groups of probes designed for detection of particular polymorphisms). Such arrays can be used to analyze multiple different polymorphisms. Detection blocks may be grouped within a single array or in multiple, separate arrays so that varying conditions (*e.g.*, conditions optimized for particular polymorphisms) may be used during the hybridization. For example, it may be desirable to provide for the detection of those polymorphisms that fall within G-C rich stretches of a genomic sequence, separately from those falling in A-T rich segments. General descriptions of using oligonucleotide arrays for detection of polymorphisms can be found, for example, in U.S. Pat. Nos. 5,858,659 and 5,837,832. In addition to oligonucleotide arrays, cDNA arrays may be used similarly in certain embodiments.

[00107] The methods described herein can include providing an array as described herein; contacting the array with a sample (*e.g.*, all or a portion of genomic DNA that includes at least a portion of a human chromosome comprising a response allele) and/or optionally, a different portion of genomic DNA (*e.g.*, a portion that includes a different portion of one or more human chromosomes), and detecting binding of a nucleic acid from the sample to the array. Optionally, the method includes amplifying nucleic acid from the sample, *e.g.*, genomic DNA that includes a portion of a human chromosome described herein, and, optionally, a region that includes another region associated with a predicted response to a method of treating SZ, SD, or SPD, prior to or during contact with the array.

[00108] In some aspects, the methods described herein can include using an array that can ascertain differential expression patterns or copy numbers of one or more genes in samples from normal and affected individuals (see, *e.g.*, Redon *et al.*, 2006). For example, arrays of probes to a marker described herein can be used to measure polymorphisms between DNA from a subject having an SSD (*e.g.*, SZ) and having a predicted response to a treatment for an SSD (*e.g.*, SZ), and control DNA, *e.g.*, DNA obtained from an individual that has SZ, SPD, or SD, and has a known response to a form of treatment for an SSD (*e.g.*, SZ). Since the clones on the array contain sequence tags, their positions on the array are accurately known relative to the genomic sequence. Different hybridization patterns between DNA from an individual afflicted with an SSD (*e.g.*, SZ) and DNA from a control individual at areas in the array corresponding to markers as described herein, and, optionally, one or

more other regions associated with an SSD (*e.g.*, SZ), are indicative of a predicted response to a treatment for an SSD (*e.g.*, SZ). Methods for array production, hybridization, and analysis are described, *e.g.*, in Snijders *et al.* (2001); Klein *et al.* (1999); Albertson *et al.* (2003); and Snijders *et al.* (2002).

5 **[00109]** In another aspect, this document provides methods of determining the absence or presence of a response allele associated with a predicted response to treatment for an SSD (*e.g.*, SZ) as described herein, using an array described above. The methods can include providing a two dimensional array having a plurality of addresses, each address of the plurality being positionally distinguishable from each other address of the plurality having a
10 unique nucleic acid capture probe, contacting the array with a first sample from a test subject who is has an SSD (*e.g.*, SZ), and comparing the binding of the first sample with one or more references, *e.g.*, binding of a sample from a subject who is known to have an SSD (*e.g.*, SZ), and/or binding of a sample from a subject who has an SSD (*e.g.*, SZ) and a known response to treatment for an SSD (*e.g.*, SZ); and comparing the binding of the first sample with the
15 binding of the second sample. In some embodiments, the methods can include contacting the array with a third sample from a cell or subject that does not have SZ; and comparing the binding of the first sample with the binding of the third sample. In some embodiments, the second and third samples are from first or second-degree relatives of the test subject. In the case of a nucleic acid hybridization, binding with a capture probe at an address of the
20 plurality, can be detected by any method known in the art, *e.g.*, by detection of a signal generated from a label attached to the nucleic acid.

III. Schizophrenia Spectrum Disorders

[00110] The methods described herein can be used to determine an individual predicted response to a method of treating a schizophrenia spectrum disorder (SSD). The
25 SSDs include schizophrenia (SZ), schizotypal personality disorder (SPD), and schizoaffective disorder (SD). Methods for diagnosing SSDs are known in the art, see, *e.g.*, the DSM-IV. See, *e.g.*, WO 2009/092032, incorporated herein by reference.

IV. Methods of Selecting and Optimizing Treatment

[00111] In some embodiments, the methods described herein include the
30 administration of one or more treatments, *e.g.*, antipsychotic medications, to a person identified as having or being at risk of developing an SSD (*e.g.*, SZ). The methods can also

include selecting a treatment regimen for a subject who has an SSD or is determined to be at risk for developing an SSD (*e.g.*, SZ), based upon the absence or presence of an allele or genotype associated with response as described herein. The determination of a treatment regimen can also be based upon the absence or presence of other risk factors, *e.g.*, as known in the art or described herein. The methods can also include administering a treatment regimen selected by a method described to a subject who has or is at risk for developing an SSD (*e.g.*, SZ) to thereby treat, reduce risk of developing, or delay further progression of the disease. A treatment regimen can include the administration of antipsychotic medications to a subject identified as having or at risk of developing an SSD (*e.g.*, SZ) before the onset of any psychotic episodes.

[00112] In some embodiments, the approach described herein uses a multiple response allele algorithm rather than a single response allele or a group of single response alleles. Algorithms can be used to derive a single value that reflects disease status, prognosis, and/or response to treatment. Highly multiplexed tools can be used to simultaneously measure multiple parameters. An advantage of using such tools is that all results can be derived from the same sample and run under the same conditions at the same time. High-level pattern recognition approaches can be applied, and a number of tools are available, including clustering approaches such as hierarchical clustering, self-organizing maps, and supervised classification algorithms (*e.g.*, support vector machines, k-nearest neighbors, and neural networks). The latter group of analytical approaches is likely to be of substantial clinical use. The basic method can include providing a biological sample (*e.g.*, a blood sample) from a individual; determining the sequence of a group of response alleles in the sample; and using an algorithm to determine a SSD score.

[00113] Algorithms for determining an individual's disease status or response to treatment, for example, can be determined for any clinical condition. The algorithms provided herein can be mathematic functions containing multiple parameters that can be quantified using, for example, medical devices, clinical evaluation scores, or biological, chemical, or physical tests of biological samples. Each mathematical function can be a weight-adjusted expression of the parameters determined to be relevant to a selected clinical condition. Univariate and multivariate analyses can be performed on data collected for each marker using conventional statistical tools (*e.g.*, not limited to: T-tests, PCA, LDA, or binary

logistic regression). An algorithm can be applied to generate a set of diagnostic scores. The algorithms generally can be expressed in the format of Formula 1:

$$\text{Diagnostic score} = f(x_1, x_2, x_3, x_4, x_5 \dots x_n) \text{ (1).}$$

The diagnostic score is a value that is the diagnostic or prognostic result, “f” is any mathematical function, “n” is any integer (*e.g.*, an integer from 1 to 10,000), and $x_1, x_2, x_3, x_4, x_5 \dots x_n$ are the “n” parameters that are, for example, measurements determined by medical devices, clinical evaluation scores, and/or test results for biological samples.

[00114] The parameters of an algorithm can be individually weighted. An example of such an algorithm is expressed in Formula 2:

$$\text{Diagnostic score} = a_1 \cdot x_1 + a_2 \cdot x_2 + a_3 \cdot x_3 + a_4 \cdot x_4 + a_5 \cdot x_5 \text{ (2).}$$

Here, x_1, x_2, x_3, x_4 , and x_5 can be measurements determined by medical devices, clinical evaluation scores, and/or test results for biological samples (*i.*, human biological samples), and a_1, a_2, a_3, a_4 , and a_5 are weight-adjusted factors for x_1, x_2, x_3, x_4 , and x_5 , respectively.

[00115] A diagnostic score can be used to quantitatively define a medical condition or disease, or the effect of a medical treatment. In a more general form, multiple diagnostic scores S_m can be generated by applying multiple formulas to specific groupings of biomarker measurements, as illustrated in Formula 3:

$$\text{Diagnostic scores } S_m = F_m(x_1, \dots x_n) \text{ (3).}$$

Multiple scores can be useful, for example, in the identification of specific types and subtypes of SSD. In some cases, the SSD is SZ. Multiple scores can also be parameters indicating patient treatment progress or the efficacy of the treatment selected. Diagnostic scores for subtypes of SSD may help aid in the selection or optimization of antipsychotics and other pharmaceuticals.

[00116] As used herein, the term “treat” or “treatment” is defined as the application or administration of a treatment regimen, *e.g.*, a therapeutic agent or modality, to a subject, *e.g.*, a patient. The subject can be a patient having an SSD (*e.g.*, SZ), a symptom of an SSD (*e.g.*, SZ), or at risk of developing (*i.e.*, a predisposition toward) an SSD (*e.g.*, SZ). The treatment can be to cure, heal, alleviate, relieve, alter, remedy, ameliorate, palliate, improve or affect an SSD (*e.g.*, SZ), the symptoms of an SSD (*e.g.*, SZ) or the predisposition

toward an SSD (*e.g.*, SZ). For example, a standard treatment regimen for schizophrenia is the administration of antipsychotic medications, which are typically antagonists acting at postsynaptic D2 dopamine receptors in the brain and can include neuroleptics and/or atypical antipsychotics. Antipsychotic medications substantially reduce the risk of relapse in the stable phase of illness. Currently accepted treatments for SZ are described in greater detail in the Practice Guideline for the Treatment of Patients With Schizophrenia American Psychiatric Association, Second Edition, American Psychiatric Association (2004), which is incorporated herein by reference in its entirety.

[00117] The methods of determining a treatment regimen and methods of treatment or prevention of SSDs as described herein can further include the step of monitoring the subject, *e.g.*, for a change (*e.g.*, an increase or decrease) in one or more of the diagnostic criteria for an SSD listed herein, or any other parameter related to clinical outcome. The subject can be monitored in one or more of the following periods: prior to beginning of treatment; during the treatment; or after one or more elements of the treatment have been administered. Monitoring can be used to evaluate the need for further treatment with the same or a different therapeutic agent or modality. Generally, a decrease in one or more of the parameters described above is indicative of the improved condition of the subject, although with red blood cell and platelet levels, an increase can be associated with the improved condition of the subject.

[00118] The methods can be used, for example, to choose between alternative treatments (*e.g.*, a particular dosage, mode of delivery, time of delivery, inclusion of adjunctive therapy, *e.g.*, administration in combination with a second agent) based on the subject's probable drug response. In some embodiments, a treatment for a subject having an SSD (*e.g.*, SZ) is selected based on the subject's response allele, and the treatment is administered to the subject. In some embodiments, various treatments or combinations of treatments can be administered based on the presence in a subject of a response allele as described herein. Various treatment regimens are known for treating SSDs including, for example, regimens as described herein.

[00119] With regards to both prophylactic and therapeutic methods of treatment of SSDs, according to the present methods treatment can be specifically tailored or modified, based on knowledge obtained from pharmacogenomics. "Pharmacogenomics," as used herein, refers to the application of genomics technologies such as structural

chromosomal analysis, to drugs in clinical development and on the market. See, for example, Eichelbaum *et al.* (1996); Linder *et al.* (1997); Wang *et al.* (2003); Weinshilboum and Wang (2004); Guttmacher and Collins (2005); Weinshilboum and Wang (2006). Specifically, as used herein, the term refers the study of how a patient's genes determine his or her response to a drug (*e.g.*, a patient's "drug response phenotype," or "drug response allele"). Drug response phenotypes that are influenced by inheritance and can vary from potentially life-threatening adverse reactions at one of the spectrum to lack of therapeutic efficacy at the other. The ability to determine whether and how a subject will respond to a particular drug can assist medical professionals in determining whether the drug should be administered to the subject, and at what dose. Thus, this document provides methods for tailoring an individual's prophylactic or therapeutic treatment according to the presence of specific drug response alleles in that individual.

[00120] Standard pharmacologic therapies for SSDs include the administration of one or more antipsychotic medications, which are typically antagonists acting at postsynaptic D2 dopamine receptors in the brain. Antipsychotic medications include conventional, or first generation, antipsychotic agents, which are sometimes referred to as neuroleptics because of their neurologic side effects, and second generation antipsychotic agents, which are less likely to exhibit neuroleptic effects and have been termed atypical antipsychotics. Typical antipsychotics can include chlorpromazine, fluphenazine, haloperidol, thiothixene, trifluoperazine, perphenazine, and thioridazine; atypical antipsychotics can include aripiprazole, risperidone, clozapine, olanzapine, quetiapine, or ziprasidone.

[00121] Information generated from pharmacogenomic research using a method described herein can be used to determine appropriate dosage and treatment regimens for prophylactic or therapeutic treatment of an individual. This knowledge, when applied to dosing or drug selection, can avoid adverse reactions or therapeutic failure and thus enhance therapeutic or prophylactic efficiency when administering a therapeutic composition (*e.g.*, a cytotoxic agent or combination of cytotoxic agents) to a patient as a means of treating or preventing progression of SSDs.

[00122] In some cases, a physician or clinician may consider applying knowledge obtained in relevant pharmacogenomics studies (*e.g.*, using a method described herein) when determining whether to administer a pharmaceutical composition such as an antipsychotic agent or a combination of antipsychotic agents to a subject. In other cases, a

physician or clinician may consider applying such knowledge when determining the dosage or frequency of treatments (*e.g.*, administration of antipsychotic agent or combination of antipsychotic agents to a patient). As one example, a physician or clinician can determine (or have determined by, for example, a laboratory) the presence of one or more response alleles
5 in a subject as described herein, and optionally one or more other markers associated with an SSD (*e.g.*, SZ) or response to a treatment, of one or a group of subjects, *e.g.*, clinical patients, or subjects who may be participating in a clinical trial, *e.g.*, a trial designed to test the efficacy of a pharmaceutical composition (*e.g.*, an antipsychotic or combination of antipsychotic agents); the physician or clinician can then correlate the genetic makeup of the
10 subjects with their response to the pharmaceutical composition.

[00123] As another example, information regarding a response allele as described herein can be used to stratify or select a subject population for a clinical trial. The information can, in some embodiments, be used to stratify individuals that exhibit or are likely to exhibit a toxic response to a treatment from those that will not. In other cases, the
15 information can be used to separate those that will be non-responders from those who will be responders. The alleles described herein can be used in pharmacogenomics-based design and manage the conduct of a clinical trial, *e.g.*, as described in U.S. Pat. Pub. No. 2003/0108938.

[00124] As another example, information regarding a response allele as described herein, can be used to stratify or select human cells or cell lines for drug testing
20 purposes. Human cells are useful for studying the effect of a polymorphism on physiological function, and for identifying and/or evaluating potential therapeutic agents for the treatment of SSDs, *e.g.*, anti-psychotics. Thus the methods can include performing the present methods on genetic material from a cell line. The information can, in some embodiments, be used to separate cells that respond or are expected to respond to particular drugs from those that do
25 not respond, *e.g.*, which cells show altered second messenger signaling.

[00125] Also included herein are compositions and methods for the identification and treatment of subjects who have a predicted response to a treatment for an SSD (*e.g.*, SZ), such that a theranostic approach can be taken to test such individuals to predict the effectiveness of a particular therapeutic intervention (*e.g.*, a pharmaceutical or
30 non-pharmaceutical intervention as described herein) and to alter the intervention to (1) reduce the risk of developing adverse outcomes and (2) enhance the effectiveness of the intervention. Thus, the methods and compositions described herein also provide a means of

optimizing the treatment of a subject having such a disorder. Provided herein is a theranostic approach to treating and preventing SSDs, by integrating diagnostics and therapeutics to improve the real-time treatment of a subject. Practically, this means creating tests that can identify which patients are most suited to a particular therapy, and providing feedback on
5 how well a drug is working to optimize treatment regimens.

[00126] Within the clinical trial setting, a theranostic method as described herein can provide key information to optimize trial design, monitor efficacy, and enhance drug safety. For instance, “trial design” theranostics can be used for patient stratification, determination of patient eligibility (inclusion/exclusion), creation of homogeneous treatment
10 groups, and selection of patient samples that are representative of the general population. Such theranostic tests can therefore provide the means for patient efficacy enrichment, thereby minimizing the number of individuals needed for trial recruitment. “Efficacy” theranostics are useful for monitoring therapy and assessing efficacy criteria. Finally, “safety” theranostics can be used to prevent adverse drug reactions or avoid medication error.

[00127] The methods described herein can include retrospective analysis of clinical trial data as well, both at the subject level and for the entire trial, to detect correlations between an allele as described herein and any measurable or quantifiable parameter relating to the outcome of the treatment, *e.g.*, efficacy (the results of which may be binary (*i.e.*, yes and no) as well as along a continuum), side-effect profile (*e.g.*, weight gain,
20 metabolic dysfunction, lipid dysfunction, movement disorders, or extrapyramidal symptoms), treatment maintenance and discontinuation rates, return to work status, hospitalizations, suicidality, total healthcare cost, social functioning scales, response to non-pharmacological treatments, and/or dose response curves. The results of these correlations can then be used to influence decision-making, *e.g.*, regarding treatment or therapeutic strategies, provision of
25 services, and/or payment. For example, a correlation between a positive outcome parameter (*e.g.*, high efficacy, low side effect profile, high treatment maintenance/low discontinuation rates, good return to work status, low hospitalizations, low suicidality, low total healthcare cost, high social function scale, favorable response to non-pharmacological treatments, and/or acceptable dose response curves) and a selected allele or genotype can influence treatment
30 such that the treatment is recommended or selected for a subject having the selected allele or genotype.

[00128] This document also provides methods and materials to assist medical or research professionals in determining whether a particular treatment regimen is optimal. Medical professionals can be, for example, doctors, nurses, medical laboratory technologists, and pharmacists. Research professionals can be, for example, principle investigators, research technicians, postdoctoral trainees, and graduate students. A professional can be assisted by (1) determining whether specific polymorphic variants are present in a biological sample from a subject, and (2) communicating information about polymorphic variants to that professional.

[00129] Using information about specific polymorphic variants determined using a method described herein, a medical professional can take one or more actions that can affect patient care. For example, a medical professional can record information in the patient's medical record regarding the patient's likely response to a given treatment for an SSD (*e.g.*, SZ). In some cases, a medical professional can record information regarding a treatment assessment, or otherwise transform the patient's medical record, to reflect the patient's current treatment and response allele(s). In some cases, a medical professional can review and evaluate a patient's entire medical record and assess multiple treatment strategies for clinical intervention of a patient's condition.

[00130] A medical professional can initiate or modify treatment after receiving information regarding a patient's response allele(s), for example. In some cases, a medical professional can recommend a change in therapy based on the subject's response allele(s). In some cases, a medical professional can enroll a patient in a clinical trial for, by way of example, detecting correlations between an allele or genotype as described herein and any measurable or quantifiable parameter relating to the outcome of the treatment as described above.

[00131] A medical professional can communicate information regarding a patient's expected response to a treatment to a patient or a patient's family. In some cases, a medical professional can provide a patient and/or a patient's family with information regarding SSDs and response assessment information, including treatment options, prognosis, and referrals to specialists. In some cases, a medical professional can provide a copy of a patient's medical records to a specialist.

[00132] A research professional can apply information regarding a subject's response allele(s) to advance scientific research. For example, a researcher can compile data on specific polymorphic variants. In some cases, a research professional can obtain a subject's response allele(s) as described herein to evaluate a subject's enrollment, or continued participation, in a research study or clinical trial. In some cases, a research professional can communicate information regarding a subject's response allele(s) to a medical professional. In some cases, a research professional can refer a subject to a medical professional.

[00133] Any appropriate method can be used to communicate information to another person (*e.g.*, a professional). For example, information can be given directly or indirectly to a professional. For example, a laboratory technician can input a patient's polymorphic variant alleles as described herein into a computer-based record. In some cases, information is communicated by making a physical alteration to medical or research records. For example, a medical professional can make a permanent notation or flag a medical record for communicating the response allele determination to other medical professionals reviewing the record. In addition, any type of communication can be used to communicate allelic, genotypic, and/or treatment information. For example, mail, e-mail, telephone, and face-to-face interactions can be used. The information also can be communicated to a professional by making that information electronically available to the professional. For example, the information can be communicated to a professional by placing the information on a computer database such that the professional can access the information. In addition, the information can be communicated to a hospital, clinic, or research facility serving as an agent for the professional.

V. Articles of Manufacture

[00134] Also provided herein are articles of manufacture comprising a probe that hybridizes with a region of human chromosome as described herein and can be used to detect a polymorphism described herein. For example, any of the probes for detecting polymorphisms described herein can be combined with packaging material to generate articles of manufacture or kits. The kit can include one or more other elements including: instructions for use; and other reagents such as a label or an agent useful for attaching a label to the probe. Instructions for use can include instructions for diagnostic applications of the probe for predicting response to a treatment for SSDs in a method described herein. Other instructions can include instructions for attaching a label to the probe, instructions for

performing in situ analysis with the probe, and/or instructions for obtaining a sample to be analyzed from a subject. In some cases, the kit can include a labeled probe that hybridizes to a region of human chromosome as described herein.

[00135] The kit can also include one or more additional reference or control probes that hybridize to the same chromosome or another chromosome or portion thereof that can have an abnormality associated with a particular response. A kit that includes additional probes can further include labels, *e.g.*, one or more of the same or different labels for the probes. In other embodiments, the additional probe or probes provided with the kit can be a labeled probe or probes. When the kit further includes one or more additional probe or probes, the kit can further provide instructions for the use of the additional probe or probes. Kits for use in self-testing can also be provided. Such test kits can include devices and instructions that a subject can use to obtain a biological sample (*e.g.*, buccal cells, blood) without the aid of a health care provider. For example, buccal cells can be obtained using a buccal swab or brush, or using mouthwash.

[00136] Kits as provided herein can also include a mailer (*e.g.*, a postage paid envelope or mailing pack) that can be used to return the sample for analysis, *e.g.*, to a laboratory. The kit can include one or more containers for the sample, or the sample can be in a standard blood collection vial. The kit can also include one or more of an informed consent form, a test requisition form, and instructions on how to use the kit in a method described herein. Methods for using such kits are also included herein. One or more of the forms (*e.g.*, the test requisition form) and the container holding the sample can be coded, for example, with a bar code for identifying the subject who provided the sample.

VI. Databases and Reports

[00137] Also provided herein are databases that include a list of polymorphisms as described herein, and wherein the list is largely or entirely limited to polymorphisms identified as useful for predicting a subject's response to a treatment for an SSD (*e.g.*, SZ) as described herein. The list is stored, *e.g.*, on a flat file or computer-readable medium. The databases can further include information regarding one or more subjects, *e.g.*, whether a subject is affected or unaffected, clinical information such as endophenotype, age of onset of symptoms, any treatments administered and outcomes (*e.g.*, data relevant to pharmacogenomics, diagnostics or theranostics), and other details, *e.g.*, about the disorder in

the subject, or environmental or other genetic factors. The databases can be used to detect correlations between a particular allele or genotype and the information regarding the subject.

[00138] The methods described herein can also include the generation of reports, *e.g.*, for use by a patient, care giver, payor, or researcher, that include information regarding a subject's response allele(s), and optionally further information such as treatments administered, treatment history, medical history, predicted response, and actual response. The reports can be recorded in a tangible medium, *e.g.*, a computer-readable disk, a solid state memory device, or an optical storage device.

VII. Engineered Cells

[00139] Also provided herein are engineered cells that harbor one or more polymorphisms described herein, *e.g.*, one or more response alleles. Such cells are useful for studying the effect of a polymorphism on physiological function, and for identifying and/or evaluating potential therapeutic agents such as anti-psychotics for the treatment of an SSD (*e.g.*, SZ).

[00140] As one example, included herein are cells in which one or more of the various alleles of the genes described herein has been re-created that is associated with a response to a specific treatment. Methods are known in the art for generating cells, *e.g.*, by homologous recombination between the endogenous gene and an exogenous DNA molecule introduced into a cell, *e.g.*, a cell of an animal. In some cases, the cells can be used to generate transgenic animals using methods known in the art.

[00141] The cells are preferably mammalian cells (*e.g.*, neuronal type cells) in which an endogenous gene has been altered to include a polymorphism as described herein. Techniques such as targeted homologous recombinations, can be used to insert the heterologous DNA as described in, *e.g.*, U.S. Pat. No. 5,272,071; WO 91/06667.

VIII. Examples

[00142] The following examples are included to demonstrate preferred embodiments of the invention. It should be appreciated by those of skill in the art that the techniques disclosed in the examples which follow represent techniques discovered by the inventor to function well in the practice of the invention, and thus can be considered to

constitute preferred modes for its practice. However, those of skill in the art should, in light of the present disclosure, appreciate that many changes can be made in the specific embodiments which are disclosed and still obtain a like or similar result without departing from the spirit and scope of the invention.

5 **Example 1 – Markers associated with antipsychotic response**

[00143] The Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE), a large federally funded clinical trial designed to assess the efficacy of antipsychotics in a real world setting, is a valuable resource for determining the role of genes in drug response (Lieberman *et al.*, 2005; Stroup *et al.*, 2003).

10 [00144] The design of the CATIE study has been described in detail by others (Lieberman *et al.*, 2005; Stroup *et al.*, 2003). Briefly, 1460 subjects were randomly assigned one of several antipsychotics and those who did not respond or chose to quit their current medication were re-randomized to another drug.

15 [00145] As part of the CATIE trial, SNP genotyping was performed for roughly half of the trial participants (Sullivan *et al.*, 2008). Treatment response and baseline phenotype data for the CATIE trial were made available to the inventors through the NIMH Center for Collaborative Genetic Studies on Mental Disorders (CCGMSD). Prior analysis of a sample comprising all 417 patients with schizophrenia and 419 unaffected controls self-reported as having exclusively European ancestry confirmed that this patient population
20 contained no population stratification (Sullivan *et al.*, 2008).

