

expression analysis, where suicide completers were found to have significantly higher ACP1 expression than non-suicide victims (12). The strongest association signal from another GWAS of suicide attempt on the bipolar disorder (STEP-BD, WTCCC, UCL) came from the intergenic chromosome 10 marker rs1466846; this finding was not replicated in the replication sample (GAIN, TGEN, German) (10). A GWAS on suicidality scores, which are derived from the SCAN interview, was conducted with a major depression sample from the RADIANT study (11). The suicidality score captures suicide severity from suicide ideation to attempt. The most significant findings from the RADIANT sample failed to replicate in the German replication sample.

[0005] At the present time, there is a lack of meaningful genetic predictors of suicidal behavior. Thus, there is a need in the art for diagnostic assays and tests to identify subjects at risk for suicide. Further there is a need in the art to genetic markers and kits that can be used to identify subjects at risk for suicide.

SUMMARY OF THE INVENTION

[0006] The present ~~invention~~ disclosure relates to risk markers for suicide. More specifically, the present ~~invention~~ disclosure relates to genetic risk markers for suicide and use thereof.

[0007] According to one aspect of the present invention disclosure, there is provided a method of identifying a subject at risk for suicide comprising identifying in a biological sample from the subject one or more genetic markers associated with suicide, at least one marker being defined by rs2491144 (SEQ ID NO:1), wherein the presence of the G allele in marker rs2491144 identifies the subject is at increased risk for suicide.

[0008] According to the present ~~invention~~ disclosure, there is provided a method as described above and herein further comprising identifying one or more additional genetic markers associated with suicide in the biological sample from the subject, the one or more additional genetic markers being defined by the group consisting of rs9315639 (SEQ ID NO:2), rs11082138 (SEQ ID NO:3), rs11697517 (SEQ ID NO:4), and rs2186437 (SEQ ID NO:5), wherein the presence of any of the C allele in marker

rs9315639, the C allele in marker rs11082138, the T allele in marker rs11697517, and C allele in marker rs2186437 identifies the subject is at increased risk for suicide.

[0009] According to the present ~~invention~~disclosure, there is also provided a method as described above and herein, further comprising a step of obtaining the biological sample from the subject.

[0010] According to the present ~~invention~~disclosure, there is also provided a method as described above and herein wherein the biological sample is a sample from blood, saliva, spinal fluid, brain biopsy, cultured cells obtained from the subject, stool, urine, autopsy samples, or frozen sections taken for histological purposes.

[0011] According to the present ~~invention~~disclosure, there is also provided a method as described above and herein wherein the step of identifying in a biological sample from the subject one or more genetic markers associated with suicide comprises PCR analysis, sequencing, 5' exonuclease fluorescence assay, probe hybridization or a combination thereof.

[0012] According to the present ~~invention~~disclosure, there is also provided a method as described above and herein wherein the subject is a subject diagnosed with a mental illness.

[0013] According to the present ~~invention~~disclosure there is also provided a method as described above and herein wherein the mental illness is selected from the group consisting of depression, schizophrenia, schizoaffective disorder, bipolar disorder, personality disorder, seasonal affective disorder, anxiety disorder, and post traumatic stress disorder.

[0014] According to the present ~~invention~~disclosure there is also provided a method as described above and herein wherein the subject exhibits one or more clinical symptoms of a mental illness.

[0015] According to the present ~~invention~~disclosure there is also provided a method as described above and herein wherein the subject exhibits one or more symptoms of a mental illness selected from the group consisting of depression, schizophrenia,

schizoaffective disorder, bipolar disorder, personality disorder, seasonal affective disorder, anxiety disorder, and post traumatic stress disorder.

[0016] According to the present ~~invention~~-disclosure there is also provided a method as described above and herein further comprising receiving, in a computer system, the subject's genotype for the one or more genetic markers associated with suicide and the identifying step is performed by the computer system.

[0017] According to the present ~~invention~~-disclosure there is also provided a method as described above and herein wherein the subject's genotype is received directly from equipment used in determining the patient's genotype.

[0018] According to the present ~~invention~~-disclosure there is also provided a method as described above and herein further comprising receiving, in a computer system, the patient's diagnosis.

