SUMMARY OF THE INVENTION

The present inventors have performed genome wide association study on several large patient cohorts and have successfully identified a number of target genes harboring copy number variations associated with autism and ASD. Thus, in accordance with the present invention, kits are provided for performance of a method for detecting a propensity for developing autism or autistic spectrum disorder is provided. An exemplary kit comprises means for obtaining a sample from a patient and testing the sample for the presence or absence of at least one deletion containing CNV in a target polynucleotide, wherein if the CNV is present, the patient has an increased risk for developing autism and/or autistic spectrum disorder. In a preferred embodiment, the deletion containing CNV is selected from the group of CNVs provided in Table II. In another embodiment, the kit includes reagents for performing the step of detecting the presence of said CNV and further comprises specific reagents for performing a process selected from the group consisting of detection of specific hybridization, measurement of allele size, restriction fragment length polymorphism analysis, allele-specific hybridization analysis, single base primer extension reaction, and sequencing of an amplified polynucleotide.

In one aspect, there is provided a kit for use in a method for detecting a propensity for developing autism or autistic spectrum disorder, the kit comprising:

a) providing a plurality of nucleic acids comprising CNVs present in autistic or ASD patients identified using genome wide association studies of large patient cohorts, said CNVs being listed in Table II;

a) means for obtaining a sample from a patient and isolating nucleic acid therefrom;

b) reagents suitable for identifying the presence or absence of at least one deletion containing CNV in a target polynucleotide and means for creating a report from from said identifying.

In one aspect, there is provided a method for identifying agents which alter neuronal signaling and/or morphology, comprising:

a) providing cells expressing a nucleic acid sequence comprising at least one CNV as described herein;

b) providing cells which express the cognate wild type sequences corresponding to the CNV of step a);

c) contacting the cells of steps a) and b) with a test agent and

d) analyzing whether said agent alters neuronal signaling and/or morphology of cells of step a) relative to those of step b), thereby identifying agents which alter neuronal signaling and morphology.

In one aspect, there is provided the use of a therapeutically effective amount of at least one agent which is known to be efficacious in the signaling pathway adversely affected by the presence of said CNV, in the manufacture of a medicament for treating autism or ASD in a human subject determined to have at least copy number variation (CNV) associated with an autistic or ASD phenotype, said at least one CNV being selected from the group consisting of CNVs set out in Table 2.

In one aspect, there is provided a kit for detecting a propensity for developing autism or autistic spectrum disorder, the kit comprising:

a) reagents suitable for obtaining a sample from a patient and isolating nucleic acid therefrom;

b) reagents suitable for amplifying the nucleic acid of step a);

c) a microarray comprising nucleic acids of known sequence with the amplified nucleic acids of step b), thereby identifying the presence or absence of at least one deletion containing CNV in a target polynucleotide, said CNV being listed in Table II; and means for creating a report indicating that if said CNV is present, said patient has an increased risk for developing autism and/or autistic spectrum disorder.

In another aspect, the present invention provides a method for identifying agents which alter neuronal signaling and/or morphology. An exemplary method entails providing cells expressing at least one CNV listed in Table 2 and cells which express the cognate wild type sequences corresponding to the CNV containing sequence, contacting both cell types with a test agent and analyzing whether the agent alters neuronal signaling and/or morphology of cells comprising the CNV relative to those which lack the genetic alteration, thereby identifying agents which alter neuronal signaling and morphology in CNV containing cells. In cases where the CNV is a deletion, vectors encoding such CNVs contain nucleic acids flanking the affected region of deletion of a suitable length, such that cloning and transformation of cells with the CNV containing nucleic acid is possible.

Also provided is a method of treating autism or ASD in a human subject determined to have at least copy number variation (CNV) associated with an autistic or ASD phenotype, said at least one CNV being selected from the group consisting of CNVs set out in Table 2, the method comprising administering to said human subject a therapeutically effective amount of at least one agent which is known to be

c) contacting the cells of steps a) and b) with a test agent and

d) analyzing whether said agent alters neuronal signaling and/or morphology of cells of step a) relative to those of step b), thereby identifying agents which alter neuronal signaling and morphology.

7. Use of a therapeutically effective amount of at least one agent which is known to be efficacious in the signaling pathway adversely affected by the presence of said CNV, in the manufacture of a medicament for treating autism or ASD in a human subject determined to have at least copy number variation (CNV) associated with an autistic or ASD phenotype, said at least one CNV being selected from the group consisting of CNVs set out in Table 2.

8. The use of claim 7, wherein said CNV containing gene is selected from the group consisting of ATP10A, GABRA5, GABRB3, GABRG3, GGTLC2, HBII-52-45, HBII-52-46, IPW, LOC648691, LOC96610, MAGEL2, MIR650, MKRN3, NCRNA00221, NDN, OCA2, OR4S2, PAR-SN, PAR1, PAR5, POM121L1P, PRAME, SNORD107, SNORD108, SNORD109A, SNORD109B, SNORD115-11, SNORD115-29, SNORD115-36, SNORD115-43, SNORD115-44, SNORD115-48, SNORD64, SNRPN, SNURF, UBE3A, ZNF280A, ZNF280B.

9. The use of claim 7, wherein said agent alters GABA signaling and is listed in Table 3 or Table 4.

10. The use of claim 9, wherein said gene is selected from the group consisting of GABRA5, GABRA3, GABRB3 and said agent is topiramide.

11. A kit for detecting a propensity for developing autism or autistic spectrum disorder, the kit comprising:

a) reagents suitable for obtaining a sample from a patient and isolating nucleic acid therefrom;

b) reagents suitable for amplifying the nucleic acid of step a);

c) a microarray comprising nucleic acids of known sequence with the amplified nucleic acids of step b), thereby identifying the presence or absence of at least one deletion containing CNV in a target polynucleotide, said CNV being listed