[00146] As described in detail below, the inventors used the genotyping results from CCGMSD combined with disease status, PANSS scores, and clinical drug response data, to design a custom genotyping platform that evaluated novel SNPs for possible utility in predicting responses to antipsychotic medications (Liu *et al.*, 2012).

25 [00147] For the CATIE study, individual cases were diagnosed as having SZ based on DSM-III/IV criteria. Treatment response for all patients was assessed using the Positive and Negative Syndrome Scale (PANSS) (Kay *et al.*, 1987; Kay *et al.*, 1989; Leucht *et al.*, 2005). PANSS rating was performed at baseline (after a minimum 7 day drug free period) and at various time points throughout the study. To avoid possible bias in post hoc
30 selection of a treatment response variable, the inventors used the mixed model repeated

measures (MMRM) approach developed by van den Oord and coworkers (van den Oord *et al.*, 2009). Briefly, this model assumes 30-day delay for treatment effects, which was adjusted by baseline PANSS; it also models random effect by introducing random intercept allowing the intercepts to be different across subjects (Liu *et al.*, 2012).

5 **[00148]** **Selection of genes for novel analysis.** An initial list of candidate loci was generated based on genetic association analyses using genotypes and phenotypes provided by the CCGSMD. Phenotypes for the CATIE study included baseline psychopathology and drug response variables described in detail by others (Lieberman *et al.*, 2005; Stroup *et al.*, 2003; Sullivan *et al.*, 2008). Case control status and genotypes for the
10 GAIN schizophrenia (version phs000021.v2.p1) and bipolar disorder (version phs000017.v3.p1) sample sets were obtained from the Database of Genotypes and Phenotypes (dbGaP), Bethesda (MD): National Center for Biotechnology Information, National Library of Medicine (Manolio *et al.*, 2007).

[00149] Initial screens using the CATIE sample involved genetic association of
15 quantitative traits by linear regression using PLINK (version 1.04) (Purcell *et al.*, 2007). The pharmacogenomic (PGx) phenotypes used for the screen were change in PANSS (percent relative to baseline) at last observation carried forward (Hamer *et al.*, 2009) and time to “all cause” discontinuation, the primary endpoint of the CATIE Trial (Stroup *et al.*, 2003), for each of the five antipsychotics included in the trial. Genes having one or more SNPs within
20 the transcribed region with P values $\leq 10^{-2}$ or associated intergenic SNPs with P values $\leq 10^{-3}$ were included in the initial PGx list. Similarly, screening was performed using association with baseline PANSS values. Genes having SNPs within the transcribed region associating with PANSS Total Score, or PANSS Positive, Negative or General subscale scores ($P \leq 10^{-2}$) or with any of the 30 individual PANSS items ($P \leq 10^{-3}$) were included.

25 **[00150]** Additional candidate loci were selected by case/control comparisons employing the GAIN consortium schizophrenia and bipolar disorder samples using an additive genetic model in PLINK. Genes with one or more SNPs within the transcribed region with P values $\leq 10^{-3}$ were included on the initial list.

[00151] To further focus the analysis, the final candidate gene list included
30 only those loci with two or more SNPs meeting the above criteria. A total of about 2,700

genes passed this triage. Of these, approximately 700 contained blocks of linkage disequilibrium (in Caucasians) poorly covered by the original CCGSMD genotypes.

[00152] Selection of novel haplotype-tagging SNPs for the custom chip. To maximize coverage of the transcribed regions of the selected genes, the inventors identified
5 blocks of linkage disequilibrium (LD) that were poorly represented by the genotypes provided by the CATIE consortium. Databases were constructed for SNPs mapping in the transcribed regions and within 5 kb in either direction using both CCGSMD-provided genotypes and genotypes downloaded from the international HapMap Project (on the world wide web at hapmap.ncbi.nlm.nih.gov/).

[00153] The Haploview program (Barrett *et al.*, 2005; Barrett *et al.*, 2009) (version 4.1) was used separately on each data set to define haplotype blocks and tagging SNPs (using an r^2 threshold of 0.8 to define tagging SNPs, and considering only haplotypes of frequency ≥ 0.01) and a database was generated that compared the resulting LD blocks for
10 both samples in a contiguous manner based on the position of each SNP in the genome. Tagging SNPs from the HapMap Project, having minor allele frequencies of ≥ 0.01 and
15 falling between the LD blocks in the CATIE sample, were selected for further analysis.

[00154] In addition, 2,060 SNPs with possible functional significance were included. Data on the functional class of SNPs (synonymous, non-synonymous, 3' or 5' UTRs) were downloaded from the NCBI database. The list of SNPs potentially affecting
20 miRNA binding sites was obtained from PolymiRTS Database 2.0 (Bao *et al.*, 2007; Ziebarth *et al.*, 2012). SNPs with non-intronic functional annotations and with a minor allele frequency ≥ 0.01 , based on NCBI resources, were selected. The list of putative functional SNPs was compared with the list of SNPs used to tag LD blocks, and redundancies were removed.

[00155] So as to ensure that newly analyzed SNPs would provide the richest possible source of genetic information, as a final triage the inventors excluded most SNPs that could be imputed with high probability using the genotype data provided by the CATIE consortium. Briefly, the approximately 450,000 genotypes already available were used to impute SNP genotypes on a genome-wide basis with the BEAGLE program (version 3.0.4;
25 Browning *et al.*, 2009) using the HapMap Caucasian (CEU) trios as reference. This produced
30 an output of imputed genotypes along with an assigned probability for each imputed

genotype. The inventors next created a database that contained only SNPs with a mean imputed probability ≥ 0.8 across all of the CATIE samples and used this as an exclusion list for SNP selection.

[00156] Design of Infinium HD iSelect custom BeadChip. The above process identified approximately 10,000 SNPs. In addition, for quality control (QC) and confirmatory purposes, the inventors included 281 SNPs previously genotyped by the CATIE group and approximately 500 SNPs previously evaluated by the inventors in non-CATIE schizophrenia or bipolar patients. Finally, to test the feasibility of using Illumina's iSelect BeadChip platform to detect for copy number variant (CNV) regions, the inventors included 200 SNPs that they had identified as CNV in the GAIN sample using the Affymetrix Genome-Wide Human SNP Array 6.0 platform.

[00157] The inventors designed a 10,000 bead, iSelect BeadChip obtained from Illumina Inc. (San Diego, CA). The assay design requirements (approximately 30% of SNPs require 2 beads rather than 1) required a further reduction in the number of SNPs. To accommodate this, approximately 3,500 SNPs were eliminated due to the fact that they were included solely to capture LD blocks in large genes that displayed genetic association with only two of the many analyzed phenotypes. Of the ~8,500 SNPs remaining, about 9% could not be accommodated by the iSelect platform as determined by Illumina's bioinformatics analysis.

[00158] In total, 7,584 SNPs located in or near 1,711 genes were included on the BeadChip. Of this total, 7,303 SNPs have not been previously analyzed for the CATIE sample. The majority of these (4,719 in or near 638 genes) covered gaps between LD blocks in candidate loci. The remaining 2,584 SNPs (in 1,445 genes) have putative functional significance or prior evidence in other sample sets suggesting a role in schizophrenia or bipolar disorder.

[00159] FIG. 1 summarizes the functional classification for the SNPs included on the custom iSelect BeadChip. Most of the SNPs are intronic (68.9%) and were included to cover LD blocks not well represented in the CATIE-provided genotypes. Additionally, the BeadChip had relatively high representations of SNPs categorized as intergenic (12.2%), 3' UTR (13.1%), and non-synonymous coding (4.0%). The smallest functional categories were 5' UTR (1.4%) and synonymous coding (0.4%) variants.

[00160] Methods for identification of novel haplotype-tagging SNPs prediction response to antipsychotic medications. The design of the CATIE study, including details of consent for genetic analyses, has been described in detail by others (Lieberman *et al.*, 2005; Stroup *et al.*, 2003; Sullivan *et al.*, 2008). Only retrospective genetic analyses, judged to be exempt from human studies requirements by an IRB, were conducted in the current study. Consented DNA samples were obtained from the Rutgers University Cell and DNA Repository in collaboration with CCGSMD. The inventors genotyped a total of 407 DNA samples from Caucasian patients who participated in the CATIE study, distributed as follows in Phase I of the trial: olanzapine, 93; perphenazine, 76; quetiapine, 94; risperidone, 97; ziprasidone, 47. All of these patients self-reported as having exclusively European ancestry. This same patient population was described in detail in a previous study that confirmed that there is no hidden population stratification in the sample (Sullivan *et al.*, 2008). The inventors genotyped an additional 429 samples (215 schizophrenia and 214 bipolar patients) from the GAIN consortium for QC purposes to allow comparisons to the previous genotypes obtained from dbGaP for these samples using the Affymetrix Genome-Wide Human SNP Array 6.0 (on the world wide web at ncbi.nlm.nih.gov/sites/entrez?db=gap).

[00161] Genotyping was performed on a fee for service basis according to Illumina's standard operating procedures. Raw intensity files were processed using Illumina® BeadStudio version 1.7.4 software. At the suggested general call threshold of 0.4, a total of 267 SNPs failed initial QC and were not analyzed further. Only two of these had been previously genotyped in the CATIE sample. For the 7,317 SNPs that passed this initial QC, the genotyping success rate across all samples was 98.9% (median 99.4%). Eighteen of these SNPs had success rates <80% and were not used for subsequent genetic analyses. On an individual sample basis, median genotyping success rates for the remaining SNPs across all SNPs averaged 96.1% (median 96.2%).

[00162] To allow comparison to previously published PGx findings for CATIE and to avoid possible bias in post-hoc selection of a treatment response variable, the inventors used the mixed model repeated measures (MMRM) approach developed by Van den Oord and coworkers (van den Oord *et al.*, 2009; McClay *et al.*, 2011). Briefly, this method models random effects by introducing random slopes for treatment effects, allowing treatment effects to be different across subjects. The MMRM approach serves to increase the statistical power

to detect genetic associations by increasing the precision in measuring change in PANSS Total Score (PANSS-T) by accounting for variance due to baseline PANSS-T, and treatment, as well as smoothing out the random fluctuations in PANSS-T between visits due to various uncontrolled variables.

5 **[00163]** Change in PANSS-T was modeled for Phases 1, 1b, and 2 of the CATIE Study using a model that assumed a 30 day lag period with a constant drug effect after that point (van den Oord *et al.*, 2009). Sample sizes for each of the drugs were as follows: olanzapine, 134; perphenazine, 75; quetiapine, 124; risperidone, 134; ziprasidone, 74. With a type 1 error rate of 0.05, a sample size of 124 gives 80% power for a SNP that
10 explains 6% of the variance in the regression model, and a sample size of 71 gives 80% power for a SNP that explains 10% of the variance in the regression model. Though genotyping results were obtained for 7,303 SNPs not previously evaluated for CATIE, genetic association analysis was limited to 6,789 of these SNPs passing QC and having minor allele frequencies $\geq 3\%$ in the combined sample of 836 CATIE and GAIN Caucasian patients.
15 For these, the inventors tested the null hypothesis that there was no difference in mean PANSS-T change for patients carrying the minor allele of the SNP for the particular antipsychotic drug (additive model). The change in PANSS-T score was used as a continuous dependent variable using the SVS version 7.3.1 software package (Golden Helix Inc. Bozeman, MT). Quantile-Quantile (QQ) plots were prepared using the R statistical
20 package version 2.14.1. For comparison purposes, original CATIE-provided SNP genotypes in specific genes were evaluated using the same genetic analysis. Haplotype association integrating newly generated and original genotypes for specific regions was carried out in SVS using haplotype blocks predefined by Haploview software.

[00164] FIG. 2 shows the QQ plots for each of the five drugs for the 6,789
25 SNPs not previously evaluated in CATIE (MAF $\geq 3\%$ within the individual drug arm). These results indicate that the custom BeadChip design resulted in a modest enrichment for SNPs influencing response to four of the five antipsychotics, with quetiapine being the sole exception.

[00165] The newly generated genotypes were integrated with those provided by
30 the CATIE consortium followed by association analysis with the identical patient samples. This analysis confirmed that most of the SNPs tag novel haplotypes or genetically isolated regions that could not have been detected or imputed using the original CATIE genotypes.

For example, twelve of the 20 most significant SNPs define novel haplotypes, and 11 of these 12 are sufficient to tag the particular haplotype.

Example 2 – Novel haplotype-tagging SNPs impacting response for olanzapine

[00166] Table 1A provides numerous examples of SNP alleles that predict good response to olanzapine, and table 1B provides numerous examples of SNP alleles that predict poor response to olanzapine. Tables 1A and 1B report the SNPs, SNP-alleles, P values, and Beta weights (in PANSS-Total units) from the linear regression for SNPs that affect response to olanzapine. A negative beta weight indicates that the allele is associated with a decrease in PANSS-T score, corresponding to greater improvement (or lowering) of symptom burden. A positive beta weight indicates that the allele is associated with an increase in PANSS-T score, corresponding to a worsening (or increase) of symptom burden. For each of the SNPs listed the reference SNP (rs) number is provided, which provides the known sequence context for the given SNP (see, *e.g.*, National Center for Biotechnology Information (NCBI) SNP database available on the world wide web at ncbi.nlm.nih.gov/snp).

TABLE 1A: Alleles Influencing Good Response to Olanzapine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
CSMD1	17070785	A	-9.11	1.66E-04
PTPRN2	221253	C	-13.90	3.33E-04
KIAA0182	12149202	A	-5.74	5.40E-04
FREMI	16932300	C	-7.73	5.83E-04
CNTNAP2	7792198	A	-5.80	5.87E-04
PCDH15	10825137	A	-4.89	9.66E-04
PDGFD ; DDI1	2279789	C	-4.42	1.51E-03
ROBO2	4343667	C	-4.96	1.64E-03
CNTN4	4685501	T	-4.63	1.89E-03
NAB1	2293765	A	-4.60	1.99E-03
CNTN4	1554561	T	-4.50	1.99E-03
GPC6	9301876	A	-4.68	2.44E-03
SCN3A	10048748	C	-5.44	2.89E-03
RBFOX1	7194775	C	-4.37	3.95E-03
CA10	741682	A	-5.58	4.08E-03
CSMD1	2724972	G	-4.69	4.38E-03
SLC16A9	16913940	A	-6.05	4.80E-03
CSMD1	7815861	C	-5.06	5.09E-03
PKNOX2	1044314	G	-4.14	5.48E-03
PSD3	7016207	C	-6.20	5.65E-03

TABLE 1A: Alleles Influencing Good Response to Olanzapine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
CLIC5	35822882	G	-14.90	5.87E-03
NELL1	4244549	C	-4.96	5.96E-03
KITLG	995029	C	-7.22	6.13E-03
FBN3	2287937	C	-5.34	6.29E-03
LIMCH1	7659262	A	-5.30	6.97E-03
DENND5B	11615961	A	-3.73	7.70E-03
HPS4	16982178	A	-5.47	8.26E-03
ERBB4	7558615	C	-7.96	8.29E-03
WNT5B	2240513	C	-3.80	8.68E-03
ANO2	7959306	A	-4.98	8.81E-03
ADTRP	6929400	C	-3.98	8.91E-03
PPARG	9809905	G	-3.74	9.59E-03
LOC100129345	12435621	G	-6.10	9.63E-03
JPH2	1055689	C	-4.34	9.80E-03
CHN2	10486608	C	-5.68	1.01E-02
CSMD1	2724973	A	-5.11	1.01E-02
CDH23	10823827	G	-4.02	1.03E-02
ANK3	4611159	A	-6.48	1.06E-02
NOS1AP	1504424	C	-9.99	1.07E-02
GALNTL4	923259	A	-4.61	1.14E-02
NAB1	4853724	C	-4.61	1.16E-02
VDAC1	6880980	G	-7.14	1.17E-02
ELOVL7	13358053	C	-5.16	1.24E-02
CNTNAP2	12670106	A	-3.60	1.24E-02
DLG2	2512676	G	-4.08	1.25E-02
CACNA2D3	1568982	C	-5.10	1.27E-02
LYN	7840325	A	-3.83	1.27E-02
CDH20	1539996	C	-4.47	1.28E-02
CGNL1	12913924	A	-4.44	1.29E-02
CNTNAP2	9640235	A	-3.70	1.30E-02
CPNE4	1381078	C	-5.23	1.33E-02
NTNG2	1810887	A	-3.65	1.33E-02
SCD5	10516679	C	-4.54	1.40E-02
ZNF804A	2369593	A	-6.03	1.41E-02
OPCML	12417211	C	-4.66	1.45E-02
GRIN3A	2485528	C	-4.11	1.48E-02
WDR48	1053516	A	-3.88	1.53E-02
HPCAL1	887981	C	-4.41	1.56E-02
IFT74	10511795	C	-6.93	1.66E-02
IFT74	10511797	C	-6.93	1.66E-02
FMN2	7543271	A	-3.63	1.67E-02
FBN3	35999680	A	-11.00	1.70E-02
MAGI2	6952164	A	-3.96	1.78E-02
BRE ;	13031756	A	-3.42	1.81E-02

TABLE 1A: Alleles Influencing Good Response to Olanzapine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
LOC100505716				
GRIA1	514381	C	-4.02	1.84E-02
KIAA1797	7030093	C	-3.95	1.95E-02
FAM46C	866111	A	-5.43	2.02E-02
TRPM3	3010423	A	-3.88	2.06E-02
GRB10	2329486	A	-4.28	2.07E-02
SLIT1	4917756	A	-4.75	2.13E-02
CACNA2D3	4642090	C	-5.21	2.16E-02
PHACTR3	6026976	A	-6.55	2.17E-02
NCAM2	2826730	C	-4.63	2.18E-02
FKTN	34787999	A	-3.75	2.18E-02
CTBP2	11599580	C	-12.50	2.19E-02
XPR1	1061015	C	-3.61	2.22E-02
SRRM4	4767785	C	-3.51	2.30E-02
LOC100130887	10887024	A	-3.49	2.30E-02
RGS6	11624306	A	-4.26	2.31E-02
SEPT9	34587622	C	-5.29	2.37E-02
CNTNAP2	2249958	C	-4.95	2.37E-02
ANK3	12354956	A	-4.59	2.51E-02
CYP4V2	1053094	T	-3.41	2.56E-02
ERBB4	6712295	A	-3.95	2.61E-02
SAMD12	2514591	A	-4.58	2.65E-02
CSMD1	2616996	G	-3.79	2.67E-02
ZNF169	9409513	C	-3.28	2.69E-02
SGCZ	1454583	C	-4.20	2.71E-02
XPR1	1061016	C	-3.44	2.72E-02
SGCZ	1454580	C	-3.57	2.73E-02
DENND5B	708200	G	-3.11	2.81E-02
FMNL2	12612608	A	-3.44	2.82E-02
CGNL1	1908202	C	-3.79	2.83E-02
GPC6	1538195	G	-3.40	2.86E-02
CAMK2D	13113625	C	-3.68	2.87E-02
APCDD1	1045584	G	-3.41	2.88E-02
RORA	12910376	C	-3.38	2.90E-02
MACROD2	461651	A	-3.59	2.92E-02
ITPR1	11717244	C	-3.53	2.94E-02
GAS7	9904524	G	-4.96	2.95E-02
MEPE	3749575	A	-8.95	2.97E-02
PARD3B	17283257	A	-3.82	2.97E-02
RIMS1	9446639	C	-3.56	2.97E-02
BIK	5996274	A	-4.94	3.09E-02
PCP4L1	6671288	C	-4.15	3.17E-02
PI4KA ; SERPIND1	78656	C	-7.22	3.22E-02

TABLE 1A: Alleles Influencing Good Response to Olanzapine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
MTIF3	12585587	A	-4.37	3.26E-02
SLC35F3	12759054	C	-3.34	3.27E-02
FMNL2	4664113	C	-4.25	3.30E-02
DLGAP1	561434	A	-4.43	3.32E-02
FHIT	971866	A	-5.07	3.33E-02
CDH13	3743621	C	-5.54	3.35E-02
FAM173B	12652786	C	-3.39	3.35E-02
RASGEF1C	2278661	C	-3.04	3.37E-02
MAGI2	848813	C	-4.34	3.39E-02
GRM8	17865066	A	-7.97	3.40E-02
GRM8	17865434	C	-7.97	3.40E-02
CACNA1B	12352971	G	-4.21	3.40E-02
SEC16B	16852158	C	-6.45	3.47E-02
PCDH17	7319102	A	-3.47	3.49E-02
IL15	3806798	A	-4.33	3.50E-02
KCND2	10953911	G	-5.26	3.53E-02
KCND2	718805	A	-5.26	3.53E-02
MCPH1	930557	C	-3.78	3.57E-02
HTR1B	11568817	G	-3.16	3.59E-02
SLC6A5	1443547	A	-3.31	3.68E-02
ARHGAP31	751607	A	-4.30	3.69E-02
LRP1B	4591293	A	-3.04	3.74E-02
EML1	34198557	C	-4.01	3.77E-02
SGCZ	10503525	C	-3.05	3.79E-02
PTPRT	6030084	A	-2.96	3.79E-02
SPOCK1	1051854	G	-6.02	3.80E-02
KCNH1	4282878	C	-3.08	3.81E-02
FSTL5	13127909	C	-4.60	3.83E-02
NTRK2	4142909	C	-3.81	3.83E-02
NRXN1	11885824	A	-5.21	3.89E-02
KLHL29	17045819	C	-4.81	3.93E-02
KDM4C	35389625	C	-11.20	3.97E-02
ERBB4	7565257	A	-3.44	4.03E-02
GAN	1345895	A	-3.53	4.07E-02
RNF144A	7605141	C	-4.00	4.13E-02
ATP10A	2291351	A	-4.99	4.15E-02
ANK3	2893823	A	-4.47	4.15E-02
SLC16A4	12126959	A	-4.16	4.17E-02
NTSR2	7602721	C	-4.08	4.20E-02
WDR90	1057835	A	-3.10	4.24E-02
FAM170A	2162856	A	-3.06	4.25E-02
AGAP1	4663220	T	-3.07	4.27E-02
PKP4	11680160	A	-4.33	4.28E-02
JPH2	2064381	A	-3.06	4.28E-02

TABLE 1A: Alleles Influencing Good Response to Olanzapine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
MACROD2	6079429	A	-4.72	4.29E-02
ARVCF	2238794	C	-3.11	4.32E-02
KAZN	12130605	C	-3.66	4.33E-02
EXOC2	9405889	C	-3.21	4.34E-02
ANK3	10821660	G	-4.45	4.41E-02
CACNG4	7219571	A	-5.84	4.42E-02
IL1RAP	2361835	A	-3.93	4.42E-02
IL1RAP	7642607	A	-3.93	4.42E-02
IL1RAP	7642797	A	-3.93	4.42E-02
NTRK2	1490403	A	-3.10	4.51E-02
LDB2	872478	C	-3.53	4.62E-02
FGF14	2390674	A	-4.22	4.67E-02
PRDM2	6429793	A	-3.13	4.73E-02
ZNF169	9409514	C	-3.04	4.77E-02
MAGI2	12705833	G	-2.87	4.79E-02
ERG	9981408	G	-3.15	4.80E-02
SGCZ	13278000	A	-2.91	4.83E-02
EHD4	1048166	C	-3.04	4.85E-02
EHD4	1048175	C	-3.04	4.85E-02
CPNE5	12194367	T	-3.14	4.92E-02
PEBP4	13271643	C	-5.41	4.95E-02
KCND2	11765060	C	-5.30	4.95E-02
NTRK2	1490407	G	-3.00	4.96E-02
IFT74	4463511	C	-3.77	4.99E-02
DLGAP1	498419	A	-3.07	4.99E-02
ADAMTS9-AS2	17071651	C	-3.03	4.99E-02

TABLE 1B: Alleles Influencing Poor Response to Olanzapine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
PLAGL1 ; LOC100652728	2247408	C	5.63	2.07E-04
PLAGL1 ; LOC100652728	3819811	A	5.72	2.43E-04
ZNF71	11881987	A	5.24	7.21E-04
DGKD	838718	A	4.46	1.03E-03
SEMA5A	707637	A	5.81	1.54E-03
GRIN3A	4324970	C	4.89	2.15E-03
DLG2	11234192	G	7.12	2.54E-03
DLG2	555867	A	5.41	2.64E-03
PARK2	7769196	A	4.70	2.82E-03
DLG2	1943687	G	5.36	2.84E-03
SEMA5A	1457768	A	6.95	3.05E-03
IL17RD	9311641	C	7.27	3.26E-03
TPH2	1872824	C	4.41	3.43E-03
RAP1GAP2	10805	G	3.98	3.51E-03
GRIK3	12059346	C	8.94	3.70E-03
SEMA3F	1046956	A	4.65	3.90E-03
PCDH15	2384470	C	4.71	4.00E-03