[0019] According to the present ~~invention~~-disclosure there is also provided a method as described above and herein further comprising a step of outputting an indication of whether or not the subject is at increased risk for suicide.

[0020] According to the present ~~invention~~-disclosure there is also provided a method as described above and herein wherein the indication of whether or not the subject is at increased risk for suicide is represented on a patient specific report.

[0021] According to another aspect of the present ~~invention~~-disclosure, there is also provided a computer readable medium containing executable instructions that when executed cause one or a plurality of processors to receive a subject's genotype for one or more genetic markers associated with suicide selected from the group consisting of rs2491144 (SEQ ID NO:1), rs9315639 (SEQ ID NO:2), rs11082138 (SEQ ID NO:3), rs11697517 (SEQ ID NO:4), and rs2186437 (SEQ ID NO:5); identify the presence of any of the G allele in marker rs2491144 (SEQ ID NO:1), the C allele in marker rs9315639 (SEQ ID NO:2), the C allele in marker rs11082138 (SEQ ID NO:3), the T allele in marker rs11697517 (SEQ ID NO:4), and C allele in marker rs2186437 (SEQ ID NO:5), and output an indication that the subject is at increased risk for suicide if at least the G allele in

marker rs2491144 (SEQ ID NO:1) is present or a null result if the G allele in marker rs2491144 (SEQ ID NO:1) is absent.

[0021a] In yet another aspect of the present disclosure, there is provided a method for reducing the risk of suicide in a subject identified as being at increased risk for suicide according to the method as described above and herein, the method comprising one or more of

a) monitoring the subject;

b) counseling the subject;

c) testing or screening the subject for mental illness or one or more symptoms that are associated with mental illness or suicide,

d) testing the biological sample comprising genomic DNA or a second biological sample obtained from the subject for one or more additional genetic markers, nucleotide sequences, proteins, metabolites or any combination thereof;

e) removing or reducing access to compounds, compositions, articles or cues which increase suicide risk, or

any combination thereof.

[0022] According to the present ~~invention~~ disclosure, there is also provided a method for reducing the risk of suicide in a subject identified as being at increased risk for suicide according to the method as described above and herein, the method comprising one or more of

a) treating the subject with medication, non-medicinal therapy or a combination thereof;

b) monitoring the subject;

c) counseling the subject;

d) testing or screening the subject for mental illness or one or more symptoms that are associated with mental illness or suicide,

e) testing the biological sample comprising genomic DNA or a second biological sample obtained from the subject for one or more additional genetic markers, nucleotide sequences, proteins, metabolites or any combination thereof;

f) removing or reducing access to compounds, compositions, articles or cues which increase suicide risk, or

any combination thereof.

[0023] According to the present ~~invention~~-disclosure there is also provided a method as described above and herein wherein treating the subject with medication comprises administering one or more antipsychotics, mood stabilizers, antidepressants, anticonvulsants, antianxiolytics, or any combination thereof.

[0024] According to the present ~~invention~~-disclosure there is also provided a method as described above and herein wherein the medication comprises clozapine, lithium, or ketamine.

[0025] According to the present ~~invention-disclosure~~ there is also provided a method as described above and herein wherein the non-medicinal therapy comprises electroconvulsive or electroshock therapy, magnetic seizure therapy, transcranial magnetic stimulation, cognitive behavioral therapy, dialectical behavioral therapy, risk dissipation group therapy, deep brain stimulation, or a combination thereof.

[0026] According to the present ~~invention-disclosure~~ there is also provided a method as described above and herein wherein said testing or screening the subject for mental illness or one or more symptoms associated with suicide or mental illness comprises testing or screening the subject for depression, schizophrenia, schizoaffective disorder, bipolar disorder, obsessive compulsive disorder, personality disorder, seasonal affective disorder, addiction, drug abuse, alcoholism, problem gambling, increased anxiety, anxiety disorder, feelings of worthlessness, psychotic symptoms, delusions, hallucinations, agitation, restlessness, irritability, aggression or anger.