TABLE 1B: Alleles Influencing Poor Response to Olanzapine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
NPAS3	12887270	A	4.39	4.21E-03
MAGI2	798338	A	4.21	4.42E-03
AK5	12565526	A	4.31	4.47E-03
FAM19A1	13094092	C	4.61	4.96E-03
PPA2	923587	C	3.86	5.78E-03
PTGER3	5682	C	3.94	5.87E-03
CNTNAP2	802022	C	4.37	5.89E-03
DLG2	7122815	A	5.32	6.00E-03
CNTNAP2	2710157	C	4.14	7.13E-03
DLGAP2	6992443	A	7.39	7.82E-03
UNC13C	10152907	A	4.17	7.95E-03
COL22A1	7819082	C	6.88	8.17E-03
SYN3	17772478	A	14.30	8.29E-03
PCLO	12666717	A	4.00	9.02E-03
PCDH15	16937849	C	5.08	9.43E-03
CNTNAP2	1608958	C	4.24	9.50E-03
CNTNAP2	10488348	C	4.34	9.70E-03
CNTNAP2	12670862	C	4.44	9.95E-03
PLD1	416158	A	5.42	1.02E-02
ANK3	10740023	C	4.34	1.12E-02
ANK3	2061486	A	4.34	1.12E-02
NALCN	8000980	C	6.10	1.16E-02
INS-IGF2 ; IGF2	3213221	C	3.82	1.27E-02
MTIF3	17085633	C	3.95	1.27E-02
TSNAX-DISC1	1411776	A	4.78	1.30E-02
DGKD	838717	A	3.57	1.32E-02
TMC8	454138	C	3.66	1.42E-02
CSMD1	595834	C	4.55	1.42E-02
KCNJ2	9914095	A	5.26	1.44E-02
DLG2	4505088	G	5.13	1.45E-02
SLC1A3	891189	A	3.70	1.50E-02
KLHL32	13203153	A	4.22	1.57E-02
WWC1	10042345	C	3.55	1.59E-02
KCNN2	4466150	C	4.33	1.61E-02
ARVCF	1990276	C	3.93	1.68E-02
KCNQ1	800336	A	4.07	1.71E-02
CNTN4	1178491	A	3.53	1.83E-02
CSMD1	4875769	A	3.68	1.85E-02
NALCN	17622020	A	4.15	1.86E-02
CSMD3	1895013	A	6.99	1.86E-02
CNTN4	2727902	G	3.43	1.88E-02
GPSM1	7853207	C	3.92	1.88E-02
SLC25A18	1044497	C	4.56	1.90E-02
CTNNA3	1941996	A	4.19	1.97E-02
ITPR1	4685786	A	4.76	1.98E-02
CDH13	16958456	A	4.39	2.02E-02
SYNPR	11920956	G	3.33	2.05E-02
IGF2R	8191754	C	5.13	2.06E-02
PRICKLE2	704378	C	3.56	2.08E-02
SLC35F3	4564211	G	5.81	2.12E-02
C9orf84	7869279	C	3.61	2.14E-02
PLCB1	6086410	C	3.80	2.14E-02
DOK6	2034022	A	3.18	2.19E-02
CDH13	11150543	A	3.84	2.20E-02
GFRA1	2694766	A	3.53	2.23E-02

TABLE 1B: Alleles Influencing Poor Response to Olanzapine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
ATXN3	2896196	C	4.67	2.30E-02
ERC2	2047566	C	3.62	2.32E-02
FAM186A	6580742	C	4.84	2.34E-02
PACRG	12526892	C	3.72	2.35E-02
KCNIP1	10050842	A	3.26	2.36E-02
CNTNAP2	10263151	C	3.55	2.36E-02
PARD3B	10209145	C	3.22	2.37E-02
IGF1R	867431	A	3.54	2.38E-02
ITGA1	1047483	A	3.59	2.39E-02
ITGA1	6895049	G	3.59	2.39E-02
ASAP1	7387355	A	4.03	2.39E-02
ARVCF	917479	G	3.43	2.42E-02
F13A1	5987	A	4.35	2.44E-02
PCDH15	12772330	A	4.54	2.53E-02
DLG2	1943691	A	3.34	2.54E-02
ALS2	7572898	C	4.17	2.58E-02
LOC100505973	1537080	A	3.73	2.64E-02
ASPHD2	34902186	A	6.30	2.81E-02
CNTNAP2	6957194	A	3.62	2.82E-02
SLC25A21	848097	C	3.49	2.83E-02
ARVCF	2240717	C	3.44	2.88E-02
MICAL2	10765924	A	3.75	2.88E-02
PRUNE2	1425286	C	5.79	2.88E-02
SAMD4A	1211170	A	3.19	2.90E-02
MBP	12456475	C	3.74	2.90E-02
NALCN	17622124	C	4.06	2.92E-02
CSMD1	6558759	C	4.48	2.92E-02
TRPC4	1570608	G	3.19	2.96E-02
RARB	4393871	C	3.36	2.99E-02
SORCS3	2496017	A	4.21	3.01E-02
LRP1B	736602	A	3.73	3.02E-02
TMC5	16972065	C	6.03	3.05E-02
RBFOX2	6000085	C	7.29	3.07E-02
LOC100505501	7837298	C	3.52	3.08E-02
CDH13	12596958	C	3.52	3.10E-02
BLZF1	2275300	G	7.78	3.12E-02
NEDD4L	474743	C	3.02	3.13E-02
CSMD1	6988561	G	3.42	3.14E-02
DAOA-AS1	12584489	A	6.56	3.15E-02
ATP2B2	34903	A	3.12	3.22E-02
DLG2	10792782	A	3.19	3.33E-02
PPP1R9A	10485996	A	4.41	3.34E-02
KCNIP1	50057	A	3.80	3.36E-02
SEMA5A	1505067	C	3.12	3.40E-02
DLG2	7103862	C	3.15	3.40E-02
KLHL29	4665614	C	3.41	3.47E-02
DLG2	553071	A	3.44	3.59E-02
CTNNA2	408144	A	3.02	3.60E-02
ERCC6	2228527	A	3.86	3.64E-02
PARK2	10945755	C	3.71	3.68E-02
ZNF638	2257136	G	5.82	3.69E-02
ANGPT1	1954727	C	3.32	3.72E-02
CERK	801720	G	3.33	3.77E-02
PTPRN2	4716835	A	4.80	3.78E-02
GPM6A ; LOC100506176	13136033	A	3.37	3.81E-02

TABLE 1B: Alleles Influencing Poor Response to Olanzapine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
QRFPR	11737010	A	3.32	3.82E-02
SDK1	659182	C	3.60	3.83E-02
ASAP1	11992957	C	3.15	3.84E-02
CNTNAP2	11984392	C	3.29	3.84E-02
GPSM1	3812550	A	3.35	3.86E-02
CSMD1	667595	C	4.33	3.86E-02
C8orf34	2591003	A	3.76	3.87E-02
CNTNAP2	10240221	A	3.17	3.89E-02
RNF144A	309304	A	3.06	3.93E-02
NAV3	770108	C	3.40	3.93E-02
PCLO	2057899	C	3.10	3.96E-02
ERBB4	10200506	A	3.80	3.97E-02
CNTNAP2	17585288	C	4.39	3.97E-02
FHIT	1350636	A	3.20	4.04E-02
SULT4A1	4823149	C	3.22	4.04E-02
PSD3	7001013	C	4.49	4.06E-02
PPP1R9A	7776891	C	5.52	4.07E-02
QRFPR	11098616	A	3.26	4.13E-02
SLC35F3	4418678	G	5.94	4.16E-02
CTNNA2	6711371	G	2.90	4.17E-02
CREB5	714500	A	3.64	4.17E-02
KIAA0182	11640338	A	2.80	4.22E-02
GPC6	1924384	A	2.90	4.22E-02
LINC00114	2836659	A	3.24	4.29E-02
CSMD1	2449210	C	2.89	4.30E-02
PDE10A	515579	A	3.03	4.39E-02
ARNT2	1020398	C	3.32	4.41E-02
ATP2B2	42445	A	3.53	4.42E-02
FMN2	10926139	C	3.60	4.47E-02
ITPR1	9831960	A	3.15	4.48E-02
NRXN3	17108086	G	3.25	4.53E-02
WBSCR17	2158735	C	2.97	4.54E-02
CTNNA2	450658	C	2.88	4.58E-02
GNG2	1890699	A	3.22	4.58E-02
PID1	3755302	A	3.70	4.66E-02
ATP2B2	3774155	A	3.48	4.71E-02
MAGI1	17432146	C	4.14	4.81E-02
FBXO4	9292832	A	6.56	4.84E-02
GOT2	11861897	A	10.70	4.88E-02
TMEM132B	16919368	A	6.87	4.90E-02
CACNA2D1	258657	C	3.30	4.91E-02
CREB5	1468447	A	3.38	4.91E-02
LRP1B	16847247	A	3.42	4.96E-02
ARNTL	10766074	C	4.48	4.97E-02
CSMD1	688579	A	3.89	4.98E-02

Example 3 – Novel haplotype-tagging SNPs impacting response for perphenazine

[00167] Table 2A provides numerous examples of SNP alleles that predict good response to perphenazine, and table 2B provides numerous examples of SNP alleles that predict poor response to perphenazine. Tables 2A and 2B report the SNPs, SNP-alleles, P

values, and Beta weights (in PANSS-Total units) from the linear regression for SNPs that affect response to perphenazine. A negative beta weight indicates that the allele is associated with a decrease in PANSS-T score, corresponding to greater improvement (or lowering) of symptom burden. A positive beta weight indicates that the allele is associated with an increase in PANSS-T score, corresponding to a worsening (or increase) of symptom burden.

TABLE 2A: Alleles Influencing Good Response to Perphenazine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
MCPH1	11774231	C	-17.25	7.72E-06
ARNTL	7126225	C	-48.45	1.68E-05
PRKCE	2278773	C	-24.74	1.69E-05
MCPH1	17570753	A	-14.24	2.25E-05
CDH13	2116971	C	-7.81	2.09E-04
SKOR2	9952628	G	-6.54	3.41E-04
SKOR2	2247784	T	-6.70	7.77E-04
CACNA2D3	2139683	A	-6.99	9.18E-04
MACROD2	8117909	A	-6.85	1.17E-03
NAALADL2	9826737	C	-12.68	1.21E-03
NALCN	8000980	C	-9.07	1.39E-03
ETV1	10236596	G	-26.20	1.51E-03
KATNAL2	9304340	A	-6.42	1.77E-03
CDH13	11647270	A	-6.77	1.95E-03
AMPH	35024632	G	-18.32	2.02E-03
SAMD12	12550842	A	-6.03	2.32E-03
FERD3L	10254337	C	-7.16	2.78E-03
CLSTN2	17397077	A	-11.68	3.03E-03
PLCXD2	4491869	G	-8.82	3.28E-03
SDK1	7812170	A	-5.18	3.36E-03
MACROD2	4813204	G	-5.86	3.40E-03
CACNA2D1	2299158	C	-7.30	3.58E-03
DYNC1I1	1488519	C	-9.02	3.73E-03
ITGAD	4889654	A	-6.12	3.79E-03
STK31	6963309	A	-6.41	3.82E-03
SAMD12	13256262	G	-5.69	3.96E-03
NPAS3	10145961	A	-5.50	4.10E-03
PLCXD2	4325897	A	-7.83	4.13E-03
CCDC165	566890	G	-8.56	4.38E-03
CACNB2	2148184	A	-8.11	4.54E-03
HSPA12A	17095095	A	-10.43	4.72E-03
CLSTN2	9852679	C	-10.67	5.00E-03
CDH10	12653077	G	-7.40	5.03E-03
FER1L6 ; FER1L6-AS1	7840702	A	-9.95	5.14E-03
DNAH17	4969188	C	-6.96	5.15E-03
FSTL5	2314105	G	-14.83	5.87E-03
RIBC2	738227	A	-5.30	6.36E-03
OPCML	4937724	A	-5.20	6.37E-03
ERBB4	6435681	A	-6.98	6.42E-03
OPCML	7110211	G	-5.28	6.49E-03
TRIO	6554852	A	-5.92	6.65E-03
EPHB2	2165331	A	-5.81	6.66E-03
CDH13	8059696	C	-6.18	6.77E-03
NPY	1859291	A	-11.20	6.85E-03
NPY	3857723	A	-11.20	6.85E-03

TABLE 2A: Alleles Influencing Good Response to Perphenazine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
KCNK10	10483994	G	-11.75	7.02E-03
PSMD14	9713	A	-5.59	7.13E-03
OPCML	12796925	A	-8.66	7.30E-03
KCNA10	34970857	C	-8.98	7.52E-03
PLCB1	3761168	G	-11.05	7.69E-03
CCDC93	11556267	A	-7.87	7.75E-03
SCLT1	3113489	A	-6.25	8.86E-03
CSMD3	7018166	G	-6.22	9.00E-03
GFRA2	11990425	C	-4.91	9.37E-03
FHIT	2736780	C	-5.66	9.39E-03
PTDSS1	2319815	A	-5.10	9.51E-03
RBFOX3	8074560	A	-6.31	9.58E-03
ATXN1	3116712	A	-13.38	1.01E-02
CA10	1503055	G	-4.68	1.02E-02
LYPD6	1196666	C	-7.49	1.05E-02
NAB1	1023568	T	-4.61	1.05E-02
NPAS3	8007455	A	-5.13	1.07E-02
GRB10	2329486	A	-6.15	1.13E-02
NEBL	313788	A	-7.16	1.14E-02
NEDD4L	292450	C	-6.26	1.18E-02
BAALC ; LOC100499183	10099640	C	-11.68	1.19E-02
HTR1B	2226183	A	-8.13	1.20E-02
NKAIN3	4379439	C	-7.05	1.20E-02
SLC18A2	363343	A	-6.50	1.20E-02
SLC18A2	363420	C	-6.50	1.20E-02
RIBC2	1022478	C	-5.40	1.25E-02
FSTL5	6829185	G	-6.00	1.27E-02
BLZF1	2275299	C	-4.54	1.36E-02
SYNRG	7207076	G	-4.62	1.37E-02
MMP27	12099177	A	-7.40	1.41E-02
DLGAP2	7830545	C	-6.27	1.42E-02
MCPH1 ; ANGPT2	2242005	A	-10.70	1.46E-02
ACCN1	28936	A	-4.88	1.50E-02
INADL	1286823	A	-8.68	1.53E-02
CNTN4	1153512	A	-5.05	1.53E-02
DYNC1I1	17638044	C	-7.44	1.55E-02
SHROOM3	4380545	A	-5.77	1.63E-02
GNG2	1253669	G	-4.63	1.63E-02
NBEA	7325781	A	-4.95	1.69E-02
PACRG	1001491	C	-5.13	1.70E-02
LINC00299	11904044	C	-9.49	1.72E-02
TSNAX-DISC1	1411776	A	-6.54	1.76E-02
PPARGC1A	2970870	C	-5.07	1.85E-02
RASGRP1	4567661	A	-4.50	1.88E-02
CAST	10515244	C	-7.45	1.94E-02
CAST	11750400	A	-7.45	1.94E-02
WWOX	16948667	A	-7.20	1.94E-02
PCSK6	735163	C	-7.93	1.96E-02
SYNE1	17082273	G	-7.89	2.02E-02
IKZF2	7607184	C	-4.92	2.03E-02
SDK1	17133426	C	-5.37	2.05E-02
FAM186A	12809349	C	-15.98	2.06E-02
NRXN3	2199796	A	-7.51	2.08E-02
ATF6	1135983	C	-8.60	2.09E-02
LOC100505806	1614229	A	-6.21	2.12E-02

TABLE 2A: Alleles Influencing Good Response to Perphenazine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
LOC100505806	1651285	A	-6.21	2.12E-02
CSMD1	3802296	C	-6.00	2.20E-02
CDH13	3844414	A	-7.93	2.29E-02
CCDC165	651219	A	-5.12	2.30E-02
RORA	341400	A	-8.45	2.33E-02
CLSTN2	16850488	C	-5.52	2.36E-02
ATRN	1064833	C	-5.12	2.40E-02
PTPRN2	896773	A	-11.19	2.51E-02
ST8SIA1	2160631	C	-4.96	2.54E-02
KCNB2	17762432	A	-4.29	2.56E-02
SKOR2	2137287	A	-4.91	2.57E-02
CERS5	2242507	A	-4.58	2.57E-02
RBFOX3	1077693	C	-5.53	2.70E-02
AKAP9	6960867	A	-4.40	2.71E-02
GNG2	1253671	G	-4.31	2.79E-02
GABRR2	3798256	T	-3.73	2.82E-02
FBLN7	3811643	C	-5.64	2.92E-02
FBLN7	4849050	C	-5.64	2.92E-02
PDE1C	1115731	A	-4.83	2.95E-02
CSMD1	12549644	A	-6.45	2.96E-02
EPHB2	4655120	A	-5.20	2.99E-02
DLG2	1226063	A	-5.35	3.00E-02
RYR2	2065985	T	-4.65	3.04E-02
DGKI	2113578	C	-4.49	3.05E-02
CD247	1052231	A	-6.34	3.07E-02
GRB10	11772525	A	-5.26	3.12E-02
SVEP1	7865430	C	-7.14	3.18E-02
COMMD1	7583942	C	-4.97	3.24E-02
MGAT2	1011373	C	-8.70	3.26E-02
NRCAM	2284290	C	-4.61	3.26E-02
MAGI2	319863	C	-4.63	3.30E-02
NKAIN3	2353366	G	-5.75	3.33E-02
NCS1	11552451	C	-6.39	3.34E-02
ROBO1	17313732	A	-4.38	3.37E-02
PREX1	6095246	A	-4.55	3.38E-02
ARHGAP21	7092130	C	-7.47	3.40E-02
LOC100506689	611419	A	-5.59	3.43E-02
ZNF536	12972537	G	-4.55	3.45E-02
ZNF536	4805590	C	-4.55	3.45E-02
FHIT	9831415	C	-6.80	3.47E-02
NALCN	2390621	C	-4.18	3.54E-02
RYR2	12133002	G	-4.46	3.55E-02
FERD3L	10268160	C	-6.16	3.58E-02
GPC6	8002366	C	-7.79	3.60E-02
CCDC50	6774730	G	-8.06	3.62E-02
ITPR1	4685810	C	-4.72	3.63E-02
ATRN	2250106	A	-4.24	3.67E-02
ATRN	2250338	C	-4.24	3.67E-02
MTUS2	9805210	A	-6.73	3.69E-02
ELOVL7	2219333	A	-11.36	3.70E-02
CHMP6	1128687	C	-4.13	3.70E-02
GABRR2	10944441	A	-6.04	3.71E-02
DCAF11	3825583	A	-9.18	3.72E-02
C19orf45	475923	A	-4.18	3.80E-02
CDH13	17701213	C	-6.29	3.82E-02

TABLE 2A: Alleles Influencing Good Response to Perphenazine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
LEPREL1	9290920	A	-4.86	3.92E-02
NBEA	12871646	A	-8.23	3.98E-02
MACROD2	6080110	G	-3.92	3.99E-02
PTPN5	7946254	C	-14.23	4.00E-02
CELF2	7091228	A	-4.40	4.06E-02
MUC7	6826961	C	-5.13	4.10E-02
TRPC4	9603241	A	-5.08	4.13E-02
SGCZ	6530806	G	-5.20	4.20E-02
LINC00308	2827687	C	-6.71	4.23E-02
CSMD1	2623630	A	-4.35	4.27E-02
SGCZ	1480696	C	-4.91	4.29E-02
SLC17A8	11568537	C	-4.11	4.30E-02
ACYP2	843719	A	-4.02	4.30E-02
CNTNAP2	17171006	C	-17.03	4.34E-02
DLC1	6981968	A	-4.32	4.49E-02
PTGER3	5675	C	-5.23	4.50E-02
MYO5B	12457962	A	-8.39	4.54E-02
PTPRG	3817458	C	-5.54	4.56E-02
MAGI2	38108	C	-4.37	4.61E-02
DNAH9	12453566	G	-5.40	4.62E-02
DNAH9	2058039	C	-5.40	4.62E-02
ATRNL1	4751924	C	-3.70	4.68E-02
RYR3	2676023	C	-5.04	4.70E-02
ROBO2	1470571	C	-4.26	4.73E-02
NRXN3	2219848	A	-4.11	4.80E-02
FHIT	17396765	C	-6.22	4.81E-02
CHMP6	1128705	C	-3.91	4.81E-02
SGCZ	10095307	A	-5.03	4.84E-02
TBC1D2B	4886989	C	-4.78	4.84E-02
WWOX	2062894	C	-3.63	4.85E-02
ELFN2	1076934	A	-3.35	4.87E-02
PCSK6	900414	A	-4.77	4.88E-02
PLCG2	4243215	A	-4.99	4.93E-02
OPCML	7944972	A	-3.86	4.94E-02
PARK2	6455765	A	-4.75	4.98E-02

TABLE 2B: Alleles Influencing Poor Response to Perphenazine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
MAML3	11100483	A	7.28	4.83E-04
GABBR2	2808534	A	7.07	8.05E-04
CSMD1	7813376	C	6.19	1.24E-03
PIP5K1B	953390	C	6.34	2.02E-03
CSMD1	6558885	A	8.38	2.28E-03
GABBR2	1177531	A	7.09	2.71E-03
SPINK1	4705203	A	7.81	2.75E-03
UNC13C	574138	A	6.27	3.03E-03
ROBO1	444598	C	5.84	3.36E-03
NBAS	10929356	G	5.46	4.91E-03
COL4A3 ; LOC654841	12464886	C	6.69	4.95E-03
CADPS2	718764	A	6.75	5.16E-03
NTSR2	7602721	C	7.29	5.82E-03
ROBO1	6762005	T	5.47	6.09E-03
CLSTN2	2042705	C	6.23	6.24E-03

TABLE 2B: Alleles Influencing Poor Response to Perphenazine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
NKAIN3	10448028	C	5.85	6.87E-03
NRXN3	2216901	C	6.60	6.93E-03
KLHL32	850587	T	5.44	7.58E-03
RNF144B	6927583	G	8.72	8.25E-03
PLCB1	6086680	A	5.81	8.35E-03
CA10	17607202	C	5.47	8.38E-03
PARK2	9458561	C	5.53	9.33E-03
NBAS	12692258	A	6.21	9.35E-03
CDH13	6565109	A	5.12	9.39E-03
EGF14	3007763	A	5.71	9.50E-03
TSPAN13	3807509	C	4.75	9.53E-03
MTSS1	6999708	C	5.72	9.71E-03
PHIP	9350797	A	5.51	1.01E-02
KCNQ1 ; KCNQ1OT1	231358	C	4.98	1.10E-02
CTNND2	6875838	A	5.02	1.14E-02
FLJ35024	875587	A	6.14	1.14E-02
GNAS	6064716	C	8.71	1.21E-02
MAGI1	17073748	A	7.64	1.29E-02
RAB6B	7644124	C	5.16	1.33E-02
NPAS3	10135876	C	5.11	1.38E-02
ZFPM2	2920048	C	7.44	1.48E-02
DLG2	2512676	G	5.77	1.49E-02
KCNQ3	10097662	A	6.38	1.55E-02
PCDH10	11731618	G	5.70	1.56E-02
PCDH10	13130047	A	5.70	1.56E-02
KCNB2	17828687	A	4.68	1.59E-02
PCLO	2877	C	5.03	1.61E-02
MYT1L	17338616	A	4.98	1.62E-02
NECAB1	1055146	C	5.00	1.63E-02
DOK5	2840	C	6.51	1.63E-02
CA10	1909923	T	4.41	1.68E-02
SMARCA2	10081778	C	5.32	1.71E-02
NBEA	10507424	A	5.28	1.72E-02
SLC7A14	4955729	C	4.45	1.73E-02
AGL	2307129	A	6.78	1.73E-02
NPAS3	1952595	A	4.95	1.80E-02
GABBR2	12552470	A	6.50	1.84E-02
KCNMA1	11002064	C	4.58	1.89E-02
COL4A3 ; LOC654841	4603754	C	5.01	1.91E-02
KCNQ1	2237869	A	5.73	1.92E-02
MACROD2	12480304	G	6.03	1.97E-02
FERMT1	2295434	A	4.89	1.98E-02
FLJ35024	693934	A	4.79	1.99E-02
MAP1B	10062773	A	4.46	2.12E-02
CNOT2	7969013	C	5.27	2.17E-02
PDE4D	16889901	A	4.77	2.20E-02
LOC100129434	2216327	C	9.55	2.20E-02
CA10	7210687	C	4.35	2.24E-02
KCNB1	3331	C	11.40	2.24E-02
SGCZ	12114757	C	6.02	2.27E-02
ELMOD1	10890742	A	4.79	2.28E-02
NEDD9	6933985	C	5.45	2.28E-02
NKAIN3	7388305	C	4.89	2.31E-02
CA10	1503056	G	4.35	2.38E-02
ACCS	178506	A	4.48	2.38E-02

TABLE 2B: Alleles Influencing Poor Response to Perphenazine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
MEPE	3749575	A	7.44	2.42E-02
KCNIP4	16870818	G	4.73	2.50E-02
NRXN3	9671249	C	6.47	2.53E-02
FMN2	10926208	A	5.97	2.54E-02
DGKB	10240641	A	4.26	2.56E-02
MAGI2	12668963	A	4.68	2.61E-02
NRXN3	221516	A	8.25	2.61E-02
ATP2B2	11708983	A	5.93	2.62E-02
PACRG	6922278	C	4.15	2.83E-02
MACROD2	6043223	C	5.97	2.88E-02
KCNMA1	7907070	A	4.22	2.92E-02
EMID2	10447812	A	11.83	2.96E-02
CSMD1	2948644	T	4.04	2.99E-02
LOC100505985	9349534	T	4.60	3.02E-02
KCNQ1	11023485	A	4.50	3.10E-02
SPINK1	10035432	A	5.44	3.11E-02
SLC22A16	3778650	A	5.11	3.19E-02
EPAS1	13428739	C	7.26	3.22E-02
TSPAN9	7980107	C	4.46	3.29E-02
PARK2	2022996	A	5.01	3.31E-02
PRKG1	10998789	A	4.58	3.33E-02
TRPM3	1336380	G	4.43	3.34E-02
PIK3C2G	10770363	A	3.86	3.35E-02
TSPAN9	7308849	C	4.43	3.36E-02
VCAN	3797782	A	4.40	3.37E-02
NRG3	10509433	C	8.87	3.41E-02
ATP2B2	11712897	C	5.68	3.44E-02
RGS7	261827	C	4.13	3.50E-02
CA10	203032	C	4.12	3.51E-02
NAV2	2625323	G	5.73	3.54E-02
EXOC2	17134263	C	7.56	3.57E-02
NBEA	9530787	G	4.50	3.60E-02
GABBR2	2808532	A	6.15	3.62E-02
PTPR1	208243	A	3.99	3.63E-02
NBAS	10179251	A	5.22	3.71E-02
PON1	705382	C	4.00	3.76E-02
MACROD2	6043211	C	5.78	3.76E-02
KCNB2	4738266	C	4.46	3.87E-02
SLC1A1	17755777	C	4.61	3.88E-02
FAM104A	4969023	C	8.27	3.90E-02
RYSR2	1362840	G	4.46	3.98E-02
ASTN2	1321922	C	5.15	3.99E-02
KCNQ3	2597351	C	5.95	4.00E-02
ITPR1	11705928	A	4.79	4.05E-02
ITPR1	9809124	A	4.79	4.05E-02
DPP10	36044503	A	5.73	4.06E-02
CCDC165	663178	T	3.95	4.14E-02
IGSF22	4237729	C	4.39	4.19E-02
CA10	9900811	T	3.82	4.24E-02
NCAM2	2826890	G	4.00	4.24E-02
GRHL2	11787301	A	4.85	4.33E-02
SHC3	4877046	A	5.02	4.37E-02
PDE1C	30602	A	3.96	4.38E-02
ESRRG	9441544	C	4.86	4.38E-02
CTNNA2	13019601	A	3.95	4.40E-02

TABLE 2B: Alleles Influencing Poor Response to Perphenazine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
GRID2	17330509	C	3.84	4.43E-02
SLC4A1AP	9678851	A	4.04	4.51E-02
ERC2	4974115	C	3.89	4.53E-02
STXBP5L	7618583	C	7.00	4.56E-02
PCDH7	13150083	A	4.48	4.59E-02
ITPR1	1873850	C	4.66	4.77E-02
PACRG	6455871	C	3.83	4.83E-02
NPAS3	10134571	A	5.63	4.95E-02
PIKFYVE	12622556	A	5.03	4.97E-02

Example 4 – Novel haplotype-tagging SNPs impacting response for quetiapine

[00168] Table 3A provides numerous examples of SNP alleles that predict good response to quetiapine, and table 3B provides numerous examples of SNP alleles that predict poor response to quetiapine. Tables 3A and 3B report the SNPs, SNP-alleles, P values, and Beta weights (in PANSS-Total units) from the linear regression for SNPs that affect response to quetiapine. A negative beta weight indicates that the allele is associated with a decrease in PANSS-T score, corresponding to greater improvement (or lowering) of symptom burden. A positive beta weight indicates that the allele is associated with an increase in PANSS-T score, corresponding to a worsening (or increase) of symptom burden.

TABLE 3A: Alleles Influencing Good Response to Quetiapine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
HTR1B	2226183	A	-7.38	7.98E-04
NLGN1	6772978	A	-7.25	9.98E-04
CNTN4	4684366	C	-5.69	1.32E-03
GREM2	9697	C	-6.83	1.46E-03
FHIT	12636662	A	-4.62	2.18E-03
PCDH15	2384470	C	-5.21	2.33E-03
ARSB	25414	C	-9.37	2.37E-03
COL22A1	4311658	G	-5.04	2.37E-03
COL22A1	4442151	C	-5.04	2.37E-03
DYNC1I1	17638044	C	-8.72	2.39E-03
RGS7	2678780	A	-4.56	2.47E-03
ETV1	41505	C	-4.08	2.62E-03
GRID2	1433667	C	-4.87	2.84E-03
ETV1	17167676	G	-5.27	2.86E-03
PTGER3	5675	C	-6.55	2.95E-03
NALCN	12877625	C	-4.40	2.97E-03
CNTNAP2	7804277	A	-4.78	3.01E-03
LDB2	872478	C	-5.04	3.22E-03
NPFFR2	11940196	A	-4.66	3.56E-03
HTR1B	11568817	G	-4.41	3.57E-03

TABLE 3A: Alleles Influencing Good Response to Quetiapine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
ETV1	2073532	C	-4.97	3.58E-03
ETV1	2073533	A	-4.97	3.58E-03
ETV1	41506	A	-4.97	3.58E-03
LRP1B	4954861	C	-4.43	3.63E-03
TMEFF2	3768703	C	-4.56	3.70E-03
ARMC3	7098947	A	-7.36	3.91E-03
L3MBTL4	3811	A	-4.75	3.99E-03
PLCG2	12925104	C	-5.09	4.24E-03
PSD3	17595804	A	-9.06	4.33E-03
PPP2R2B	17524553	A	-6.53	4.36E-03
DCC	11875845	C	-5.85	4.66E-03
CSMD1	17066296	A	-7.67	4.71E-03
TMEFF2	4853493	G	-4.70	4.75E-03
DOK6	12960929	A	-4.43	5.25E-03
SLC6A1	1170694	A	-5.04	5.46E-03
NLGN1	1980298	C	-4.13	5.83E-03
FHIT	4145506	A	-4.76	6.05E-03
EPHA6	13080770	C	-5.82	6.11E-03
FHIT	398105	A	-3.75	6.22E-03
LRP1B	10496858	C	-4.35	6.35E-03
ERC2	4974115	C	-4.27	6.62E-03
DCTN4	11954652	C	-8.63	6.67E-03
MACROD2	6514537	T	-3.87	6.83E-03
RGS7	1878729	C	-4.01	7.24E-03
SVEP1	1410045	A	-5.03	7.49E-03
RORA	8037420	C	-4.03	8.07E-03
TRAPPC10	2838476	C	-5.10	8.67E-03
CA10	203032	C	-3.83	8.90E-03
DNAH5	4549527	A	-6.52	9.33E-03
BNIP2	1057059	G	-4.03	9.40E-03
NRG3	1937972	A	-4.41	9.75E-03
SEPT9	2627222	C	-14.60	9.78E-03
KYNU	351678	G	-4.09	9.95E-03
MSR1	12675467	C	-8.89	1.00E-02
MSR1	918	A	-8.89	1.00E-02
CDH7	2291343	A	-4.21	1.01E-02
TLN2	16945912	C	-13.51	1.04E-02
ZNF532	3737506	G	-10.25	1.04E-02
PHIP	9350797	A	-4.32	1.04E-02
GFRA1	2694766	A	-3.82	1.07E-02
CNTNAP2	6957194	A	-4.24	1.10E-02
SEPT9	448767	A	-14.90	1.11E-02
CCDC93	17569222	C	-8.74	1.13E-02
CNTN4	767460	A	-4.52	1.15E-02
CSMD1	10503264	A	-4.17	1.15E-02
NCS1	887534	G	-5.89	1.17E-02
LOC286094	7007485	A	-4.14	1.17E-02
CACNA2D1	7811209	A	-4.74	1.18E-02
KCNIP4	2011495	C	-4.09	1.20E-02
MYO10	27878	A	-3.71	1.25E-02
OPCML	7940198	A	-5.30	1.28E-02
GALNTL4	4910339	A	-6.50	1.37E-02
DGKB	2024038	C	-4.71	1.37E-02
DLG2	10898304	C	-3.65	1.41E-02

TABLE 3A: Alleles Influencing Good Response to Quetiapine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
DYNC1I1	1488519	C	-7.20	1.48E-02
NRG3	11194491	C	-3.99	1.52E-02
MSI2	9912674	A	-4.89	1.55E-02
ATF6	1135983	C	-7.15	1.56E-02
RYS3	12906601	C	-5.99	1.56E-02
GPR97	7193154	C	-5.36	1.57E-02
THADA	6754589	A	-4.13	1.57E-02
SLCO3A1	12708589	C	-3.72	1.57E-02
PARK2	9365365	C	-4.64	1.61E-02
CNTNAP2	17170957	G	-4.57	1.63E-02
PIK3CG	3173908	C	-4.53	1.67E-02
GRM5	3824927	G	-3.45	1.70E-02
KCNQ1	11022855	C	-6.87	1.75E-02
PARD3B	2197691	A	-4.14	1.80E-02
NALCN	12874108	A	-3.89	1.87E-02
NALCN	9513862	C	-3.89	1.87E-02
ARHGAP15	9287353	C	-3.91	1.94E-02
CDH7	12607785	A	-3.69	1.94E-02
CDH7	4580293	C	-3.69	1.94E-02
DOK6	7228021	G	-3.57	1.95E-02
LRP1B	2380943	C	-3.47	1.96E-02
TRIM9	882413	C	-4.35	2.00E-02
HAAO	3755540	C	-3.79	2.01E-02
CDH13	8048616	C	-3.49	2.03E-02
PTPRT	876523	C	-3.45	2.06E-02
CACNA2D3	9861155	A	-4.28	2.07E-02
INMT-FAM188B ;				
FAM188B	10230286	A	-3.51	2.09E-02
CTNNA2	10520244	C	-6.07	2.12E-02
RIMBP2	12305517	C	-5.62	2.16E-02
C13orf35	4907727	C	-3.58	2.16E-02
MSR1	6981231	C	-7.67	2.17E-02
FMNL2	1155779	C	-3.41	2.20E-02
SDK2	4969114	A	-3.33	2.22E-02
WWOX	7203676	C	-3.87	2.23E-02
CPLX2	2243404	C	-4.30	2.25E-02
MYO10	26317	A	-3.80	2.25E-02
CNTN6	7646412	A	-4.64	2.28E-02
CTNNA2	10201249	A	-4.77	2.33E-02
OPCML	3920986	G	-3.72	2.33E-02
KCNB1	34467662	C	-9.06	2.39E-02
ESRRG	9441544	C	-4.04	2.40E-02
TMC1	10869183	T	-3.43	2.41E-02
MCPH1	2515509	C	-5.16	2.44E-02
SHC3	10122011	C	-3.43	2.47E-02
GALNTL4	4909979	C	-5.30	2.49E-02
CA10	7210687	C	-3.24	2.52E-02
OPCML	3018407	A	-3.48	2.60E-02
GRM8	17865066	A	-10.79	2.61E-02
GRM8	17865434	C	-10.79	2.61E-02
KCNQ3	17659416	A	-4.39	2.67E-02
NLGN1	2861338	A	-3.51	2.69E-02

TABLE 3A: Alleles Influencing Good Response to Quetiapine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
INMT- FAM188B ; FAM188B	11972565	A	-3.53	2.70E-02
DENND4C	2666797	C	-3.79	2.72E-02
DGKD	838717	A	-3.38	2.74E-02
ATP2B2	11712897	C	-3.54	2.77E-02
LRP1B	34488772	A	-8.41	2.80E-02
PRKG1	1904018	C	-3.09	2.81E-02
CERK	78424	A	-3.60	2.86E-02
C15orf41	8027206	A	-3.40	2.90E-02
NRG3	12767532	G	-3.66	2.93E-02
CTNNA2	17018593	A	-4.25	2.95E-02
GRID2	1836115	A	-3.53	3.01E-02
LRFN2	2078460	A	-3.67	3.06E-02
OPCML	3019855	C	-3.40	3.16E-02
KCNIP4	10516363	A	-3.43	3.20E-02
STX11	3734228	C	-9.67	3.21E-02
STX11	6912580	C	-9.67	3.21E-02
SORBS1	4572071	A	-3.66	3.25E-02
NPAS3	927763	G	-4.45	3.26E-02
ST8SIA1	4606528	C	-3.84	3.26E-02
DLC1	12677920	A	-3.35	3.27E-02
SLC35F3	12087906	G	-9.04	3.30E-02
FOXP1	831440	C	-3.67	3.37E-02
CCBE1	12606241	G	-4.12	3.38E-02
PLCG2	4889447	C	-5.77	3.48E-02
TMT2C	7974520	A	-3.64	3.49E-02
ROBO2	1470571	C	-3.69	3.50E-02
CHRM3	4659552	A	-3.02	3.50E-02
RGS7	10802943	C	-2.99	3.52E-02
JAG1	6074164	A	-4.59	3.54E-02
EXOC2	17135234	A	-4.93	3.55E-02
SAMD4A	8011374	C	-3.17	3.60E-02
CNTNAP2	10240221	A	-3.22	3.63E-02
ITPR2	11048710	A	-3.75	3.74E-02
ERG	10854385	A	-4.00	3.76E-02
GPR116	9395218	C	-4.73	3.77E-02
FMN2	1020709	C	-3.38	3.77E-02
FLJ38109	11167681	C	-3.35	3.82E-02
KCNQ1	422314	C	-3.18	3.83E-02
USP10	2012708	C	-3.05	3.86E-02
CA10	17607202	C	-3.10	3.87E-02
SGCZ	12155874	A	-3.08	3.89E-02
LDB2	3805320	A	-3.16	3.90E-02
TGIF1	12606927	A	-3.49	4.02E-02
FBXL2	6772365	C	-3.45	4.07E-02
PARD3B	7589114	C	-3.18	4.08E-02
TSC1	1050700	A	-3.29	4.13E-02
GRID2	13103135	C	-3.66	4.20E-02
IYD	2076286	A	-6.69	4.24E-02
CLSTN2	10513102	C	-4.05	4.28E-02
RPRD1A	4799835	A	-3.76	4.31E-02
SORBS1	4918911	C	-3.34	4.32E-02
GNG2	1343870	G	-3.12	4.37E-02

TABLE 3A: Alleles Influencing Good Response to Quetiapine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
NCAM2	12483671	A	-3.47	4.38E-02
EXOC2	1747599	G	-3.71	4.44E-02
AKAP9	35759833	C	-4.62	4.46E-02
DLG2	7101982	C	-2.93	4.47E-02
CDH13	3935908	G	-2.89	4.47E-02
PLXDC2	989767	A	-3.31	4.48E-02
CSMD1	2616996	G	-3.44	4.49E-02
PIKFYVE	17699982	A	-4.12	4.51E-02
CSMD1	2724971	A	-3.06	4.51E-02
OSBPL1A	275861	C	-3.06	4.55E-02
RBFOX1	7194775	C	-2.88	4.58E-02
MYT1L	17338616	A	-2.88	4.58E-02
CSMD1	2740865	C	-3.52	4.60E-02
IL1RAP	2361835	A	-4.37	4.63E-02
IL1RAP	7642607	A	-4.37	4.63E-02
IL1RAP	7642797	A	-4.37	4.63E-02
FAM186A	12809349	C	-10.53	4.68E-02
CCDC85A	6704684	A	-3.94	4.68E-02
RYR2	17626494	A	-3.72	4.68E-02
NAV3	1731723	C	-4.81	4.69E-02
HYDIN	1774423	C	-4.48	4.70E-02
CSMD1	2617002	A	-3.54	4.71E-02
MACROD2	1233774	A	-3.02	4.77E-02
FMN2	9729725	C	-3.65	4.81E-02
ITGA1	1047483	A	-3.26	4.82E-02
ITGA1	6895049	G	-3.26	4.82E-02
MSI2	9905296	C	-4.56	4.85E-02
CSMD1	2724973	A	-4.25	4.86E-02
WBSCR17	10238468	C	-3.15	4.88E-02
CTNND2	13362481	C	-3.24	4.90E-02
NRG3	585597	C	-3.13	4.91E-02
SORBS1	955759	A	-3.24	4.95E-02
SNCA	356198	A	-3.59	4.96E-02
ARHGAP21	7090524	A	-3.39	4.98E-02

TABLE 3B: Alleles Influencing Poor Response to Quetiapine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
KCNMA1	35793	C	13.23	1.81E-04
SORBS1	11188339	C	6.46	6.12E-04
NPAS3	10148780	C	5.96	1.11E-03
NRG3	1739780	A	6.18	1.28E-03
NPAS3	8013252	C	5.97	1.69E-03
SORBS1	10882612	C	5.96	1.73E-03
GRIN3A	4324970	C	4.65	2.08E-03
ROBO2	13323053	A	4.24	2.78E-03
NAV2	2625319	A	4.76	2.80E-03
COL4A4	1320407	G	4.69	2.90E-03
NAV2	2585757	G	5.09	3.46E-03
MYO3B	33962844	A	5.07	3.65E-03
CSMD1	4875309	C	5.79	3.69E-03
LOC100289230	4703054	A	4.73	4.63E-03
DOK6	12456201	C	4.39	4.71E-03

TABLE 3B: Alleles Influencing Poor Response to Quetiapine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
DGKB	13242030	C	7.37	5.07E-03
GRIN3A	2485528	T	4.23	5.60E-03
ADTRP	6929400	C	4.67	5.63E-03
ADAMTS9	7615657	C	4.25	5.72E-03
CA10	1503055	G	3.85	6.35E-03
PTPRT	6102904	C	6.55	6.49E-03
CA10	1909923	C	3.84	6.67E-03
CSMD1	2948644	G	4.15	6.79E-03
ANK3	3897459	C	4.50	6.92E-03
CA10	9900811	G	3.96	6.94E-03
KAZN	4661549	C	3.91	7.84E-03
GPM6A	2333250	A	5.13	7.98E-03
PTPRG	17066238	G	8.98	7.98E-03
NRP2	11678877	A	4.07	8.69E-03
MGAT2	1011373	C	12.58	9.21E-03
NLGN1	4894648	A	4.76	9.80E-03
BTN3A1	10447391	G	5.08	9.94E-03
BTN3A1	3208734	C	5.08	9.94E-03
BTN3A1	4711109	A	5.08	9.94E-03
PLA2G2D	578459	A	3.79	1.01E-02
NLGN1	1421422	A	4.73	1.03E-02
PRICKLE2	695938	C	6.98	1.04E-02
MAGI2	740967	C	4.68	1.21E-02
PCSK6	12910197	A	4.96	1.24E-02
CLSTN2	1346134	C	4.60	1.29E-02
MACROD2	6034267	C	5.13	1.36E-02
RIBC2	1022478	C	3.91	1.41E-02
CRISPLD1	17295835	C	4.29	1.42E-02
FHIT	602197	C	4.42	1.43E-02
TFB1M	428447	C	4.05	1.47E-02
PDE4D	1995166	C	3.62	1.48E-02
EPHB1	2400398	A	4.93	1.48E-02
DUOX2	2554452	A	3.94	1.58E-02
ATXN1	2237186	C	5.75	1.60E-02
SMEK2	3748945	A	4.30	1.62E-02
NELL1	1793004	C	4.10	1.64E-02
ERG	2226375	C	4.18	1.64E-02
CACNA2D1	10954673	C	4.83	1.64E-02
SMARCA2	16937852	C	3.77	1.65E-02
PRKCE	7601378	A	4.08	1.70E-02
PJA2	33730	A	3.50	1.72E-02
ZFPM2	16873402	C	4.01	1.72E-02
EMID2	10228469	C	3.62	1.73E-02
SFRP1	17574424	C	4.16	1.78E-02
ACCN1	28936	A	3.93	1.87E-02
CSMD1	2720811	A	3.85	1.91E-02
MAGI2	2885559	C	3.66	1.94E-02
GALNT9	11246993	A	3.98	2.00E-02
SOBP	10554	A	5.23	2.00E-02
CDH13	3743621	C	5.41	2.11E-02
PLCG2	11863650	A	3.64	2.15E-02
MACROD2	204093	C	3.65	2.15E-02
UNC13C	2456976	C	3.77	2.18E-02
RNF144B	17626032	A	4.32	2.18E-02
CREB3L2	10954592	C	6.16	2.18E-02

TABLE 3B: Alleles Influencing Poor Response to Quetiapine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
MACROD2	4813204	G	3.45	2.19E-02
LOC100128590 ;				
SLC8A1	11690292	A	3.43	2.22E-02
KCNK2	4573492	A	3.30	2.35E-02
NAV3	1479024	C	3.35	2.37E-02
NLGN1	990634	C	4.20	2.37E-02
CA10	1503056	A	3.20	2.39E-02
OPCML	7944972	A	3.49	2.45E-02
MACROD2	16994969	A	3.94	2.46E-02
MAGI2	2364341	A	5.37	2.48E-02
PSD3	930023	A	5.05	2.49E-02
MAGI2	6466510	G	3.84	2.50E-02
NBEA	1041304	G	4.11	2.51E-02
CDH13	4783304	C	3.46	2.57E-02
ABCA4	1801466	A	6.64	2.58E-02
CADPS	13067730	C	3.18	2.60E-02
RYR2	7532996	A	3.78	2.60E-02
MUSK	16915435	A	4.31	2.64E-02
NCEH1	4490388	A	3.62	2.65E-02
KCNJ3	3111008	G	3.36	2.80E-02
ATXN1	1399220	A	3.65	2.84E-02
DGKB	38273	C	4.16	2.84E-02
SNTG1	2449960	C	7.09	2.86E-02
RARB	4393871	C	3.40	2.90E-02
MUSK	3001124	C	3.24	2.92E-02
OPCML	4937724	A	3.27	2.93E-02
OPCML	7110211	G	3.27	2.93E-02
EPHA7	345741	G	5.39	2.93E-02
NAV2	10766588	A	3.47	3.00E-02
ATP2B2	4684689	C	2.89	3.07E-02
NALCN	1333761	A	3.14	3.13E-02
DOK6	9965360	A	3.49	3.16E-02
MYO3A	3006260	C	8.20	3.17E-02
IRF8	11647876	A	3.90	3.23E-02
IRF8	9308366	A	3.90	3.23E-02
RGS7	3912106	C	3.22	3.25E-02
NFIL3	12683158	C	6.47	3.30E-02
CSMD1	2720851	G	3.26	3.36E-02
LOC100128590 ;				
SLC8A1	404226	A	3.12	3.47E-02
CNTN4	6787604	A	3.45	3.51E-02
EPHB1	2138213	C	4.38	3.51E-02
MAGI2	6949412	A	3.72	3.52E-02
LOC100128590 ;				
SLC8A1	11894296	C	3.84	3.52E-02
EMID2	10953346	C	4.83	3.55E-02
SEMA5A	3026309	A	7.70	3.59E-02
CLSTN2	4683773	A	3.61	3.60E-02
OPCML	12796925	A	5.44	3.62E-02
NLGN1	10936778	A	3.67	3.63E-02
MUSK	10980573	A	4.19	3.65E-02
NCAM2	2826692	A	3.47	3.68E-02
NEDD4L	12961713	A	3.84	3.68E-02
FOXP1	831078	A	3.23	3.72E-02
KIAA0182	11640338	A	3.21	3.75E-02

TABLE 3B: Alleles Influencing Poor Response to Quetiapine

Gene	NCBI RS#	Allele	Beta(PANSS)	P
TMEM132E	998637	C	3.16	3.79E-02
TMEM132E	998638	C	3.16	3.79E-02
CADPS	6785029	C	3.22	3.80E-02
KCNMA1	7921994	C	3.56	3.80E-02
CA10	4794301	A	3.15	3.81E-02
SELT	6777911	A	3.24	3.83E-02
NRCAM	11561991	A	3.43	3.86E-02
LRRK1	2924835	A	3.15	3.88E-02
DLG2	1943687	G	3.55	3.94E-02
PACRG	9295202	A	3.20	4.01E-02
MIR3974	1513050	C	3.68	4.03E-02
FREM1	7041710	C	4.50	4.04E-02
MDGA2	7160311	C	4.24	4.05E-02
ADAMTS9 ;				
ADAMTS9-AS2	36115950	A	7.23	4.05E-02
MAP1B	10062773	A	2.93	4.06E-02
NRCAM	10241406	A	3.78	4.07E-02
CTNND2	2023916	A	2.87	4.09E-02
PTPRT	6030291	C	4.15	4.10E-02
SEC23B	6075350	C	3.51	4.11E-02
PKP4	2193707	C	3.32	4.13E-02
PDE4D	6886495	C	4.69	4.14E-02
C19orf45	475923	A	3.30	4.24E-02
CNTN6	12490675	C	3.56	4.24E-02
DOK6	8095385	C	3.18	4.27E-02
MYO10	153708	C	3.19	4.28E-02
RAB6B	1104916	A	3.31	4.29E-02
RAB6B	940900	A	3.31	4.29E-02
CTNND2	1494694	A	5.54	4.29E-02
RYR3	1514033	C	2.91	4.30E-02
RAB6B	2692677	C	3.31	4.30E-02
RIBC2	738227	A	3.08	4.31E-02
ARNTL	4757142	A	3.21	4.37E-02
KIAA0182	754710	C	3.16	4.38E-02
SH2D4B	7097169	A	3.37	4.39E-02
DOK6	4353548	G	3.41	4.46E-02
RGS7	984402	C	3.27	4.47E-02
INPP4A	4851142	A	3.61	4.47E-02
ROBO2	10514734	C	5.22	4.47E-02
MAGI1	17073748	A	3.71	4.54E-02
CNTNAP2	6464862	A	3.30	4.55E-02
NPY	16141	C	3.03	4.59E-02
CCDC85A	888279	C	3.27	4.68E-02
NPY	10951003	A	4.91	4.72E-02
RAB6B	940898	A	3.33	4.80E-02
PSD3	13278489	A	5.41	4.81E-02
TOX	448650	C	3.40	4.90E-02
DPP6	6961280	A	4.05	4.93E-02
CACNG2	2283997	C	3.34	4.96E-02
PLCB1	6118218	A	4.06	4.96E-02
HAAO	2241850	A	2.99	4.98E-02
KCNB2	1107217	A	3.17	4.98E-02
PREX2	4336596	C	3.19	4.99E-02

Example 5 – Novel haplotype-tagging SNPs impacting response for risperidone

[00169] Table 4A provides numerous examples of SNP alleles that predict good response to risperidone, and table 4B provides numerous examples of SNP alleles that predict poor response to risperidone. Tables 4A and 4B report the SNPs, SNP-alleles, P values, and Beta weights (in PANSS-Total units) from the linear regression for SNPs that affect response to risperidone. A negative beta weight indicates that the allele is associated with a decrease in PANSS-T score, corresponding to greater improvement (or lowering) of symptom burden. A positive beta weight indicates that the allele is associated with an increase in PANSS-T score, corresponding to a worsening (or increase) of symptom burden.