[0027] According to a further aspect of the present ~~invention-disclosure~~ there is also provided a kit comprising,

a) one or more primers to amplify a nucleotide sequence that comprises the polymorphism as defined in:

rs2491144 (SEQ ID NO:1) or a fragment thereof comprising the polymorphic site, or the complement of SEQ ID NO:1 or a fragment thereof comprising the polymorphic site;

rs9315639 (SEQ ID NO:2) or a fragment thereof comprising the polymorphic site, or the complement of SEQ ID NO:2 or a fragment thereof comprising the polymorphic site;

rs11082138 (SEQ ID NO:3) or a fragment thereof comprising the polymorphic site, or the complement of SEQ ID NO:3 or a fragment thereof comprising the polymorphic site;

rs11697517 (SEQ ID NO:4) or a fragment thereof comprising the polymorphic site, or the complement of SEQ ID NO:4 or a fragment thereof comprising the polymorphic site,

rs2186437 (SEQ ID NO:5) or a fragment thereof comprising the polymorphic site, or the complement of SEQ ID NO:5 or a fragment thereof comprising the polymorphic site,

or any combination thereof;

b) one or more probes that hybridize to SEQ ID NOs:1, 2, 3, 4, or 5, or the complement thereof, over a region of nucleotides comprising the polymorphic site, wherein said probe hybridizes to a particular variant of the polymorphism at the polymorphic site;

c) one or more reagents and/or products comprising buffers, nucleotides, DNA amplifying enzymes, or any combination thereof;

d) one or more reagents, components and/or products for genotyping the polymorphisms of SEQ ID NO:1, 2, 3, 4, 5, their complements or any combination thereof,

e) one or more reagents, components and/or products for performing a DNA sequencing reaction that determines the sequence of SEQ ID NO: 1, 2, 3, 4, 5, their complements or any combination thereof,

f) a gene chip or nucleotide sequence array comprising a plurality of nucleotide sequences comprising or consisting of any one or combination of SEQ ID NOs:1-5, a fragment thereof comprising the polymorphic site or their complements;

g) one or more instructions for using the components as described herein, practicing the methods as described herein, interpreting the data obtained from practicing the methods, or any combination thereof;

h) a scale, reference or the like that may be used to test, diagnose, monitor or determine symptoms of the subject;

or any combination or sub-combination of a) through h).

[0028] According to the present ~~invention~~ disclosure there is also provided a kit as defined above and herein comprising,

- a) one or more primers to amplify a nucleotide sequence that comprises the polymorphism as defined in rs2491144 (SEQ ID NO:1), rs9315639 (SEQ ID NO:2), rs11082138 (SEQ ID NO:3), rs11697517 (SEQ ID NO:4), rs2186437 (SEQ ID NO:5) or any combination thereof;
 - b) one or more probes that hybridize to SEQ ID NOs:1, 2, 3, 4, or 5, over a region of nucleotides comprising the polymorphic site, wherein said probe hybridizes to a particular variant of the polymorphism at the polymorphic site—;
 - c) one or more reagents and/or products comprising buffers, nucleotides, DNA amplifying enzymes, or any combination thereof;
 - d) one or more reagents, components and/or products for genotyping the polymorphisms of SEQ ID NO:1, 2, 3, 4, 5, or a combination thereof,
 - e) one or more reagents, components and/or products for performing a DNA sequencing reaction that determines the sequence of SEQ ID NO: 1, 2, 3, 4, 5, or a combination thereof,
 - f) a gene chip or nucleotide sequence array comprising a plurality of nucleotide sequences comprising or consisting of SEQ ID NOs:1-5, and;
 - g) one or more instructions for using the components as described herein, practicing the methods as described herein, interpreting the data obtained from practicing the methods, or any combination thereof;
 - h) a scale, reference or the like that may be used to test, diagnose, monitor or determine symptoms of the a subject;
- or any combination or sub-combination of a) through h).

[0029] This summary ~~of the invention~~ does not necessarily describe all features of the ~~invention~~present disclosure.