TABLE 4A: Alleles Influencing Good Response to Risperidone

Gene	NCBI RS#	Allele	Beta(PANSS)	P
PSMD14	9713	A	-6.27	4.99E-05
LRP1B	874295	C	-6.60	1.85E-04
TMEFF2	3738883	C	-5.02	4.11E-04
C7orf58	35793694	A	-9.50	6.74E-04
CAMK2D	17620390	A	-6.17	7.46E-04
SLC35F3	12759054	C	-5.63	7.83E-04
CREB3L2	10954592	C	-10.21	9.00E-04
CACNB4	7597215	C	-6.13	1.36E-03
DNAH17	595711	C	-5.79	1.45E-03
SLC35F3	4641353	A	-5.60	1.45E-03
EXOC2	4409224	A	-5.45	1.60E-03
NRCAM	1269658	A	-4.63	2.09E-03
MAMDC2 ; LOC100507299	2148858	C	-6.08	2.14E-03
POLR2M	11858659	C	-9.29	2.50E-03
KCNB2	349331	C	-6.87	3.18E-03
EPHA4	9758	A	-4.65	3.55E-03
NRXN3	17595443	C	-9.47	3.58E-03
DLEU2	2812200	G	-4.76	3.59E-03
PJA2	33730	A	-4.41	4.80E-03
KCNB2	4738266	C	-4.60	4.91E-03
ROBO1	35456279	A	-8.86	5.08E-03
CCDC50	35380043	A	-12.06	5.10E-03
LOC100129345	12435621	G	-5.86	5.29E-03
PLA2G2D	578459	A	-4.31	5.36E-03
RIMBP2	12305517	C	-6.36	5.46E-03
PLCG2	11639517	C	-5.59	5.63E-03
CHRM3	7551001	A	-4.04	5.65E-03
ALK	35093491	A	-14.31	6.06E-03
TMTC2	7974520	A	-4.91	6.39E-03
NALCN	614728	C	-4.30	7.04E-03
CHRM3	12093821	A	-3.83	8.04E-03
PTPRN2	3952723	A	-4.63	8.62E-03
NBN	1063054	A	-4.49	9.00E-03
EXOC2	4960043	C	-4.17	9.12E-03
IQGAP2	34950321	C	-11.04	1.05E-02

TABLE 4A: Alleles Influencing Good Response to Risperidone

Gene	NCBI RS#	Allele	Beta(PANSS)	P
DTNBP1	3213207	A	-6.69	1.05E-02
DTNBP1	760761	C	-5.39	1.05E-02
DTNBP1	2619522	G	-5.41	1.06E-02
SERPINI1	2420034	A	-3.96	1.06E-02
CDH13	12600161	C	-6.05	1.08E-02
C14orf182	11626611	C	-4.24	1.09E-02
ATRNL1	1272383	C	-7.28	1.12E-02
PCSK5	10781342	C	-4.83	1.16E-02
NPAS3	7159875	A	-4.19	1.18E-02
PJA2	958976	A	-3.84	1.20E-02
ARPP21	2280096	A	-3.72	1.20E-02
NPAS3	10133174	C	-4.15	1.22E-02
CGNL1	6493933	C	-3.82	1.26E-02
ODZ3	2726789	C	-4.79	1.31E-02
PLA2G1B	1179387	A	-5.27	1.33E-02
ITPR1	3805029	C	-4.22	1.40E-02
DGKB	2116312	C	-3.80	1.45E-02
AKAP13	1808338	C	-6.54	1.55E-02
VPS41	2240555	A	-3.96	1.55E-02
CSMD1	688579	A	-5.07	1.60E-02
MYL12B	894733	A	-4.36	1.72E-02
CSMD1	10503279	C	-3.82	1.74E-02
LOXL2	2280936	C	-3.71	1.74E-02
KAZN	2004702	A	-4.20	1.75E-02
VTI1A	3740144	C	-7.41	1.77E-02
SULT4A1	2071886	A	-4.91	1.78E-02
SULT4A1	4149442	A	-4.91	1.78E-02
CDH13	16958456	A	-5.35	1.83E-02
KCNB2	13264816	C	-5.05	1.84E-02
UNC5C	10856915	C	-3.57	1.84E-02
ARPP21	2063648	A	-3.55	1.84E-02
NPY	16141	C	-3.83	1.88E-02
PARD3B	698911	G	-4.84	1.90E-02
EVC	3774876	C	-5.51	1.95E-02
CSMD1	667595	C	-4.83	1.98E-02
EPHB2	11800828	G	-3.48	2.01E-02
BAALC	17799604	C	-4.95	2.02E-02
ABT1	12204145	A	-6.55	2.05E-02
GDA	1123	C	-4.37	2.13E-02
BAALC	4734693	C	-3.63	2.13E-02
TMEFF2	13008804	C	-3.56	2.13E-02
LRRK1	2924835	A	-3.86	2.17E-02
LRP1B	16847247	A	-3.88	2.23E-02
TMX2-CTNND1 ;				
CTNND1	12362406	A	-4.74	2.24E-02
COL22A1	10088210	C	-3.66	2.30E-02
NALCN	583880	A	-3.99	2.33E-02
NALCN	658213	C	-3.99	2.33E-02
PRKCE	11125051	G	-4.42	2.41E-02
ST8SIA2	11853992	A	-3.98	2.42E-02
QRFP	7034278	C	-6.85	2.45E-02
PARD3B	1397482	A	-3.65	2.46E-02
CGNL1	766103	G	-3.76	2.48E-02

TABLE 4A: Alleles Influencing Good Response to Risperidone

Gene	NCBI RS#	Allele	Beta(PANSS)	P
IP6K1	7634902	T	-3.33	2.48E-02
TBC1D22A	15411	C	-4.38	2.51E-02
PSD3	13277215	C	-3.20	2.58E-02
SLC2A9	6817564	A	-5.51	2.59E-02
CHN2	3793259	G	-3.76	2.62E-02
SLC41A1	1772159	A	-3.52	2.64E-02
DOK6	10163684	C	-4.80	2.66E-02
PDE1C	10228662	A	-3.50	2.70E-02
ANO2	7308729	C	-3.68	2.71E-02
DEAF1	4073590	G	-3.31	2.72E-02
TRIP12	4973228	G	-3.89	2.74E-02
HS1BP3	35579164	C	-9.52	2.79E-02
PRKCE	12619351	G	-4.24	2.82E-02
EXOC2	2473480	A	-4.99	2.99E-02
SLC2A13	4312128	A	-4.47	3.07E-02
DEAF1	17758	A	-9.35	3.09E-02
PPM1H	3825305	G	-6.45	3.09E-02
SYNE1	2813539	A	-3.29	3.15E-02
ANO2	11063846	C	-4.97	3.16E-02
CNTN4	6787604	A	-3.86	3.24E-02
CAMKV	6797500	A	-7.59	3.25E-02
ARPP21	4678793	G	-3.21	3.26E-02
CSMD1	2194358	C	-3.77	3.28E-02
FLJ45139	2836722	A	-3.24	3.30E-02
NPAS3	11156806	A	-3.12	3.30E-02
SORBS1	3740511	C	-3.52	3.31E-02
SLC2A13	10735885	A	-4.39	3.37E-02
SLC2A13	10784051	C	-4.39	3.37E-02
PLD5	4658813	A	-3.14	3.45E-02
LPHN3	1510924	G	-3.81	3.46E-02
TOX	375878	C	-4.48	3.52E-02
ST8SIA2	2290492	C	-3.95	3.56E-02
FSTL5	1542071	A	-5.10	3.57E-02
NPY	10951003	A	-4.53	3.59E-02
DOK6	12960929	A	-3.31	3.63E-02
NRG3	12415064	A	-4.72	3.65E-02
GALNTL4	11021757	C	-4.11	3.68E-02
IL17RD	4299455	A	-3.30	3.73E-02
CDH8	11075447	A	-3.50	3.76E-02
ATP10A	3816800	C	-3.17	3.77E-02
CSMD1	11136778	C	-3.39	3.78E-02
PLCB1	227131	A	-3.24	3.83E-02
RYR2	12135982	C	-5.44	3.85E-02
PCLO	2715156	A	-3.36	3.88E-02
FBXL17	999063	A	-4.69	3.90E-02
UNC5C	7681109	A	-3.18	3.91E-02
NPAS3	8014355	A	-3.81	3.95E-02
PTCHD4	9395327	C	-3.26	3.95E-02
OTOG	7130190	A	-5.31	4.04E-02
NKAIN3	7388305	C	-3.14	4.04E-02
EPAS1	12614710	G	-3.50	4.06E-02
SVEP1	10980345	C	-3.68	4.09E-02
PCSK5	10869713	C	-3.14	4.10E-02
PTPRM	565784	A	-3.89	4.16E-02

TABLE 4A: Alleles Influencing Good Response to Risperidone

Gene	NCBI RS#	Allele	Beta(PANSS)	P
CACNA2D3	7617999	A	-3.33	4.17E-02
KCNIP1	870109	A	-3.08	4.17E-02
RGS7	6689169	A	-4.69	4.21E-02
RGS7	6700378	A	-4.69	4.21E-02
WVOX	1125670	C	-3.28	4.21E-02
CSMD1	6995892	A	-3.02	4.22E-02
GPC6	10508001	C	-3.78	4.23E-02
GPC6	16948803	C	-3.78	4.23E-02
SLC35F3	6695594	A	-3.54	4.25E-02
CACNA2D3	10510770	A	-3.73	4.26E-02
UNC5C	7679033	C	-3.21	4.26E-02
KCNN3	1218583	A	-7.19	4.28E-02
ANK3	10994154	A	-4.88	4.28E-02
CERKL	2290517	A	-4.66	4.33E-02
DOK6	7228021	G	-3.12	4.42E-02
PDE10A	220805	A	-3.60	4.45E-02
CAMKMT	698826	A	-4.03	4.48E-02
RABGEF1	1060527	C	-5.59	4.52E-02
CLSTN2	1346134	C	-3.97	4.53E-02
DOK6	2886018	C	-3.55	4.56E-02
CSMD1	10108973	A	-4.10	4.62E-02
DGKB	12666221	G	-3.96	4.66E-02
NKAIN2	1382648	C	-5.84	4.67E-02
GRIN3A	10989597	A	-3.73	4.69E-02
LOC100505806	17329324	C	-6.19	4.70E-02
SORBS1	7899506	C	-3.30	4.75E-02
MTSS1	10956192	A	-4.22	4.77E-02
MAML3	7690044	G	-3.18	4.78E-02
SGCZ	17230584	C	-4.87	4.80E-02
MAGI2	12706063	C	-3.24	4.80E-02
KLF12	11841507	C	-6.52	4.82E-02
SVEP1	10816995	C	-3.55	4.86E-02
GPC5	9523734	C	-2.98	4.89E-02
EXOC2	17757367	G	-4.59	4.92E-02
PLCB1	1047383	C	-3.05	4.93E-02
PLCB1	6056229	C	-3.05	4.93E-02
RYSR2	1521746	C	-3.47	4.95E-02
PRODH	4819756	A	-3.03	4.95E-02
CCDC165	566890	G	-4.34	4.99E-02
GRID2	2904482	A	-2.82	4.99E-02

TABLE 4B: Alleles Influencing Poor Response to Risperidone

Gene	NCBI RS#	Allele	Beta(PANSS)	P
AGAP1	1869295	C	5.79	2.05E-04
NPAS3	1315115	C	8.80	3.04E-04
FER1L6 ; FER1L6-AS1	7840702	A	7.83	1.00E-03
FHIT	6446117	C	5.37	1.71E-03
DENND4C	10122709	C	6.41	2.04E-03
LRP1B	355597	C	7.77	2.10E-03
CTBP2	11245455	C	5.27	2.54E-03
MAML3	2139926	A	4.69	3.23E-03

TABLE 4B: Alleles Influencing Poor Response to Risperidone

Gene	NCBI RS#	Allele	Beta(PANSS)	P
CHRM3	4659552	A	4.43	3.99E-03
LRRK1	1048327	A	6.21	4.45E-03
NRG3	1039076	C	5.03	4.88E-03
TBC1D22A	9616150	C	6.35	5.11E-03
LRP1B	2290140	C	4.79	5.14E-03
CBLB	9832882	A	4.06	5.22E-03
APBB2	4861314	C	4.33	5.69E-03
DHODH	2288000	C	4.31	5.92E-03
RORA	1965886	C	4.92	6.07E-03
GBE1	2680277	C	4.22	6.17E-03
GLDN	2459395	A	4.98	6.26E-03
SNX21 ; ACOT8	1057276	A	15.54	6.29E-03
MSI2	8079426	A	4.37	6.75E-03
BNC2	1999032	C	3.88	7.69E-03
DENND4C	2666797	C	4.86	7.90E-03
NRXN3	8012563	A	5.86	8.52E-03
CSMD1	17071342	C	6.03	8.86E-03
CHN2	6965446	A	6.11	8.96E-03
GAS7	17759453	C	4.07	9.28E-03
SAG	7565275	A	8.22	9.56E-03
DLGAP1	498419	A	4.03	9.65E-03
SORCS2	13442	G	3.99	9.71E-03
TMX2-CTNND1	501738	C	4.62	1.01E-02
GRB10	6967612	C	3.98	1.02E-02
GRB10	7793570	C	3.98	1.02E-02
GLP1R	10305516	C	8.09	1.08E-02
ATXN3	1047795	C	4.28	1.14E-02
NCAM2	2826672	C	4.18	1.21E-02
KIAA0947	1864117	A	3.87	1.23E-02
WWOX	2062894	C	3.97	1.23E-02
SLC6A5	1443547	A	4.03	1.24E-02
CGNL1	11071315	A	4.48	1.24E-02
NXPH2	3732351	A	4.18	1.25E-02
NPAS3	4982070	C	3.76	1.30E-02
PDE4D	16889901	A	4.11	1.32E-02
SKAP1	2278868	C	3.90	1.34E-02
WWOX	9921980	C	4.43	1.39E-02
ATF3	1126700	A	7.72	1.50E-02
PCDH17	7319102	A	4.57	1.54E-02
ABI2	11682759	C	5.06	1.55E-02
ROBO1	17313129	C	5.96	1.58E-02
PTPRG	9844687	A	5.84	1.59E-02
FLJ22447	698028	C	4.43	1.61E-02
RYR2	12121792	A	3.96	1.63E-02
PKIA	2368508	A	3.76	1.65E-02
ARPP21	9311104	G	3.61	1.67E-02
PDE1C	2041517	C	3.75	1.69E-02
CBLB	9288815	G	4.73	1.70E-02
INMT-FAM188B ; FAM188B	11972565	A	3.84	1.71E-02
ITGA1	1047483	A	4.07	1.73E-02
LRP1B	13400449	A	4.02	1.75E-02
KLHL29	17045819	C	5.51	1.75E-02
ITGA1	6895049	G	4.07	1.78E-02
LOC100506731	11159707	C	4.06	1.85E-02

TABLE 4B: Alleles Influencing Poor Response to Risperidone

Gene	NCBI RS#	Allele	Beta(PANSS)	P
CBLB	13073784	C	5.22	1.89E-02
TBC1D1	2995920	A	3.62	1.91E-02
MR1	16856699	C	5.08	1.95E-02
CLASP2	4679034	A	5.85	2.06E-02
GLDN	2124874	A	4.45	2.11E-02
PIKFYVE	12622556	A	4.45	2.12E-02
CCBE1	1791322	C	3.30	2.18E-02
ARFGAP3	9607952	C	3.41	2.21E-02
NPAS3	11622789	T	3.53	2.21E-02
NOS1AP	1504424	C	10.44	2.23E-02
PLA2G4D	776721	C	3.74	2.24E-02
TMEM163	626501	A	4.47	2.26E-02
NPAS3	17525387	G	6.05	2.28E-02
RAB11FIP4	757375	C	3.52	2.30E-02
PLEKHH2	919690	C	3.66	2.36E-02
CNTNAP2	12667619	A	5.36	2.37E-02
SAMD12	11562744	A	12.92	2.37E-02
SAMD12	12540990	A	12.92	2.37E-02
SAMD12	4302874	A	12.92	2.37E-02
RORA	4775308	A	4.81	2.38E-02
ZNF365	2138564	A	3.62	2.39E-02
MICAL2	11022209	C	7.35	2.40E-02
CARD11	6967255	A	2.73	2.42E-02
GBE1	846	C	3.80	2.43E-02
GRID2	6532374	C	4.01	2.53E-02
PAPPA	16933356	C	3.93	2.56E-02
CGNL1	8027154	C	3.59	2.57E-02
LOC286190 ;				
LACTB2	1979452	C	5.18	2.57E-02
NCAM2	2826671	A	3.81	2.62E-02
SAAL1	951624	A	8.43	2.63E-02
LOC728755	7149088	A	3.64	2.68E-02
CSMD1	1442401	G	3.39	2.70E-02
PTPRF	6072649	A	4.82	2.75E-02
MTSS1	8180920	C	3.50	2.78E-02
LOC100289230	4703054	A	3.72	2.81E-02
NTRK2	630426	A	4.11	2.84E-02
CLSTN2	4450768	A	3.74	2.86E-02
FAM69A	2244496	G	6.41	2.87E-02
BIRC6	2710625	A	3.25	2.93E-02
EXOC4	17167240	A	3.69	2.95E-02
ADAMTS19	10069990	C	6.48	3.00E-02
ADAMTS19	1422472	A	6.48	3.00E-02
ADAMTS19	1465686	G	6.48	3.00E-02
CCDC165	7240959	A	3.32	3.02E-02
DLC1	10888175	C	5.25	3.08E-02
FSTL5	6826831	C	4.34	3.13E-02
LRP1B	10179688	A	4.51	3.13E-02
KCNN3	4845677	C	3.49	3.18E-02
ERBB4	1971801	A	3.49	3.18E-02
NCAM2	2826668	A	3.68	3.24E-02
CDH13	10871271	A	3.76	3.28E-02
C15orf41	12708546	A	4.61	3.35E-02
HHAT	926581	A	3.37	3.37E-02
ARL13B ; STX19	13071953	A	5.76	3.37E-02

TABLE 4B: Alleles Influencing Poor Response to Risperidone

Gene	NCBI RS#	Allele	Beta(PANSS)	P
FAM69A	4240962	A	5.73	3.38E-02
QPCT	6708310	A	6.00	3.41E-02
SYNE1	35591210	C	6.21	3.44E-02
RORA	8041466	C	3.38	3.46E-02
NAV2	11819786	A	3.70	3.46E-02
PRKG1	1937710	C	4.62	3.46E-02
DFNB31	10982201	A	3.87	3.49E-02
DFNB31	4979379	C	3.87	3.49E-02
PDE1C	11769133	A	4.10	3.50E-02
RORA	4775304	A	3.51	3.51E-02
GLDN	2168624	C	4.20	3.54E-02
SNCA	2301134	T	3.24	3.59E-02
DGKB	17168013	A	4.79	3.59E-02
MACROD2	4813205	A	3.94	3.60E-02
CAMKMT	343954	C	4.19	3.65E-02
KDM4C	12379798	C	3.04	3.69E-02
SGCZ	12114757	C	3.82	3.79E-02
NRG3	342368	A	3.62	3.82E-02
DAB2IP	12000723	C	3.79	3.82E-02
LRP1B	7558715	A	3.94	3.82E-02
SLIT2	7663557	A	5.44	3.82E-02
DOK6	12957360	G	3.11	3.95E-02
CSMD1	2616996	G	3.49	3.97E-02
HTR5A	980442	G	9.32	3.97E-02
OSBPL1A	275861	C	3.06	4.01E-02
SLIT1	4917756	A	4.36	4.01E-02
CELF2	7068732	G	3.09	4.06E-02
ABCA1	1800978	C	5.34	4.07E-02
FRMD1	3823460	C	3.34	4.08E-02
DGKB	38292	C	4.10	4.14E-02
CDH23	12260631	A	3.31	4.18E-02
NCAM2	2826674	A	3.43	4.21E-02
ATRNL1	12358411	A	3.54	4.23E-02
SULT4A1	17570873	C	4.04	4.25E-02
TMEM106B	1042949	C	3.12	4.28E-02
DGKB	1859730	C	3.32	4.36E-02
HS6ST3	2282135	C	3.72	4.37E-02
PSD3	334749	C	6.95	4.38E-02
MAGI2	12540925	C	3.39	4.39E-02
DOK6	10871643	A	3.41	4.43E-02
NAV3	2030897	C	3.62	4.45E-02
ATP2B2	4327369	C	3.36	4.49E-02
INMT-FAM188B ; FAM188B	10230286	A	3.19	4.63E-02
CLASP2	12492003	A	4.90	4.66E-02
LRP1B	970600	A	3.95	4.75E-02
THBS4	3813667	C	2.89	4.77E-02
NALCN	9557591	C	3.90	4.81E-02
LOC100506128	10913414	A	4.60	4.82E-02
KCNK10	10151231	A	5.04	4.82E-02
SORCS3	7068684	C	4.15	4.84E-02
CDH13	3935908	G	3.22	4.91E-02
NTM	487518	C	3.19	4.92E-02
VPS41	1061303	C	5.74	4.93E-02
PPM1H	17732506	G	6.16	4.94E-02

TABLE 4B: Alleles Influencing Poor Response to Risperidone

Gene	NCBI RS#	Allele	Beta(PANSS)	P
NRG3	2820111	A	3.44	4.95E-02
DPP6	10952464	A	4.13	4.95E-02
GRB10	1019000	C	3.16	4.97E-02

Example 6 – Novel haplotype-tagging SNPs impacting response for ziprasidone

[00170] Table 5A provides numerous examples of SNP alleles that predict good response to ziprasidone, and table 5B provides numerous examples of SNP alleles that predict poor response to ziprasidone. Tables 5A and 5B report the SNPs, SNP-alleles, P values, and Beta weights (in PANSS-Total units) from the linear regression for SNPs that affect response to ziprasidone. A negative beta weight indicates that the allele is associated with a decrease in PANSS-T score, corresponding to greater improvement (or lowering) of symptom burden. A positive beta weight indicates that the allele is associated with an increase in PANSS-T score, corresponding to a worsening (or increase) of symptom burden.

TABLE 5A: Alleles Influencing Good Response to Ziprasidone

Gene	NCBI RS#	Allele	Beta(PANSS)	P
CDH4	4925300	A	-7.60	6.29E-05
LYN	1546519	C	-6.40	1.31E-04
CNTN4	17194378	A	-5.87	4.41E-04
CDH4	4925199	G	-6.52	1.06E-03
KITLG	995029	C	-7.41	1.38E-03
ARHGAP31	12495539	C	-6.37	1.76E-03
HIATL1	9409550	C	-4.98	1.92E-03
LOC100616530	2319150	G	-4.97	2.27E-03
BAG3	35434411	C	-11.89	2.37E-03
NALCN	7993937	A	-6.10	2.63E-03
FHIT	17670088	A	-5.84	3.47E-03
ODZ2	17526010	C	-5.89	3.90E-03
SGCZ	1454583	C	-5.86	4.05E-03
ODZ2	11134473	A	-5.98	4.36E-03
SGCZ	2199910	A	-5.30	4.87E-03
NEDD9	17495074	C	-6.31	4.92E-03
ZNF169	7042481	A	-4.62	5.08E-03
ANK2	34270799	A	-12.77	5.33E-03
C15orf41	2111015	G	-5.95	6.03E-03
SGCZ	2168123	C	-5.61	6.35E-03
CAPZB,				
LOC644083	10799809	C	-4.47	6.74E-03
CSMD1	1531532	C	-4.55	6.77E-03
KCNB2	7465440	A	-6.79	6.97E-03
ADAMTSL1	10811035	A	-4.68	7.11E-03
TMEM181	9364984	A	-4.91	7.12E-03
METTL21A	4234080	A	-6.10	7.23E-03
PTPRG	12635719	A	-6.64	7.71E-03
ATP10A	4609818	A	-5.44	7.80E-03

TABLE 5A: Alleles Influencing Good Response to Ziprasidone

Gene	NCBI RS#	Allele	Beta(PANSS)	P
SORCS3	2496017	A	-5.64	7.82E-03
NPAS3	12100765	C	-4.85	7.84E-03
ANK3	12354956	A	-4.96	8.73E-03
LRP1B	13400449	A	-5.21	1.05E-02
VSNL1	2680832	A	-4.17	1.05E-02
LOXL2	2280936	C	-4.02	1.05E-02
RGS7	2815849	C	-6.56	1.08E-02
SYCP2	13039338	G	-14.84	1.12E-02
MAGI1	13086093	C	-4.83	1.14E-02
NALCN	1452113	G	-5.41	1.16E-02
TSPAN9	537938	A	-4.43	1.18E-02
RAB36	5751596	A	-4.38	1.19E-02
SCUBE1	5759274	A	-3.96	1.19E-02
DYNCH1	916758	C	-5.76	1.21E-02
RC3H1	2103640	A	-4.75	1.21E-02
NXPH1	17150874	C	-7.08	1.22E-02
SLC1A3	891189	G	-4.27	1.23E-02
GLP1R	1820	A	-9.85	1.28E-02
DFNB31	4979379	C	-5.48	1.28E-02
CNTN4	908490	A	-4.24	1.29E-02
CSMD1	12549644	A	-5.91	1.30E-02
CDH7	974080	C	-5.07	1.34E-02
CDH13	17701213	C	-7.08	1.38E-02
HYDIN	1774416	C	-6.82	1.38E-02
EYA4	6569879	A	-4.60	1.38E-02
SHC3	10122011	C	-4.18	1.45E-02
PES1	42942	A	-7.23	1.46E-02
PRKG1	10997954	C	-4.51	1.50E-02
ADAMTS19	4836459	A	-5.20	1.55E-02
PDE1C	11769133	A	-6.03	1.58E-02
HAAO	3755540	C	-4.79	1.61E-02
CTNNA3, LRRTM3	7902006	C	-6.58	1.62E-02
CAPZB, LOC644083	6698682	G	-4.02	1.67E-02
ODZ2	1421991	A	-8.64	1.70E-02
ADAMTSL1	4977432	C	-6.16	1.70E-02
MTSS1	891541	C	-4.72	1.71E-02
LIMCH1	1377349	G	-4.89	1.72E-02
SRRM4	1568923	C	-4.43	1.74E-02
NRXN3	2199796	A	-7.27	1.75E-02
NALCN	1289556	G	-4.33	1.75E-02
QRFPR	11098616	A	-4.20	1.80E-02
SDK1	17133636	A	-7.23	1.81E-02
MAGI2	7789112	A	-3.86	1.81E-02
SGCZ	17574120	G	-3.93	1.83E-02
SDK1	10807838	C	-3.75	1.86E-02
ODZ2	4868807	C	-6.30	1.87E-02
PLCG2	7197832	A	-4.46	1.91E-02
NCKAP5	281580	A	-4.17	1.91E-02
FGF5	3733336	A	-4.10	1.92E-02
ADAMTSL1	10811036	C	-5.69	1.95E-02
INPP4A	12988976	A	-8.49	1.96E-02
TSPAN11	3741868	A	-9.20	2.04E-02
GABRP	11745599	A	-4.76	2.06E-02

TABLE 5A: Alleles Influencing Good Response to Ziprasidone

Gene	NCBI RS#	Allele	Beta(PANSS)	P
FBXL17	288173	C	-5.30	2.10E-02
GRM8	17865092	C	-8.62	2.12E-02
F5	6018	G	-9.77	2.16E-02
MICAL2	11022209	C	-6.38	2.16E-02
MAML3	7690044	G	-3.98	2.17E-02
CDH7	2291343	A	-4.73	2.19E-02
FBXL17	288180	C	-5.29	2.22E-02
GABBR2	2304391	A	-6.08	2.23E-02
SHC3	944478	T	-3.75	2.25E-02
PLD5	2809995	A	-3.66	2.25E-02
KLHL29	934373	A	-4.12	2.26E-02
DOK6	1790602	C	-7.75	2.28E-02
MSI2	17834337	A	-7.74	2.30E-02
ODZ2	1421988	G	-3.89	2.31E-02
ODZ2	1421978	C	-3.77	2.34E-02
QRFPR	11737010	A	-4.04	2.38E-02
LIMCH1	1377348	C	-4.63	2.44E-02
KLHL29	1709304	A	-3.63	2.51E-02
ODZ2	6879227	A	-4.60	2.56E-02
ODZ2	2973664	A	-4.60	2.56E-02
RYR3	16970951	A	-4.41	2.56E-02
CDH13	17768659	C	-5.59	2.58E-02
LOC100289130,				
GPX1	1800668	C	-4.24	2.61E-02
LIMCH1	1453043	C	-4.24	2.62E-02
DGKD	838718	A	-3.93	2.62E-02
PARK2	9458300	A	-4.78	2.66E-02
SCD5	7657237	C	-5.76	2.69E-02
CDS1	1372971	A	-3.82	2.72E-02
ATF6	6427628	A	-6.77	2.73E-02
RORA	340005	A	-3.68	2.73E-02
TMEM106B	1042949	C	-3.36	2.81E-02
KCNJ3	2591172	G	-3.86	2.86E-02
CDH13	8053315	G	-4.37	2.93E-02
CDH7	12607785	A	-4.48	2.95E-02
CDH7	4580293	C	-4.48	2.95E-02
NCAM2	6518020	G	-3.47	2.96E-02
PRUNE2	620552	C	-4.74	2.97E-02
PRUNE2	512110	C	-4.74	2.97E-02
DGKD	838717	A	-3.87	2.97E-02
CPLX2	3749801	C	-8.65	3.00E-02
C15orf41	2381887	A	-4.31	3.01E-02
MAGI1	2306379	C	-4.50	3.02E-02
SGCZ	1454580	C	-3.75	3.02E-02
FHIT	2736792	A	-3.87	3.03E-02
TRPC4	3812841	A	-3.71	3.05E-02
OPCML	11223232	A	-3.85	3.06E-02
GIGYF2	2289915	A	-4.58	3.10E-02
PTPRG	11721138	C	-5.79	3.15E-02
PTPRG	9832251	C	-5.79	3.15E-02
SPIB	1137895	C	-4.27	3.17E-02
CDH23	7902757	C	-9.95	3.18E-02
NELL1	12223203	A	-4.29	3.18E-02
VSNL1	1996610	C	-3.56	3.19E-02
NCKAP5	12999715	A	-4.14	3.24E-02

TABLE 5A: Alleles Influencing Good Response to Ziprasidone

Gene	NCBI RS#	Allele	Beta(PANSS)	P
NRXN3	10146690	A	-4.73	3.28E-02
NRXN3	12147298	A	-5.05	3.30E-02
DENND5B	3741876	A	-5.69	3.34E-02
USH2A	11117573	A	-4.59	3.35E-02
NLGN1	3980098	G	-3.61	3.38E-02
MAGI2	6949538	A	-5.38	3.44E-02
BMP7	17480735	A	-6.71	3.51E-02
PCLO	17210284	C	-3.87	3.56E-02
CDH4	6142887	C	-12.39	3.57E-02
GALNTL4	10741551	C	-4.13	3.58E-02
CACNB2	6482385	C	-3.79	3.58E-02
SH2D4B	7097169	A	-4.18	3.62E-02
KIAA0182	11640338	A	-3.84	3.70E-02
SDK1	4722654	A	-3.38	3.71E-02
CDH13	7185276	A	-4.77	3.90E-02
LRR4C	10768581	C	-3.50	3.98E-02
NRXN3	2192426	G	-3.26	3.98E-02
WVOX	9921059	G	-3.54	4.04E-02
SH3GL3	2730082	A	-3.92	4.08E-02
ABCA13	11983883	G	-5.63	4.10E-02
TBXAS1	193948	G	-3.59	4.14E-02
RYS2	4659797	A	-6.26	4.16E-02
ARHGAP31	751607	A	-5.36	4.23E-02
SLC22A23	9392478	C	-3.36	4.23E-02
DOCK1	2229603	A	-20.43	4.26E-02
ADCY8	913818	A	-6.73	4.28E-02
CTBP2	2938009	G	-3.60	4.37E-02
PARK2	9295174	C	-4.36	4.42E-02
DLC1	2027	A	-10.36	4.43E-02
MAGI1	2372067	A	-3.56	4.44E-02
CACNA1E	638132	A	-3.71	4.45E-02
COL6A3	4663722	C	-6.40	4.49E-02
SNRNP27	1048139	A	-4.89	4.49E-02
PTPR	1569549	A	-5.49	4.50E-02
FBXL2	12330707	A	-3.98	4.50E-02
COL6A3	36117715	A	-8.54	4.58E-02
LIMCH1	11735207	C	-3.72	4.63E-02
RORA	8037420	C	-3.55	4.64E-02
PDE1C	10951313	C	-3.25	4.68E-02
MACROD2	1013112	A	-3.35	4.73E-02
RGS7	2678780	A	-4.17	4.78E-02
GAS7	7216101	A	-5.42	4.79E-02
PCDH17	9537776	A	-3.46	4.80E-02
STK10	15963	C	-4.48	4.84E-02
GRK5	4623810	G	-3.45	4.85E-02
KCNJ3	3106660	C	-10.17	4.86E-02
CELSR3	6773261	A	-5.90	4.87E-02
DFNB31	10982201	A	-4.35	4.88E-02
TSPAN5	10020677	A	-3.50	4.88E-02
TMEM132B	2240497	A	-3.32	4.89E-02
LRR4C	4375425	A	-3.39	4.90E-02
SHROOM3	12710873	A	-4.25	4.95E-02
CELSR3	3821875	C	-6.04	4.97E-02

TABLE 5B: Alleles Influencing a Poor Response to Ziprasidone

Gene	NCBI RS#	Allele	Beta(PANSS)	P
BMPRI1B	17023107	C	23.68	2.51E-05
UNC5C	17023119	C	23.68	2.51E-05
NALCN	9585618	C	5.77	4.79E-04
SLIT2	12233652	A	6.24	7.97E-04
BLZF1	2275299	C	5.37	1.00E-03
NBAS	12692258	A	6.91	1.05E-03
NALCN	651737	C	5.83	1.30E-03
NALCN	614728	C	5.38	1.59E-03
GRIA1	10036589	C	7.42	1.76E-03
NALCN	583880	A	5.65	1.77E-03
NALCN	658213	C	5.65	1.77E-03
PSD3	335244	C	5.20	2.03E-03
MACROD2	13043406	C	10.71	2.24E-03
MUSK	16915435	A	6.63	3.26E-03
MUSK	10980573	A	6.94	3.58E-03
ITGA1	1047483	T	5.06	4.25E-03
ITGA1	6895049	T	5.06	4.25E-03
TRPM3	10780982	G	4.73	4.53E-03
PARD3B	10490272	A	5.76	4.69E-03
FMN2	6699880	A	5.71	5.05E-03
PARD3B	724605	A	5.16	5.22E-03
CDH4	6061338	C	5.64	5.68E-03
WWC1	10042345	C	4.82	5.98E-03
S100BBP	1284365	C	5.91	6.05E-03
BCL2L11	6753785	G	4.22	6.28E-03
VSNL1	7593881	C	4.68	6.47E-03
PTPRG	12495140	T	4.56	6.51E-03
CDS1	1120	C	5.55	6.60E-03
PARD3B	12613874	A	4.30	6.81E-03
EPHB1	1004551	A	4.85	7.80E-03
NALCN	9557581	C	4.45	7.87E-03
APBB2	4861314	C	4.65	9.10E-03
EPHB1	1980139	G	6.04	9.18E-03
DAPK1	1007394	C	3.89	9.22E-03
SLC25A21	17105059	C	5.72	9.44E-03
DAPK1	3118854	C	3.93	9.71E-03
TMEFF2	13008804	C	4.18	1.01E-02
CNTNAP2	2692132	A	4.56	1.05E-02
KCNIP1	50057	A	4.83	1.12E-02
CTNNA2	2862025	C	5.49	1.13E-02
TRPM3	10511991	A	4.80	1.15E-02
GRID2	992995	A	4.30	1.18E-02
ARNTL	4757138	A	4.61	1.19E-02
ARNTL	2279287	A	4.61	1.19E-02
ARNTL	2279286	C	4.61	1.19E-02
ARNTL	2279285	A	4.61	1.19E-02
ARNTL	2279284	A	4.61	1.19E-02
ERC2	187205	C	4.56	1.27E-02
SYNE1	1408461	A	4.28	1.29E-02
ARNTL	10766075	C	4.40	1.32E-02
RYR2	10925398	A	4.43	1.36E-02
RHOG	4597058	C	4.73	1.45E-02
DPYSL5	1371614	C	4.32	1.47E-02
DLGAP1	11081059	A	4.61	1.50E-02
NKAIN2	9372762	A	4.09	1.51E-02

TABLE 5B: Alleles Influencing a Poor Response to Ziprasidone

Gene	NCBI RS#	Allele	Beta(PANSS)	P
DLGAP1	1791398	A	4.60	1.51E-02
NBEA	9600401	C	7.63	1.55E-02
UTRN	12204734	A	5.75	1.56E-02
EXOC2	17755910	C	6.16	1.61E-02
COL4A4	1320407	G	4.07	1.62E-02
ZNF169	10993153	C	6.00	1.65E-02
CACNA2D1	37090	A	3.78	1.74E-02
DAPK1	3128480	C	3.49	1.76E-02
PACRG	1333955	G	3.72	1.76E-02
UTRN	9321977	G	4.91	1.76E-02
PRKCE	7601378	A	4.37	1.77E-02
PKP4	2193707	C	4.55	1.78E-02
KCNMA1	6480850	C	3.76	1.79E-02
SEMA3E	2723017	A	5.51	1.85E-02
DLG2	921452	A	6.03	1.89E-02
GPC5	9523734	C	3.59	2.03E-02
DGKI	2278829	A	4.10	2.03E-02
TBC1D1	12643286	A	4.58	2.04E-02
FGF14	2390674	A	5.74	2.08E-02
PTPRN2	3952723	A	4.52	2.20E-02
ULK1	10902469	C	10.56	2.24E-02
KCNMA1	1907727	C	4.82	2.31E-02
PLA2R1	3109389	C	5.49	2.33E-02
SLC35F3	10157061	T	3.93	2.34E-02
CNTN5	10790978	G	4.47	2.35E-02
UTRN	10457761	C	4.87	2.43E-02
CCDC50	35380043	A	9.56	2.47E-02
INSC	17507577	A	6.31	2.49E-02
SDK1	10233166	A	3.63	2.52E-02
KCNK9	2542425	A	3.93	2.52E-02
CDH13	7186797	C	3.56	2.54E-02
CTNNA2	12713991	G	3.89	2.61E-02
TMEFF2	3738883	C	3.72	2.62E-02
EXOC2	17757367	G	5.83	2.65E-02
RAB11FIP4	1076185	G	4.77	2.70E-02
PDE4D	6450528	G	4.12	2.71E-02
FREM1	16932300	C	8.78	2.71E-02
RARB	871963	A	3.48	2.77E-02
TPH2	1386493	C	4.05	2.80E-02
ATP10A	12050652	C	3.36	2.81E-02
MICAL2	11022220	A	4.96	2.81E-02
LRP1B	10193058	A	3.88	2.83E-02
CDH13	17289333	G	4.62	2.88E-02
C12orf5	1046165	C	4.84	2.88E-02
SYT13	3816205	A	5.87	2.90E-02
ARHGAP19-SLIT1	3758587	C	4.32	2.92E-02
DPYSL5	10181727	C	3.46	2.97E-02
DPYSL5	1057115	C	3.46	2.97E-02
CTNND2	6879413	C	4.80	3.02E-02
CCBE1	1791322	C	3.49	3.03E-02
CDH13	8182105	C	5.35	3.04E-02
FSTL5	13141680	C	4.27	3.07E-02
DLG2	7109065	C	5.32	3.11E-02
SYT13	7395419	A	4.47	3.12E-02
SYT13	7395421	A	4.47	3.12E-02

TABLE 5B: Alleles Influencing a Poor Response to Ziprasidone

Gene	NCBI RS#	Allele	Beta(PANSS)	P
UBL3	9578136	C	4.30	3.13E-02
UBL3	957189	C	4.30	3.13E-02
CTBP2	3781412	C	3.59	3.22E-02
SAMD4A	1211170	A	3.78	3.25E-02
NAV3	964639	A	3.43	3.27E-02
KYNU	10496935	C	3.80	3.31E-02
CACNA2D3	1851043	C	3.78	3.35E-02
PSD3	335221	C	3.76	3.36E-02
FMN2	7530215	G	4.40	3.38E-02
CSMD1	13271457	A	3.73	3.40E-02
KIAA1797	9886755	C	4.95	3.51E-02
NRXN3	8017544	C	3.61	3.71E-02
NCKAP5	16841277	A	4.16	3.82E-02
F5	2187952	A	3.71	3.89E-02
CHN2	6965446	A	5.17	3.95E-02
ROBO1	9855098	A	4.32	3.96E-02
MBP	6565924	A	3.70	3.99E-02
MICAL2	12274943	C	3.87	4.03E-02
MIER1	6681625	A	14.71	4.04E-02
PTGS2	20417	C	5.28	4.05E-02
MAGI2	2885559	C	3.54	4.07E-02
CSMD1	7813376	C	3.88	4.18E-02
DLG2	7937832	G	3.88	4.20E-02
COL22A1	7000416	C	3.71	4.25E-02
CDH23	10999803	C	6.66	4.27E-02
MIR1270-1	7247683	C	3.68	4.29E-02
AKAP6	4647899	A	4.17	4.32E-02
ARHGEF10	14375	G	4.92	4.33E-02
TPH2	1872824	C	3.47	4.35E-02
SLCO3A1	4312282	A	4.01	4.37E-02
CCDC88C	7146512	C	3.50	4.39E-02
MTO1	1713862	C	6.02	4.41E-02
CNTN4	13086027	A	4.04	4.44E-02
DOK6	9989625	C	3.48	4.45E-02
SLC1A3	10491374	G	3.56	4.48E-02
C10orf112	10763975	A	5.05	4.49E-02
GRIN3A	4324970	C	3.28	4.50E-02
FHIT	492836	T	3.39	4.50E-02
WWOX	13335579	C	3.41	4.50E-02
MBP	4890788	C	3.49	4.50E-02
PCSK6	4965881	C	3.99	4.51E-02
PCSK6	7166590	A	3.99	4.51E-02
FMN2	994277	A	3.35	4.52E-02
TPH2	1386482	A	3.37	4.57E-02
TRDN	11759636	A	4.15	4.64E-02
CNTNAP2	6964783	C	3.45	4.65E-02
CRISPLD2	16974880	G	3.69	4.65E-02
MMP16	10103111	C	4.39	4.66E-02
CTNND2	6859430	C	6.30	4.71E-02
MIOX	1055271	C	3.47	4.72E-02
PTPRN2	6978278	A	3.79	4.77E-02
COL4A4	12468501	A	4.32	4.79E-02
TMC8	11655790	C	8.46	4.79E-02
TRPM6	9650767	A	3.55	4.81E-02
ZXDC	7131	C	3.61	4.81E-02

TABLE 5B: Alleles Influencing a Poor Response to Ziprasidone

Gene	NCBI RS#	Allele	Beta(PANSS)	P
GRID2	10004009	A	3.45	4.88E-02
SH3GL3	1491578	C	4.27	4.89E-02
NAALADL2	7640306	A	3.97	4.95E-02
LRP1B	13398962	C	4.86	5.00E-02

Example 7 – Identification of SNPs tagging the same haplotypes

[00171] The inventors determined which of the various SNPs that impact antipsychotic response, correlate with one another indicating that they, in fact, tag the same haplotype. To determine which of the various SNP genotypes for SNPs in Tables 1-5 correlate with one another, the inventors calculated the pair-wise correlation coefficient using *cor* function in R (version 2.15.1). This was done for each antipsychotic drug separately so that correlation coefficients were calculated for pairs of SNPs within Table 1, within Table 2, within Table 3, within Table 4, and within Table 5. Two SNPs were considered correlated if their Pearson correlation coefficient $r \geq 0.8$ (or $r^2 \geq 0.64$). Note that this approach identifies SNPs that are redundant in terms of tagging haplotypes in that SNPs with correlated genotypes, by definition, tag the same haplotype. The inventors define such SNPs as being members of the same “correlating cluster”.

[00172] Tables 6 to 10 show SNPs that both impact the response to the same antipsychotic medication, and that are members of the same correlating cluster, thus tagging the same haplotype. Table 6 shows correlating clusters for olanzapine, Table 7 for perphenazine, Table 8 for quetiapine, Table 9 for risperidone, and Table 10 for ziprasidone. Any SNP from Tables 1-5 that is not listed in the corresponding Table 6-10 uniquely tags a haplotype and is not part of any of the listed correlating clusters.

TABLE 6: Correlating Clusters for Olanzapine

Cluster	Correlated SNPs
01	rs6895049;rs1047483
02	rs1048175;rs1048166
03	rs10511795;rs10511797
04	rs1061015;rs1061016
05	rs7103862;rs4505088;rs7122815;rs555867;rs10792782;rs11234192;rs1943687;rs1943691
06	rs718805;rs10953911;rs11765060
07	rs11737010;rs11098616
08	rs2057899;rs12666717
09	rs9640235;rs802022;rs10240221;rs12670106;rs1608958;rs2710157
10	rs10503525;rs13278000
11	rs1490407;rs1490403
12	rs4685501;rs1554561
13	rs4642090;rs1568982
14	rs17622020;rs17622124
15	rs17865434;rs17865066
16	rs10740023;rs10821660;rs4611159;rs2061486;rs2893823
17	rs7853207;rs3812550
18	rs2247408;rs3819811
19	rs3774155;rs42445
20	rs2485528;rs4324970
21	rs408144;rs450658;rs6711371
22	rs688579;rs595834;rs667595
23	rs11615961;rs708200
24	rs2361835;rs7642607;rs7642797
25	rs838717;rs838718
26	rs2240717;rs917479
27	rs9409513;rs9409514

TABLE 7: Correlating Clusters for Perphenazine

Cluster	Correlated SNPs
01	rs4705203;rs10035432
02	rs11750400;rs10515244
03	rs1128687;rs1128705
04	rs9809124;rs11705928;rs1873850
05	rs11712897;rs11708983
06	rs13130047;rs11731618
07	rs17570753;rs11774231
08	rs2058039;rs12453566
09	rs6043211;rs6043223;rs12480304
10	rs1253669;rs1253671
11	rs4805590;rs12972537
12	rs12550842;rs13256262
13	rs1503056;rs7210687;rs1909923;rs9900811;rs203032;rs17607202;rs1503055
14	rs1614229;rs1651285
15	rs9852679;rs17397077
16	rs1488519;rs17638044
17	rs3857723;rs1859291
18	rs9458561;rs2022996
19	rs9671249;rs2216901
20	rs1064833;rs2250106;rs2250338
21	rs11772525;rs2329486
22	rs10097662;rs2597351
23	rs38108;rs319863
24	rs363420;rs363343
25	rs4849050;rs3811643
26	rs4325897;rs4491869
27	rs7110211;rs7944972;rs4937724
28	rs444598;rs6762005
29	rs6455871;rs6922278
30	rs11002064;rs7907070
31	rs7308849;rs7980107
32	rs10507424;rs9530787
33	rs17396765;rs9831415
34	rs2247784;rs9952628

TABLE 8: Correlating Clusters for Quetiapine

Cluster	Correlated SNPs
01	rs4711109;rs3208734;rs10447391
02	rs6895049;rs1047483
03	rs11188339;rs4918911;rs10882612;rs955759
04	rs4894648;rs990634;rs10936778;rs1421422
05	rs16915435;rs10980573
06	rs2692677;rs1104916;rs940900;rs940898
07	rs754710;rs11640338
08	rs9308366;rs11647876
09	rs404226;rs11690292
10	rs10230286;rs11972565
11	rs4580293;rs12607785;rs2291343
12	rs4145506;rs12636662
13	rs6981231;rs918;rs12675467
14	rs11194491;rs1937972;rs12767532
15	rs9513862;rs12874108;rs12877625
16	rs930023;rs13278489
17	rs4683773;rs1346134
18	rs1836115;rs1433667
19	rs1503056;rs9900811;rs7210687;rs1909923;rs203032;rs17607202;rs1503055
20	rs1488519;rs17638044
21	rs17865434;rs17865066
22	rs10516363;rs2011495
23	rs2073533;rs41506;rs2073532;rs41505
24	rs10496858;rs2380943;rs4954861
25	rs2625319;rs2585757
26	rs2616996;rs2720851;rs2617002;rs2720811;rs2724973
27	rs448767;rs2627222
28	rs1878729;rs984402;rs2678780;rs3912106
29	rs3018407;rs7110211;rs3019855;rs4937724
30	rs4442151;rs4311658
31	rs2485528;rs4324970
32	rs740967;rs6466510
33	rs3734228;rs6912580
34	rs12960929;rs7228021
35	rs2361835;rs7642607;rs7642797
36	rs6957194;rs7804277
37	rs10148780;rs8013252
38	rs9905296;rs9912674
39	rs998637;rs998638

TABLE 9: Correlating Clusters for Risperidone

Cluster	Correlated SNPs
01	rs1465686;rs10069990;rs1422472
02	rs7793570;rs6967612;rs1019000
03	rs342368;rs1039076
04	rs6895049;rs1047483
05	rs4312128;rs10735885;rs10784051
06	rs10980345;rs10816995
07	rs4979379;rs10982201
08	rs12619351;rs11125051
09	rs2290492;rs11853992
10	rs10230286;rs11972565
11	rs4659552;rs12093821;rs7551001
12	rs4679034;rs12492003
13	rs11562744;rs12540990;rs4302874
14	rs16958456;rs12600161
15	rs3738883;rs13008804
16	rs10508001;rs16948803
17	rs4678793;rs2280096;rs9311104;rs2063648
18	rs2124874;rs2168624
19	rs4240962;rs2244496
20	rs760761;rs2619522
21	rs846;rs2680277
22	rs2826668;rs2826671;rs2826672;rs2826674
23	rs2071886;rs4149442
24	rs12759054;rs4641353;rs6695594
25	rs1965886;rs4775304;rs8041466
26	rs658213;rs614728;rs583880
27	rs1047383;rs6056229
28	rs688579;rs667595
29	rs6689169;rs6700378
30	rs12960929;rs7228021
31	rs3740511;rs7899506
32	rs33730;rs958976

TABLE 10: Correlating Clusters for Ziprasidone

Cluster	Correlated SNPs
01	rs992995;rs10004009
02	rs9321977;rs10457761;rs12204734
03	rs6895049;rs1047483
04	rs10181727;rs1057115
05	rs2279285;rs4757138;rs2279286;rs2279284;rs2279287;rs10766075
06	rs4722654;rs10807838
07	rs4977432;rs10811036
08	rs16915435;rs10980573
09	rs4979379;rs10982201
10	rs11737010;rs11098616
11	rs1377348;rs11735207;rs1453043;rs1377349
12	rs11022220;rs12274943
13	rs4580293;rs974080;rs12607785;rs2291343
14	rs11721138;rs9832251;rs12635719
15	rs281580;rs12999715
16	rs2168123;rs1454583
17	rs17023107;rs17023119
18	rs934373;rs1709304
19	rs17755910;rs17757367
20	rs7185276;rs17768659
21	rs11081059;rs1791398
22	rs1386482;rs1872824
23	rs2680832;rs1996610
24	rs288180;rs288173
25	rs6879227;rs2973664
26	rs1007394;rs3118854;rs3128480
27	rs335221;rs335244
28	rs6773261;rs3821875
29	rs4925199;rs4925300
30	rs620552;rs512110
31	rs658213;rs614728;rs9585618;rs651737;rs1452113;rs9557581;rs583880;rs7993937
32	rs10799809;rs6698682
33	rs921452;rs7109065
34	rs4965881;rs7166590
35	rs10490272;rs724605
36	rs7395419;rs7395421
37	rs6699880;rs7530215
38	rs838717;rs838718
39	rs7042481;rs9409550
40	rs10122011;rs944478
41	rs9578136;rs957189

Example 8 - Combing the results for various tagging SNPs in a combinatorial algorithm to predict response

[00173] One skilled in the art will recognize that for uncorrelated predictors (in this case alleles of various SNPs not belonging to the same correlating cluster) for a dependent variable (in this case response to antipsychotic medication, measured by change in PANSS), the influence of the predictors is independent and additive. Therefore, the genotypes for the various SNPs can be combined to develop algorithms for prediction of drug response: those in Table 2 for olanzapine, those in Table 1 for perphenazine, those in Table 3 for quetiapine, those in Table 4 for risperidone, and those Table 5 for ziprasidone.