WHAT IS CLAIMED IS:

1. A method of identifying a subject at risk for suicide comprising identifying in a biological sample from the subject one or more genetic markers associated with suicide, at least one marker being defined by rs2491144 (SEQ ID NO:1), wherein the presence of the G allele in marker rs2491144 identifies the subject is at increased risk for suicide.

2. The method of claim 1, further comprising identifying one or more additional genetic markers associated with suicide in the biological sample from the subject, the one or more additional genetic markers being defined by the group consisting of rs9315639 (SEQ ID NO:2), rs11082138 (SEQ ID NO:3), rs11697517 (SEQ ID NO:4), and rs2186437 (SEQ ID NO:5), wherein

the presence of any of the C allele in marker rs9315639, the C allele in marker rs11082138, the T allele in marker rs11697517, and C allele in marker rs2186437 identifies the subject is at increased risk for suicide.

~~3. The method of claim 1 or 2, further comprising a step of obtaining the biological sample from the subject.~~

43. The method of any of claims 1-~~32~~, wherein the biological sample is a sample from blood, saliva, spinal fluid, brain biopsy, cultured cells obtained from the subject, stool, urine, autopsy samples, or frozen sections taken for histological purposes.

54. The method of claim 43, wherein the step of identifying in a biological sample from the subject one or more genetic markers associated with suicide comprises PCR analysis, sequencing, 5' exonuclease fluorescence assay, probe hybridization or a combination thereof.

65. The method of any of claims 1-~~54~~, wherein the subject is a subject diagnosed with a mental illness.

76. The method of claim 65, wherein the mental illness is selected from the group consisting of depression, schizophrenia, schizoaffective disorder, bipolar disorder,

personality disorder, seasonal affective disorder, anxiety disorder, and post traumatic stress disorder.

87. The method of any of claims 1-~~54~~, wherein the subject exhibits one or more clinical symptoms of a mental illness.

98. The method of claim 87, wherein the subject exhibits one or more symptoms of a mental illness selected from the group consisting of depression, schizophrenia, schizoaffective disorder, bipolar disorder, personality disorder, seasonal affective disorder, anxiety disorder, and post traumatic stress disorder.

~~109~~. The method of any of claims 1-98, further comprising receiving, in a computer system, the subject's genotype for the one or more genetic markers associated with suicide and the identifying step is performed by the computer system.

~~110~~. The method of claim ~~109~~, wherein the subject's genotype is received directly from equipment used in determining the patient's genotype.

~~1211~~. The method of claim ~~109~~ or ~~110~~, further comprising receiving, in a computer system, the patient's diagnosis.

~~1312~~. The method of any of claims ~~109-1211~~, further comprising a step of outputting an indication of whether or not the subject is at increased risk for suicide.

~~1413~~. The method of claim ~~1312~~, wherein the indication of whether or not the subject is at increased risk for suicide is represented on a patient specific report.

~~1514~~. A computer readable medium containing executable instructions that when executed cause one or a plurality of processors to

receive a subject's genotype for one or more genetic markers associated with suicide selected from the group consisting of rs2491144 (SEQ ID NO:1), rs9315639 (SEQ ID NO:2), rs11082138 (SEQ ID NO:3), rs11697517 (SEQ ID NO:4), and rs2186437 (SEQ ID NO:5);

identify the presence of any of the G allele in marker rs2491144 (SEQ ID NO:1), the C allele in marker rs9315639 (SEQ ID NO:2), the C allele in marker rs11082138

(SEQ ID NO:3), the T allele in marker rs11697517 (SEQ ID NO:4), and C allele in marker rs2186437 (SEQ ID NO:5), and

output an indication that the subject is at increased risk for suicide if at least the G allele in marker rs2491144 (SEQ ID NO:1) is present or a null result if the G allele in marker rs2491144 (SEQ ID NO:1) is absent.

15. A method for reducing the risk of suicide in a subject identified as being at increased risk for suicide according to the method of any of claims 1-14, the method comprising one or more of

~~a) treating the subject with medication, non-medicinal therapy or a combination thereof;~~

b) monitoring the subject;

c) counseling the subject;

d) testing or screening the subject for mental illness or one or more symptoms that are associated with mental illness or suicide,

e) testing the biological sample comprising genomic DNA or a second biological sample obtained from the subject for one or more additional genetic markers, nucleotide sequences, proteins, metabolites or any combination thereof;

f) removing or reducing access to compounds, compositions, articles or cues which increase suicide risk, or

any combination thereof.