[00174] As determined by the laws of Mendelian inheritance and confirmed by observations in the CATIE data set used for the examples presented in this specification, the inheritance of an allele at a given SNP is binary. Additionally, one skilled in the art will recognize that SNP alleles are unitary. Therefore, a given human subject will carry either 0, 1, or 2 copies of a given allele for any particular SNP listed in Tables 1-5.

[00175] Therefore, for all cases where SNPs are not members of a correlating cluster, the basic rules of multiple regression equations and straightforward mathematical principles make it true that:

If, N_1 = number of alleles at one SNP (SNP1) impacting response to a given drug (0, 1, 2 only); and

N_2 = number of alleles of a second SNP (SNP2) impacting response to a the same drug (0, 1, 2 only); and

β_1 = beta weight (slope) attributed SNP1; and

β_2 = beta weight (slope) attributed to SNP2; and

C = y intercept for PANSS-T change (by definition) = baseline change in PANSS-T for individuals carrying zero alleles of either predictor,

then the predicted response to the antipsychotic medication measured in change in PANSS-T is given by:

Expected change in PANSS-T = $C + \beta_1 N_1 + \beta_2 N_2$.

Similarly, this can be generalized by the formula:

Expected change in PANSS-T = $C + \sum_i \beta_i N_i$

where i = the number of SNPs from members of different correlating clusters selected from the one of Tables 6-10 corresponding to the particular drug.

* * *

5 **[00176]** All of the methods disclosed and claimed herein can be made and
executed without undue experimentation in light of the present disclosure. While the
compositions and methods of this invention have been described in terms of preferred
embodiments, it will be apparent to those of skill in the art that variations may be applied to
the methods and in the steps or in the sequence of steps of the method described herein
10 without departing from the concept, spirit and scope of the invention. More specifically, it
will be apparent that certain agents which are both chemically and physiologically related
may be substituted for the agents described herein while the same or similar results would be
achieved. All such similar substitutes and modifications apparent to those skilled in the art
are deemed to be within the spirit, scope and concept of the invention as defined by the
15 appended claims.

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The following references, to the extent that they provide exemplary procedural or other details supplementary to those set forth herein, are specifically incorporated herein by reference.

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WHAT IS CLAIMED IS:

1. A method of detecting the presence of a polymorphism in the PSMD14, LRP1B, or TMEFF2 gene and administering a treatment to a human subject, the method comprising:

(a) obtaining a genomic sample from a human subject having or at risk of developing SZ;

(b) detecting the haplotype tagged by the “A” allele of rs9713, the haplotype tagged by the “C” allele of rs874295, or the haplotype tagged by the “C” allele of rs3738883 in the genomic sample;

(c) identifying the subject having the haplotype tagged by the “A” allele of rs9713, the haplotype tagged by the “C” allele of rs874295, or the haplotype tagged by the “C” allele of rs3738883 in the genomic sample as likely to have an improved response to risperidone as compared to control subject; and

(d) administering a treatment comprising risperidone to the subject with the haplotype tagged by the “A” allele of rs9713, the haplotype tagged by the “C” allele of rs874295, or the haplotype tagged by the “C” allele of rs3738883.

2. A method of treating a human subject having or at risk of developing SZ comprising administering an effective amount of risperidone to a subject determined to have a haplotype tagged by the “A” allele of rs9713, the haplotype tagged by the “C” allele of rs874295, or the haplotype tagged by the “C” allele of rs3738883.

3. A method of detecting the presence of a polymorphism in and administering a treatment to a human subject, the method comprising:

(a) obtaining a genomic sample from a human subject having or at risk of developing SZ;

(b) detecting the haplotype tagged by an allele selected from those provided in Table 1A in the genomic sample;

(c) identifying the subject having the haplotype tagged by the allele provided in Table 1A in the genomic sample as likely to have an improved response to olanzapine as compared to control subject; and

(d) administering a treatment comprising olanzapine to the subject with the haplotype tagged by the allele provided in Table 1A.

4. A method of treating a human subject having or at risk of developing SZ comprising administering an effective amount of olanzapine to a subject determined to have a haplotype tagged by an allele selected from those provided in Table 1A.

5. The method of claim 3, further comprising detecting the haplotype tagged by two or more alleles selected from those provided in Table 1A.

6. The method of claim 5, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 6.

7. A method of detecting the presence of a polymorphism in and administering a treatment to a human subject, the method comprising:

(a) obtaining a genomic sample from a human subject having or at risk of developing SZ;

(b) detecting the haplotype tagged by an allele selected from those provided in Table 1B in the genomic sample;

(c) identifying the subject having the haplotype tagged by the allele provided in Table 1B in the genomic sample as likely to have a poor response to olanzapine as compared to control subject; and

(d) administering an antipsychotic treatment other than olanzapine to the subject with the haplotype tagged by the allele provided in Table 1B.

8. A method of treating a human subject having or at risk of developing SZ comprising administering an effective amount of an antipsychotic agent that is not olanzapine to a subject determined to have a haplotype tagged by an allele selected from those provided in Table 1B.

9. The method of claim 7, further comprising detecting the haplotype tagged by two or more alleles selected from those provided in Table 1B.

10. The method of claim 9, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 6.

11. The method of claim 7, comprising administering perphenazine, quetiapine, risperidone or ziprasidone to the subject.

12. A method of detecting the presence of a polymorphism in the CSMD1 or PTPRN2 gene and administering a treatment to a human subject, the method comprising:

(a) obtaining a genomic sample from a human subject having or at risk of developing SZ;

(b) detecting the haplotype tagged by the “A” allele of rs17070785 or the haplotype tagged by the “C” allele of rs221253 in the genomic sample;

(c) identifying the subject having the haplotype tagged by the “A” allele of rs17070785 or the haplotype tagged by the “C” allele of rs221253 in the genomic sample as likely to have an improved response to olanzapine as compared to control subject; and

(d) administering a treatment comprising olanzapine to the subject with the haplotype tagged by the “A” allele of rs17070785 or the haplotype tagged by the “C” allele of rs221253.

13. A method of treating a human subject having or at risk of developing SZ comprising administering an effective amount of olanzapine to a subject determined to have a the haplotype tagged by the “A” allele of rs17070785 or the haplotype tagged by the “C” allele of rs221253.

14. A method of detecting the presence of a polymorphism in the PLAGL1 gene and administering an antipsychotic treatment to a human subject, the method comprising:

(a) obtaining a genomic sample from a human subject having or at risk of developing SZ;

(b) detecting the haplotype tagged by the “C” allele of rs2247408 or the haplotype tagged by the “A” allele of rs3819811 in the genomic sample;

(c) identifying the subject having the haplotype tagged by the “C” allele of rs2247408 or the haplotype tagged by the “A” allele of rs3819811 in the genomic sample as likely to have a poor response to olanzapine as compared to control subject; and

(d) administering an antipsychotic treatment other than olanzapine to the subject with the haplotype tagged by the “C” allele of rs2247408 or the haplotype tagged by the “A” allele of rs3819811.

15. The method of claim 14, comprising administering perphenazine, quetiapine, risperidone or ziprasidone to the subject.

16. A method of treating a human subject having or at risk of developing SZ comprising administering an effective amount of an antipsychotic agent that is not olanzapine to a subject determined to have a haplotype tagged by the “C” allele of rs2247408 or the haplotype tagged by the “A” allele of rs3819811.

17. A method of detecting the presence of a polymorphism in and administering a treatment to a human subject, the method comprising:

(a) obtaining a genomic sample from a human subject having or at risk of developing SZ;

(b) detecting the haplotype tagged by an allele selected from those provided in Table 2A in the genomic sample;

(c) identifying the subject having the haplotype tagged by the allele provided in Table 2A in the genomic sample as likely to have an improved response to perphenazine as compared to control subject; and

(d) administering a treatment comprising perphenazine to the subject with the haplotype tagged by the allele provided in Table 2A.

18. A method of treating a human subject having or at risk of developing SZ comprising administering an effective amount of perphenazine to a subject determined to have a haplotype tagged by an allele selected from those provided in Table 2A.

19. The method of claim 17, further comprising detecting the haplotype tagged by two or more alleles selected from those provided in Table 2A.
20. The method of claim 19, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 7.
21. A method of detecting the presence of a polymorphism in and administering a treatment to a human subject, the method comprising:
- (a) obtaining a genomic sample from a human subject having or at risk of developing SZ;
 - (b) detecting the haplotype tagged by an allele selected from those provided in Table 2B in the genomic sample;
 - (c) identifying the subject having the haplotype tagged by the allele provided in Table 2B in the genomic sample as likely to have a poor response to perphenazine as compared to control subject; and
 - (d) administering an antipsychotic treatment other than perphenazine to the subject with the haplotype tagged by the allele provided in Table 2B.
22. A method of treating a human subject having or at risk of developing SZ comprising administering an effective amount of an antipsychotic agent that is not perphenazine to a subject determined to have a haplotype tagged by an allele selected from those provided in Table 2B.
23. The method of claim 21, further comprising detecting the haplotype tagged by two or more alleles selected from those provided in Table 2B.
24. The method of claim 23, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 7.
25. The method of claim 21, comprising administering olanzapine, quetiapine, risperidone or ziprasidone to the subject.

26. A method of detecting the presence of a polymorphism in the MCPH1, PRKCE, CDH13, or SKOR2 gene and administering a treatment to a human subject, the method comprising:

(a) obtaining a genomic sample from a human subject having or at risk of developing SZ;

(b) detecting the haplotype tagged by the "C" allele of rs11774231, the haplotype tagged by the "C" allele of rs2278773, the haplotype tagged by the "A" allele of rs17570753, the haplotype tagged by the "C" allele of rs2116971, or the haplotype tagged by the "G" allele of rs9952628 in the genomic sample;

(c) identifying the subject having the haplotype tagged by the "C" allele of rs11774231, the haplotype tagged by the "C" allele of rs2278773, the haplotype tagged by the "A" allele of rs17570753, the haplotype tagged by the "C" allele of rs2116971, or the haplotype tagged by the "G" allele of rs9952628 in the genomic sample as likely to have an improved response to perphenazine as compared to control subject; and

(d) administering a treatment comprising perphenazine to the subject with the haplotype tagged by the "C" allele of rs11774231, the haplotype tagged by the "C" allele of rs2278773, the haplotype tagged by the "A" allele of rs17570753, the haplotype tagged by the "C" allele of rs2116971, or the haplotype tagged by the "G" allele of rs9952628.

27. A method of treating a human subject having or at risk of developing SZ comprising administering an effective amount of perphenazine to a subject determined to have a haplotype tagged by the "C" allele of rs11774231, the haplotype tagged by the "C" allele of rs2278773, the haplotype tagged by the "A" allele of rs17570753, the haplotype tagged by the "C" allele of rs2116971, or the haplotype tagged by the "G" allele of rs9952628.

28. A method of detecting the presence of a polymorphism in the MAML3 gene and administering a treatment to a human subject, the method comprising:

(a) obtaining a genomic sample from a human subject having or at risk of developing SZ;

(b) detecting the haplotype tagged by the "A" allele of rs11100483 in the genomic sample;

(c) identifying the subject having the haplotype tagged by the “A” allele of rs11100483 in the genomic sample as likely to have a poor response to perphenazine as compared to control subject; and

(d) administering an antipsychotic treatment other than perphenazine to the subject with the haplotype tagged by the “A” allele of rs11100483.

29. A method of treating a human subject having or at risk of developing SZ comprising administering an effective amount of an antipsychotic agent that is not perphenazine to a subject determined to have a haplotype tagged by the “A” allele of rs11100483.

30. The method of claim 28, comprising administering olanzapine, quetiapine, risperidone or ziprasidone to the subject.

31. A method of detecting the presence of a polymorphism in and administering a treatment to a human subject, the method comprising:

(a) obtaining a genomic sample from a human subject having or at risk of developing SZ;

(b) detecting the haplotype tagged by an allele selected from those provided in Table 3A in the genomic sample;

(c) identifying the subject having the haplotype tagged by the allele provided in Table 3A in the genomic sample as likely to have an improved response to quetiapine as compared to control subject; and

(d) administering a treatment comprising quetiapine to the subject with the haplotype tagged by the allele provided in Table 3A.

32. A method of treating a human subject having or at risk of developing SZ comprising administering an effective amount of quetiapine to a subject determined to have a haplotype tagged by an allele selected from those provided in Table 3A.

33. The method of claim 31, further comprising detecting the haplotype tagged by two or more alleles selected from those provided in Table 3A.

34. The method of claim 33, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 8.

35. A method of detecting the presence of a polymorphism in and administering a treatment to a human subject, the method comprising:

(a) obtaining a genomic sample from a human subject having or at risk of developing SZ;

(b) detecting the haplotype tagged by an allele selected from those provided in Table 3B in the genomic sample;

(c) identifying the subject having the haplotype tagged by the allele provided in Table 3B in the genomic sample as likely to have a poor response to quetiapine as compared to control subject; and

(d) administering an antipsychotic treatment other than quetiapine to the subject with the haplotype tagged by the allele provided in Table 3B.

36. A method of treating a human subject having or at risk of developing SZ comprising administering an effective amount of an antipsychotic agent that is not quetiapine to a subject determined to have a haplotype tagged by an allele selected from those provided in Table 3B.

37. The method of claim 35, further comprising detecting the haplotype tagged by two or more alleles selected from those provided in Table 3B.

38. The method of claim 37, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 8.

39. The method of claim 35, comprising administering olanzapine, perphenazine, risperidone or ziprasidone to the subject.

40. A method of detecting the presence of a polymorphism in the KCNMA1 gene and administering a treatment to a human subject, the method comprising:

(a) obtaining a genomic sample from a human subject having or at risk of developing SZ;

(b) detecting the haplotype tagged by the "C" allele of rs35793;

(c) identifying the subject having the haplotype tagged by the “C” allele of rs35793 in the genomic sample as likely to have a poor response to quetiapine as compared to control subject; and

(d) administering an antipsychotic treatment other than quetiapine to the subject with the haplotype tagged by the “C” allele of rs35793.

41. A method of treating a human subject having or at risk of developing SZ comprising administering an effective amount of an antipsychotic agent that is not quetiapine to a subject determined to have a haplotype tagged by the “C” allele of rs35793.

42. The method of claim 40, comprising administering olanzapine, perphenazine, risperidone or ziprasidone to the subject.

43. A method of detecting the presence of a polymorphism in and administering a treatment to a human subject, the method comprising:

(a) obtaining a genomic sample from a human subject having or at risk of developing SZ;

(b) detecting the haplotype tagged by an allele selected from those provided in Table 4A in the genomic sample;

(c) identifying the subject having the haplotype tagged by the allele provided in Table 4A in the genomic sample as likely to have an improved response to risperidone as compared to control subject; and

(d) administering a treatment comprising risperidone to the subject with the haplotype tagged by the allele provided in Table 4A.

44. A method of treating a human subject having or at risk of developing SZ comprising administering an effective amount of risperidone to a subject determined to have a haplotype tagged by an allele selected from those provided in Table 4A.

45. The method of claim 43, further comprising detecting the haplotype tagged by two or more alleles selected from those provided in Table 4A.

46. The method of claim 45, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 9.

47. A method of detecting the presence of a polymorphism in and administering a treatment to a human subject, the method comprising:

(a) obtaining a genomic sample from a human subject having or at risk of developing SZ;

(b) detecting the haplotype tagged by an allele selected from those provided in Table 4B in the genomic sample;

(c) identifying the subject having the haplotype tagged by the allele provided in Table 4B in the genomic sample as likely to have a poor response to risperidone as compared to control subject; and

(d) administering an antipsychotic treatment other than risperidone to the subject with the haplotype tagged by the allele provided in Table 4B.

48. A method of treating a human subject having or at risk of developing SZ comprising administering an effective amount of an antipsychotic agent that is not risperidone to a subject determined to have a haplotype tagged by an allele selected from those provided in Table 4B.

49. The method of claim 47, further comprising detecting the haplotype tagged by two or more alleles selected from those provided in Table 4B.

50. The method of claim 49, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 9.

51. The method of claim 47, comprising administering olanzapine, perphenazine, quetiapine or ziprasidone to the subject.

52. A method of detecting the presence of a polymorphism in the AGAP1 or NPAS3 gene and administering a treatment to a human subject, the method comprising:

(a) obtaining a genomic sample from a human subject having or at risk of developing SZ;

(b) detecting the haplotype tagged by the “C” allele of rs1869295 or the haplotype tagged by the “C” allele of rs1315115 in the genomic sample;

(c) identifying the subject having the haplotype tagged by the “C” allele of rs1869295 or the haplotype tagged by the “C” allele of rs1315115 in the genomic sample as likely to have a poor response to risperidone as compared to control subject; and

(d) administering an antipsychotic treatment other than risperidone to the subject with the haplotype tagged by the “C” allele of rs1869295 or the haplotype tagged by the “C” allele of rs1315115.

53. A method of treating a human subject having or at risk of developing SZ comprising administering an effective amount of an antipsychotic agent that is not risperidone to a subject determined to have a haplotype tagged by the “C” allele of rs1869295 or the haplotype tagged by the “C” allele of rs1315115.

54. The method of claim 52, comprising administering olanzapine, perphenazine, quetiapine or ziprasidone to the subject.

55. A method of detecting the presence of a polymorphism in and administering a treatment to a human subject, the method comprising:

(a) obtaining a genomic sample from a human subject having or at risk of developing SZ;

(b) detecting the haplotype tagged by an allele selected from those provided in Table 5A in the genomic sample;

(c) identifying the subject having the haplotype tagged by the allele provided in Table 5A in the genomic sample as likely to have an improved response to ziprasidone as compared to control subject; and

(d) administering a treatment comprising ziprasidone to the subject with the haplotype tagged by the allele provided in Table 5A.

56. A method of treating a human subject having or at risk of developing SZ comprising administering an effective amount of ziprasidone to a subject determined to have a haplotype tagged by an allele selected from those provided in Table 5A.

57. The method of claim 55, further comprising detecting the haplotype tagged by two or more alleles selected from those provided in Table 5A.

58. The method of claim 57, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 10.

59. A method of detecting the presence of a polymorphism in and administering a treatment to a human subject, the method comprising:

(a) obtaining a genomic sample from a human subject having or at risk of developing SZ;

(b) detecting the haplotype tagged by an allele selected from those provided in Table 5B in the genomic sample;

(c) identifying the subject having the haplotype tagged by the allele provided in Table 5B in the genomic sample as likely to have a poor response to ziprasidone as compared to control subject; and

(d) administering an antipsychotic treatment other than ziprasidone to the subject with the haplotype tagged by the allele provided in Table 5B.

60. A method of treating a human subject having or at risk of developing SZ comprising administering an effective amount of an antipsychotic agent that is not ziprasidone to a subject determined to have a haplotype tagged by an allele selected from those provided in Table 5B.

61. The method of claim 59, further comprising detecting the haplotype tagged by two or more alleles selected from those provided in Table 5B.

62. The method of claim 61, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 10.

63. The method of claim 59, comprising administering olanzapine, perphenazine, quetiapine or risperidone to the subject.

64. A method of detecting the presence of a polymorphism in the CDH4, LYN, or CNTN4 gene and administering a treatment to a human subject, the method comprising:

(a) obtaining a genomic sample from a human subject having or at risk of developing SZ;

(b) detecting the haplotype tagged by the “A” allele of rs4925300, the haplotype tagged by the “C” allele of rs1546519, or the haplotype tagged by the “A” allele of rs17194378 in the genomic sample;

(c) identifying the subject having the haplotype tagged by the “A” allele of rs4925300, the haplotype tagged by the “C” allele of rs1546519, or the haplotype tagged by the “A” allele of rs17194378 in the genomic sample as likely to have an improved response to ziprasidone as compared to control subject; and

(d) administering a treatment comprising ziprasidone to the subject with the haplotype tagged by the “A” allele of rs4925300, the haplotype tagged by the “C” allele of rs1546519, or the haplotype tagged by the “A” allele of rs17194378.

65. A method of treating a human subject having or at risk of developing SZ comprising administering an effective amount of ziprasidone to a subject determined to have a haplotype tagged by the “A” allele of rs4925300, the haplotype tagged by the “C” allele of rs1546519, or the haplotype tagged by the “A” allele of rs17194378.

66. A method of detecting the presence of a polymorphism in the NALCN gene and administering a treatment to a human subject, the method comprising:

(a) obtaining a genomic sample from a human subject having or at risk of developing SZ;

(b) detecting the haplotype tagged by the “C” allele of rs9585618 in the genomic sample;

(c) identifying the subject having the haplotype tagged by the “C” allele of rs9585618 in the genomic sample as likely to have a poor response to ziprasidone as compared to control subject; and

(d) administering an antipsychotic treatment other than ziprasidone to the subject with the haplotype tagged by the “C” allele of rs9585618.

67. A method of treating a human subject having or at risk of developing SZ comprising administering an effective amount of an antipsychotic agent that is not ziprasidone to a subject determined to have a haplotype tagged by the “C” allele of rs9585618.
68. The method of claim 66, comprising administering olanzapine, perphenazine, quetiapine or risperidone to the subject.
69. The method of any one of claims 3-68, wherein the subject has early, intermediate, or aggressive SZ.
70. The method of any one of claims 3-68, wherein the subject has one or more risk factors associated with SZ.
71. The method of any one of claims 3-68, wherein the haplotype tagged by an allele comprises determining the number of alleles tagging the haplotype in the subject.
72. The method of any one of claims 3-68, wherein the subject has a relative afflicted with SZ or a genetically-based phenotypic trait associated with risk for SZ.
73. The method of any one of claims 3-68, wherein the subject is Caucasian or comprises European ancestry.
74. A method of identifying and administering a treatment to a human subject, the method comprising:
- (a) obtaining a genomic sample from a human subject having or at risk of developing SZ;
 - (b) detecting two or more haplotypes tagged by alleles selected from those provided in Tables 1-5 in the genomic sample;
 - (c) calculating a predicted treatment efficacy for at least two drugs selected from the group consisting of olanzapine, perphenazine, quetiapine, risperidone, and ziprasidone;
 - (d) ranking the predicted efficacy of the at least two drugs; and
 - (e) administering a treatment comprising the drug with the highest predicted efficiency to the subject based on said ranking.

75. The method of claim 74, wherein detecting two or more haplotypes tagged by an allele comprises determining the number of alleles tagging the two or more haplotypes in the subject.

76. The method of claim 75, wherein calculating a predicted treatment efficacy for a given drug comprises assigning a weighted value to each haplotype influencing response to that drug and multiplying the weighted value by the number of alleles tagging the haplotype in the subject.

77. The method of claim 75, wherein calculating a predicted treatment efficacy for a given drug comprises using the equation:

$$P = C + \sum_i \beta_i N_i$$

wherein P is the predicted treatment efficacy measured in change in PANSS-T; C is the change in PANSS-T for individuals carrying zero alleles of any response-predicting haplotype for the drug, β is the weighted value for at least a first haplotype measured in PANSS-T; N is the number of alleles tagging at least the first haplotype; and i is the number of haplotypes detected.

78. The method of claim 74, comprising a predicted treatment efficacy for three, four or five drugs selected from the group consisting of olanzapine, perphenazine, quetiapine, risperidone, and ziprasidone.

79. The method of any one of claims 74-78, wherein the subject has early, intermediate, or aggressive SZ.

80. The method of any one of claims 74-78, wherein the subject has one or more risk factors associated with SZ.

81. The method of any one of claims 74-78, wherein the subject has a relative afflicted with SZ or a genetically-based phenotypic trait associated with risk for SZ.

82. The method of any one of claims 74-78, wherein the subject is Caucasian or comprises European ancestry.

83. An in vitro method of detecting the presence of a polymorphism in a human subject, the method comprising:

(a) detecting the haplotype tagged by an allele selected from those provided in Table 1A in a genomic sample from a human subject having or at risk of developing SZ; and

(b) identifying the subject having the haplotype tagged by the allele provided in Table 1A in the genomic sample as likely to have an improved response to olanzapine as compared to a control subject.

84. The method of claim 83, further comprising detecting the haplotype tagged by two or more alleles selected from those provided in Table 1A.

85. The method of claim 84, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 6.

86. A composition comprising olanzapine for use in treating a human subject having or at risk of developing SZ, the human subject having a haplotype tagged by an allele provided in Table 1A.

87. The composition of claim 86, wherein the human subject has a haplotype tagged by two or more alleles selected from those provided in Table 1A.

88. The composition of claim 87, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 6.

89. An in vitro method of detecting the presence of a polymorphism in a human subject, the method comprising:

(a) detecting the haplotype tagged by an allele selected from those provided in Table 1B in a genomic sample from a human subject having or at risk of developing SZ; and

(b) identifying the subject having the haplotype tagged by the allele provided in Table 1B in the genomic sample as likely to have a poor response to olanzapine as compared to a control subject.

90. The method of claim 89 further comprising detecting the haplotype tagged by two or more alleles selected from those provided in Table 1B.

91. The method of claim 90, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 6.

92. A composition comprising an antipsychotic agent that is not olanzapine for use in treating a human subject having or at risk of developing SZ, the human subject having a haplotype tagged by an allele provided in Table 1B.

93. The composition of claim 92, comprising perphenazine, quetiapine, risperidone or ziprasidone.

94. The composition of claim 92, wherein the human subject has a haplotype tagged by two or more alleles selected from those provided in Table 1B.

95. The composition of claim 94, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 6.

96. An in vitro method of detecting the presence of a polymorphism in a human subject, the method comprising:

(a) detecting a haplotype tagged by the “A” allele of rs17070785 or a haplotype tagged by the “C” allele of rs221253 in a genomic sample from a human subject having or at risk of developing SZ; and

(b) identifying the subject having the haplotype tagged by the “A” allele of rs17070785 or the haplotype tagged by the “C” allele of rs221253 in the genomic sample as likely to have an improved response to olanzapine as compared to a control subject.

97. A composition comprising olanzapine for use in treating a human subject having or at risk of developing SZ, the human subject having a haplotype tagged by the “A” allele of rs17070785 or a haplotype tagged by the “C” allele of rs221253.

98. An in vitro method of detecting the presence of a polymorphism in a human subject, the method comprising:

(a) detecting a haplotype tagged by the “C” allele of rs2247408 or the haplotype tagged by the “A” allele of rs3819811 in a genomic sample from a human subject having or at risk of developing SZ; and

(b) identifying the subject having the haplotype tagged by the “C” allele of rs2247408 or the haplotype tagged by the “A” allele of rs3819811 in the genomic sample as likely to have poor response to olanzapine as compared to a control subject.

99. A composition comprising an antipsychotic agent that is not olanzapine for use in treating a human subject having or at risk of developing SZ, the human subject having a haplotype tagged by the “C” allele of rs2247408 or the haplotype tagged by the “A” allele of rs3819811.

100. The composition of claim 99, comprising perphenazine, quetiapine, risperidone or ziprasidone.

101. An in vitro method of detecting the presence of a polymorphism in a human subject, the method comprising:

(a) detecting the haplotype tagged by an allele selected from those provided in Table 2A in a genomic sample from a human subject having or at risk of developing SZ; and

(b) identifying the subject having the haplotype tagged by the allele provided in Table 2A in the genomic sample as likely to have an improved response to perphenazine as compared to a control subject.

102. The method of claim 101, further comprising detecting the haplotype tagged by two or more alleles selected from those provided in Table 2A.

103. The method of claim 102, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 7.

104. A composition comprising perphenazine for use in treating a human subject having or at risk of developing SZ, the human subject having a haplotype tagged by an allele provided in Table 2A.

105. The composition of claim 104, wherein the human subject has a haplotype tagged by two or more alleles selected from those provided in Table 2A.

106. The composition of claim 105, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 7.

107. An in vitro method of detecting the presence of a polymorphism in a human subject, the method comprising:

(a) detecting the haplotype tagged by an allele selected from those provided in Table 2B in a genomic sample from a human subject having or at risk of developing SZ; and

(b) identifying the subject having the haplotype tagged by the allele provided in Table 2B in the genomic sample as likely to have a poor response to perphenazine as compared to a control subject.

108. The method of claim 107 further comprising detecting the haplotype tagged by two or more alleles selected from those provided in Table 2B.

109. The method of claim 108, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 7.

110. A composition comprising an antipsychotic agent that is not perphenazine for use in treating a human subject having or at risk of developing SZ, the human subject having a haplotype tagged by an allele provided in Table 2B.

111. The composition of claim 110, comprising olanzapine, quetiapine, risperidone or ziprasidone.

112. The composition of claim 110, wherein the human subject has a haplotype tagged by two or more alleles selected from those provided in Table 2B.

113. The composition of claim 112, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 7.

114. An in vitro method of detecting the presence of a polymorphism in a human subject, the method comprising:

(a) detecting a haplotype tagged by the "C" allele of rs11774231, the haplotype tagged by the "C" allele of rs2278773, the haplotype tagged by the "A" allele of rs17570753, the haplotype tagged by the "C" allele of rs2116971, or the haplotype tagged by the "G" allele of rs9952628 in a genomic sample from a human subject having or at risk of developing SZ; and

(b) identifying the subject having the haplotype tagged by the "C" allele of rs11774231, the haplotype tagged by the "C" allele of rs2278773, the haplotype tagged by the "A" allele of rs17570753, the haplotype tagged by the "C" allele of rs2116971, or the

haplotype tagged by the “G” allele of rs9952628 in the genomic sample as likely to have an improved response to perphenazine as compared to a control subject.

115. A composition comprising perphenazine for use in treating a human subject having or at risk of developing SZ, the human subject having a haplotype tagged by the “C” allele of rs11774231, the haplotype tagged by the “C” allele of rs2278773, the haplotype tagged by the “A” allele of rs17570753, the haplotype tagged by the “C” allele of rs2116971, or the haplotype tagged by the “G” allele of rs9952628.

116. An in vitro method of detecting the presence of a polymorphism in a human subject, the method comprising:

(a) detecting a haplotype tagged by the “A” allele of rs11100483 in a genomic sample from a human subject having or at risk of developing SZ; and

(b) identifying the subject having the haplotype tagged by the “A” allele of rs11100483 in the genomic sample as likely to have poor response to perphenazine as compared to a control subject.

117. A composition comprising an antipsychotic agent that is not perphenazine for use in treating a human subject having or at risk of developing SZ, the human subject having a haplotype tagged by the “A” allele of rs11100483.

118. The composition of claim 117, comprising olanzapine, quetiapine, risperidone or ziprasidone.

119. An in vitro method of detecting the presence of a polymorphism in a human subject, the method comprising:

(a) detecting the haplotype tagged by an allele selected from those provided in Table 3A in a genomic sample from a human subject having or at risk of developing SZ; and

(b) identifying the subject having the haplotype tagged by the allele provided in Table 3A in the genomic sample as likely to have an improved response to quetiapine as compared to a control subject.

120. The method of claim 119, further comprising detecting the haplotype tagged by two or more alleles selected from those provided in Table 3A.

121. The method of claim 120, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 8.

122. A composition comprising quetiapine for use in treating a human subject having or at risk of developing SZ, the human subject having a haplotype tagged by an allele provided in Table 3A.

123. The composition of claim 122, wherein the human subject has a haplotype tagged by two or more alleles selected from those provided in Table 3A.

124. The composition of claim 123, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 8.

125. An in vitro method of detecting the presence of a polymorphism in a human subject, the method comprising:

(a) detecting the haplotype tagged by an allele selected from those provided in Table 3B in a genomic sample from a human subject having or at risk of developing SZ; and

(b) identifying the subject having the haplotype tagged by the allele provided in Table 3B in the genomic sample as likely to have a poor response to quetiapine as compared to a control subject.

126. The method of claim 125 further comprising detecting the haplotype tagged by two or more alleles selected from those provided in Table 3B.

127. The method of claim 126, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 8.

128. A composition comprising an antipsychotic agent that is not quetiapine for use in treating a human subject having or at risk of developing SZ, the human subject having a haplotype tagged by an allele provided in Table 3B.

129. The composition of claim 128, comprising olanzapine, perphenazine, risperidone or ziprasidone.

130. The composition of claim 128, wherein the human subject has a haplotype tagged by two or more alleles selected from those provided in Table 3B.

131. The composition of claim 130, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 8.

132. An in vitro method of detecting the presence of a polymorphism in a human subject, the method comprising:

(a) detecting a haplotype tagged by the “C” allele of rs35793 in a genomic sample from a human subject having or at risk of developing SZ; and

(b) identifying the subject having the haplotype tagged by the “C” allele of rs35793 in the genomic sample as likely to have poor response to quetiapine as compared to a control subject.

133. A composition comprising an antipsychotic agent that is not quetiapine for use in treating a human subject having or at risk of developing SZ, the human subject having a haplotype tagged by the “C” allele of rs35793.

134. The composition of claim 133, comprising olanzapine, perphenazine, risperidone or ziprasidone.

135. An in vitro method of detecting the presence of a polymorphism in a human subject, the method comprising:

(a) detecting the haplotype tagged by an allele selected from those provided in Table 4A in a genomic sample from a human subject having or at risk of developing SZ; and

(b) identifying the subject having the haplotype tagged by the allele provided in Table 4A in the genomic sample as likely to have an improved response to risperidone as compared to a control subject.

136. The method of claim 135, further comprising detecting the haplotype tagged by two or more alleles selected from those provided in Table 4A.

137. The method of claim 136, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 9.

138. A composition comprising risperidone for use in treating a human subject having or at risk of developing SZ, the human subject having a haplotype tagged by an allele provided in Table 4A.

139. The composition of claim 138, wherein the human subject has a haplotype tagged by two or more alleles selected from those provided in Table 4A.

140. The composition of claim 139, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 9.

141. An in vitro method of detecting the presence of a polymorphism in a human subject, the method comprising:

(a) detecting the haplotype tagged by an allele selected from those provided in Table 4B in a genomic sample from a human subject having or at risk of developing SZ; and

(b) identifying the subject having the haplotype tagged by the allele provided in Table 4B in the genomic sample as likely to have a poor response to risperidone as compared to a control subject.

142. The method of claim 141 further comprising detecting the haplotype tagged by two or more alleles selected from those provided in Table 4B.

143. The method of claim 142, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 9.

144. A composition comprising an antipsychotic agent that is not risperidone for use in treating a human subject having or at risk of developing SZ, the human subject having a haplotype tagged by an allele provided in Table 4B.

145. The composition of claim 144, comprising olanzapine, perphenazine, quetiapine or ziprasidone.

146. The composition of claim 144, wherein the human subject has a haplotype tagged by two or more alleles selected from those provided in Table 4B.

147. The composition of claim 146, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 9.

148. An in vitro method of detecting the presence of a polymorphism in a human subject, the method comprising:

(a) detecting a haplotype tagged by the “A” allele of rs9713, the haplotype tagged by the “C” allele of rs874295, or the haplotype tagged by the “C” allele of rs3738883 in a genomic sample from a human subject having or at risk of developing SZ; and

(b) identifying the subject having the haplotype tagged by the “A” allele of rs9713, the haplotype tagged by the “C” allele of rs874295, or the haplotype tagged by the “C” allele of rs3738883 in the genomic sample as likely to have an improved response to risperidone as compared to a control subject.

149. A composition comprising risperidone for use in treating a human subject having or at risk of developing SZ, the human subject having a haplotype tagged by the “A” allele of rs9713, the haplotype tagged by the “C” allele of rs874295, or the haplotype tagged by the “C” allele of rs3738883.

150. An in vitro method of detecting the presence of a polymorphism in a human subject, the method comprising:

(a) detecting a haplotype tagged by the “C” allele of rs1869295 or the haplotype tagged by the “C” allele of rs1315115 in a genomic sample from a human subject having or at risk of developing SZ; and

(b) identifying the subject having the haplotype tagged by the “C” allele of rs1869295 or the haplotype tagged by the “C” allele of rs1315115 in the genomic sample as likely to have poor response to risperidone as compared to a control subject.

151. A composition comprising an antipsychotic agent that is not risperidone for use in treating a human subject having or at risk of developing SZ, the human subject having a haplotype tagged by the “C” allele of rs1869295 or the haplotype tagged by the “C” allele of rs1315115.

152. The composition of claim 151, comprising olanzapine, perphenazine, quetiapine or ziprasidone.

153. An in vitro method of detecting the presence of a polymorphism in a human subject, the method comprising:

(a) detecting the haplotype tagged by an allele selected from those provided in Table 5A in a genomic sample from a human subject having or at risk of developing SZ; and

(b) identifying the subject having the haplotype tagged by the allele provided in Table 5A in the genomic sample as likely to have an improved response to ziprasidone as compared to a control subject.

154. The method of claim 153, further comprising detecting the haplotype tagged by two or more alleles selected from those provided in Table 5A.

155. The method of claim 154, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 10.

156. A composition comprising ziprasidone for use in treating a human subject having or at risk of developing SZ, the human subject having a haplotype tagged by an allele provided in Table 5A.

157. The composition of claim 156, wherein the human subject has a haplotype tagged by two or more alleles selected from those provided in Table 5A.

158. The composition of claim 157, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 10.

159. An in vitro method of detecting the presence of a polymorphism in a human subject, the method comprising:

(a) detecting the haplotype tagged by an allele selected from those provided in Table 5B in a genomic sample from a human subject having or at risk of developing SZ; and

(b) identifying the subject having the haplotype tagged by the allele provided in Table 5B in the genomic sample as likely to have a poor response to ziprasidone as compared to a control subject.

160. The method of claim 159 further comprising detecting the haplotype tagged by two or more alleles selected from those provided in Table 5B.

161. The method of claim 160, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 10.

162. A composition comprising an antipsychotic agent that is not ziprasidone for use in treating a human subject having or at risk of developing SZ, the human subject having a haplotype tagged by an allele provided in Table 5B.

163. The composition of claim 162, comprising olanzapine, perphenazine, quetiapine or risperidone.

164. The composition of claim 162, wherein the human subject has a haplotype tagged by two or more alleles selected from those provided in Table 5B.

165. The composition of claim 164, wherein said two or more alleles are alleles from two or more different correlated clusters selected from those provided in Table 10.

166. An in vitro method of detecting the presence of a polymorphism in a human subject, the method comprising:

(a) detecting a haplotype tagged by the “A” allele of rs4925300, the haplotype tagged by the “C” allele of rs1546519, or the haplotype tagged by the “A” allele of rs17194378 in a genomic sample from a human subject having or at risk of developing SZ; and

(b) identifying the subject having the haplotype tagged by the “A” allele of rs4925300, the haplotype tagged by the “C” allele of rs1546519, or the haplotype tagged by the “A” allele of rs17194378 in the genomic sample as likely to have an improved response to ziprasidone as compared to a control subject.

167. A composition comprising ziprasidone for use in treating a human subject having or at risk of developing SZ, the human subject having a haplotype tagged by the “A” allele of rs4925300, the haplotype tagged by the “C” allele of rs1546519, or the haplotype tagged by the “A” allele of rs17194378.

168. An in vitro method of detecting the presence of a polymorphism in a human subject, the method comprising:

(a) detecting a haplotype tagged by the “C” allele of rs9585618 in a genomic sample from a human subject having or at risk of developing SZ; and

(b) identifying the subject having the haplotype tagged by the “C” allele of rs9585618 in the genomic sample as likely to have poor response to ziprasidone as compared to a control subject.

169. A composition comprising an antipsychotic agent that is not ziprasidone for use in treating a human subject having or at risk of developing SZ, the human subject having a haplotype tagged by the “C” allele of rs9585618.

170. The composition of claim 169, comprising olanzapine, perphenazine, quetiapine or risperidone to the subject.

171. An in vitro assay method comprising:

(a) detecting two or more haplotypes tagged by alleles selected from those provided in Tables 1-5 in a genomic sample from a human subject having or at risk of developing SZ;

(c) calculating a predicted treatment efficacy for at least two drugs selected from the group consisting of olanzapine, perphenazine, quetiapine, risperidone, and ziprasidone; and

(d) ranking the predicted efficacy of the at least two drugs.

172. The method of claim 171, wherein detecting two or more haplotypes tagged by an allele comprises determining the number of alleles tagging the two or more haplotypes in the subject.

173. The method of claim 172, wherein calculating a predicted treatment efficacy for a given drug comprises assigning a weighted value to each haplotype influencing response to that drug and multiplying the weighted value by the number of alleles tagging the haplotype in the subject.

174. The method of claim 172, wherein calculating a predicted treatment efficacy for a given drug comprises using the equation:

$$P = C + \sum_i \beta_i N_i$$

wherein P is the predicted treatment efficacy measured in change in PANSS-T; C is the change in PANSS-T for individuals carrying zero alleles of any response-predicting haplotype for the drug, β is the weighted value for at least a first haplotype measured in PANSS-T; N is the number of alleles tagging at least the first haplotype; and i is the number of haplotypes detected.

175. The method of claim 171, comprising a predicted treatment efficacy for three, four or five drugs selected from the group consisting of olanzapine, perphenazine, quetiapine, risperidone, and ziprasidone.

176. The method or composition of any one of claims 83-175, wherein the subject has early, intermediate, or aggressive SZ.

177. The method or composition of any one of claims 83-175, wherein the subject has one or more risk factors associated with SZ.

178. The method or composition of any one of claims 83-175, wherein the haplotype tagged by an allele comprises determining the number of alleles tagging the haplotype in the subject.

179. The method or composition of any one of claims 83-175, wherein the subject has a relative afflicted with SZ or a genetically-based phenotypic trait associated with risk for SZ.

180. The method or composition of any one of claims 83-175, wherein the subject is Caucasian or comprises European ancestry.

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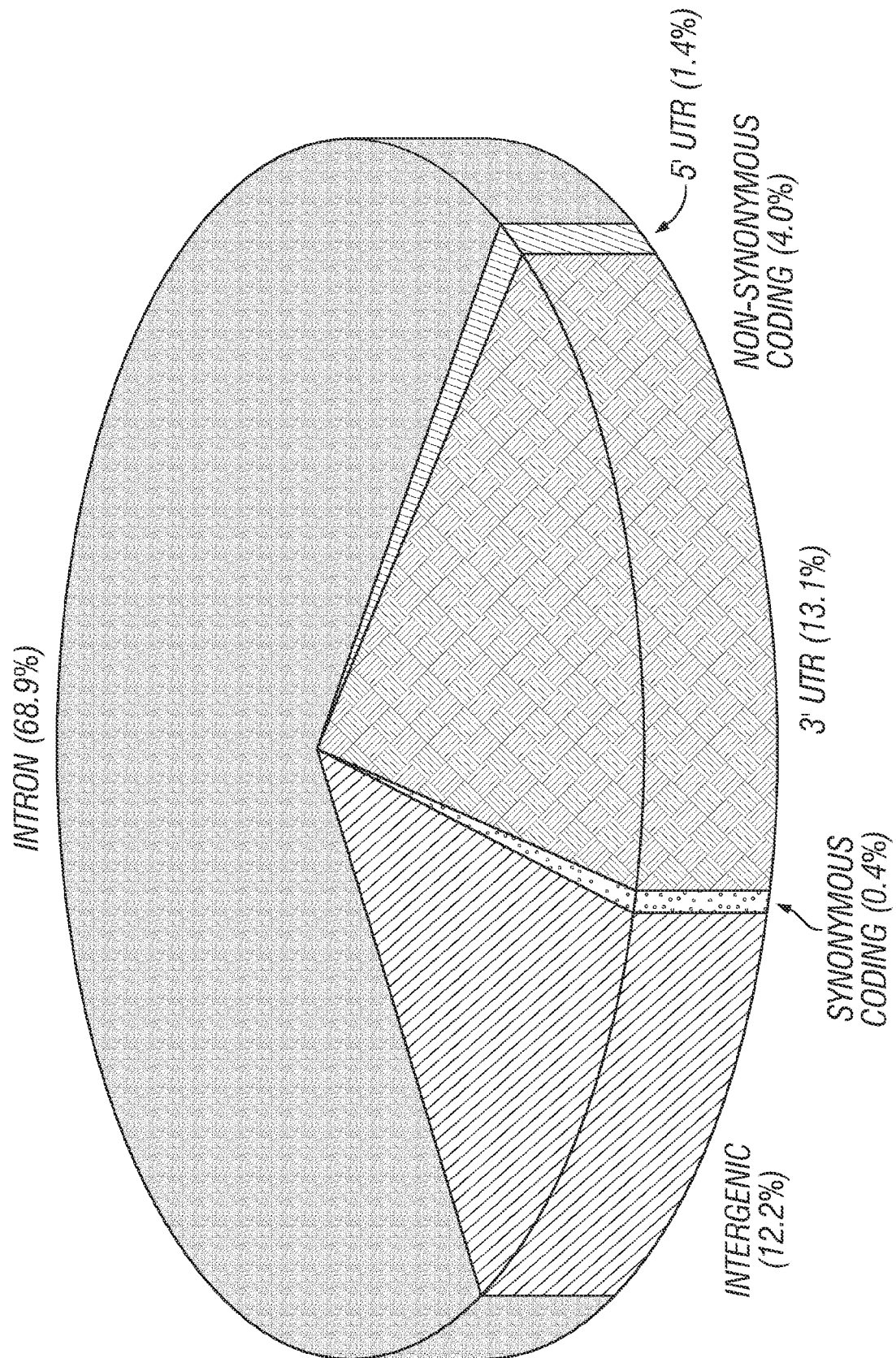


FIG. 1

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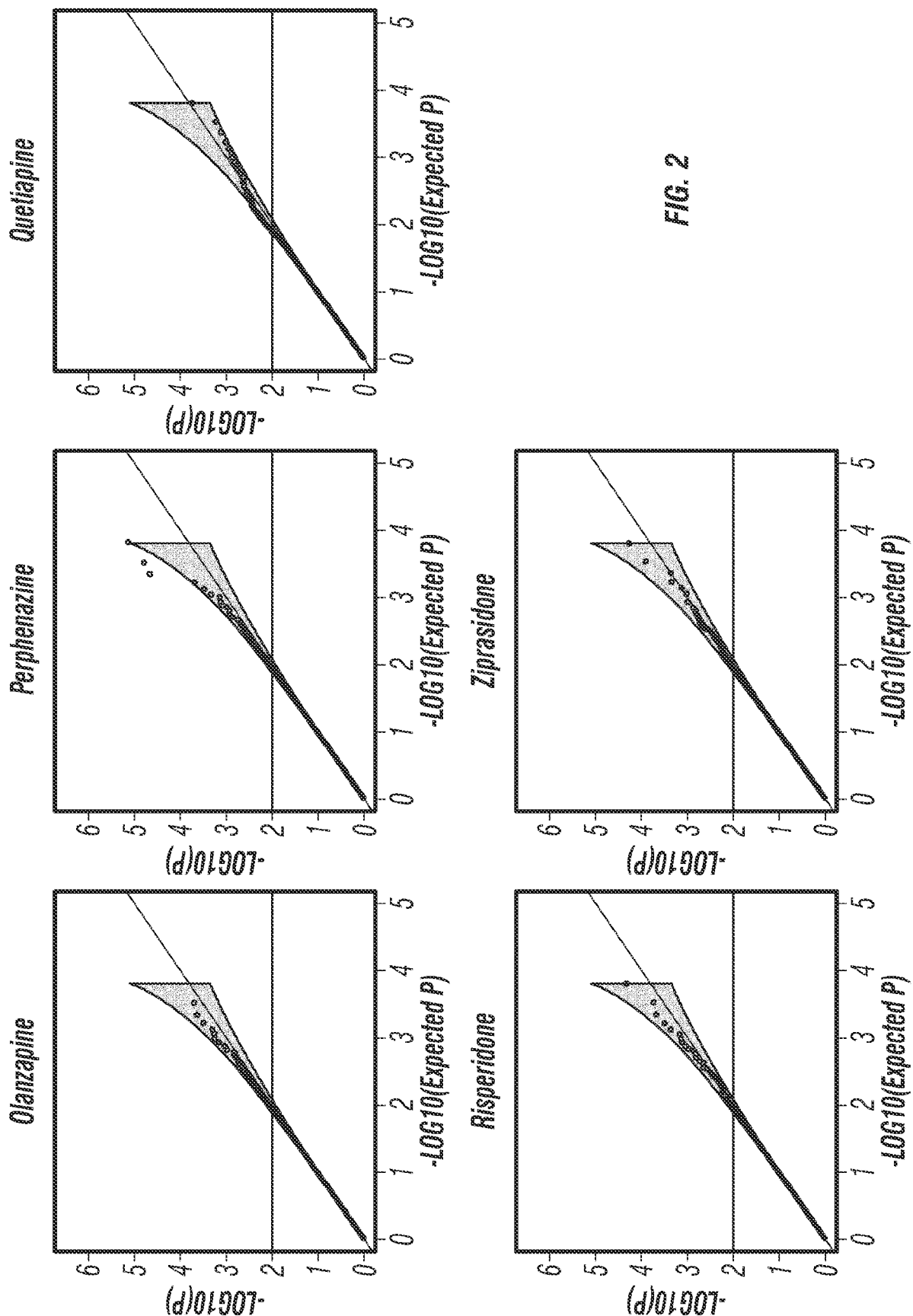


FIG. 2