16. The method of claim 15, wherein the subject had been treated with medication, non-medicinal therapy or a combination thereof.

17. The method of claim 16, wherein the subject had been treated ~~treating the subject with~~ medication comprising administering one or more antipsychotics, mood stabilizers, antidepressants, anticonvulsants, anxiolytics, or any combination thereof.

18. The method of claim 16, wherein the medication comprises clozapine, lithium, or ketamine.

19. The method of claim 16, wherein the non-medicinal therapy comprises electroconvulsive or electroshock therapy, magnetic seizure therapy, transcranial magnetic stimulation, cognitive behavioral therapy, dialectical behavioral therapy, risk dissipation group therapy, deep brain stimulation, or a combination thereof.

20. The method of claim ~~16~~15, wherein said testing or screening the subject for mental illness or one or more symptoms associated with suicide or mental illness comprises testing or screening the subject for depression, schizophrenia, schizoaffective disorder, bipolar disorder, obsessive compulsive disorder, personality disorder, seasonal affective disorder, addiction, drug abuse, alcoholism, problem gambling, increased anxiety, anxiety disorder, feelings of worthlessness, psychotic symptoms, delusions, hallucinations, agitation, restlessness, irritability, aggression or anger.

21. A kit comprising,

a) one or more primers to amplify a nucleotide sequence that comprises the polymorphism as defined in:

rs2491144 (SEQ ID NO:1) or a fragment thereof comprising the polymorphic site, or the complement of SEQ ID NO:1 or a fragment thereof comprising the polymorphic site;

rs9315639 (SEQ ID NO:2) or a fragment thereof comprising the polymorphic site, or the complement of SEQ ID NO:2 or a fragment thereof comprising the polymorphic site;

rs11082138 (SEQ ID NO:3) or a fragment thereof comprising the polymorphic site, or the complement of SEQ ID NO:3 or a fragment thereof comprising the polymorphic site;

rs11697517 (SEQ ID NO:4) or a fragment thereof comprising the polymorphic site, or the complement of SEQ ID NO:4 or a fragment thereof comprising the polymorphic site,

rs2186437 (SEQ ID NO:5) or a fragment thereof comprising the polymorphic site, or the complement of SEQ ID NO:5 or a fragment thereof comprising the polymorphic site,

or any combination thereof;

b) one or more probes that hybridize to SEQ ID NOs:1, 2, 3, 4, or 5, or the complement thereof, over a region of nucleotides comprising the polymorphic site, wherein said probe hybridizes to a particular variant of the polymorphism at the polymorphic site;

c) one or more reagents and/or products comprising buffers, nucleotides, DNA amplifying enzymes, or any combination thereof;

d) one or more reagents, components and/or products for genotyping the polymorphisms of SEQ ID NO:1, 2, 3, 4, 5, their complements or any combination thereof,

e) one or more reagents, components and/or products for performing a DNA sequencing reaction that determines the sequence of SEQ ID NO: 1, 2, 3, 4, 5, their complements or any combination thereof,

f) a gene chip or nucleotide sequence array comprising a plurality of nucleotide sequences comprising or consisting of any one or combination of SEQ ID NOs:1-5, a fragment thereof comprising the polymorphic site or their complements;

g) one or more instructions for using the components as described herein, practicing the methods as described herein, interpreting the data obtained from practicing the methods, or any combination thereof;

h) a scale, reference or the like that may be used to test, diagnose, monitor or determine symptoms of the subject;

or any combination or sub-combination of a) through h).

22. The kit of claim 21 comprising,

- a) one or more primers to amplify a nucleotide sequence that comprises the polymorphism as defined in rs2491144 (SEQ ID NO:1), rs9315639 (SEQ ID NO:2), rs11082138 (SEQ ID NO:3), rs11697517 (SEQ ID NO:4), rs2186437 (SEQ ID NO:5) or any combination thereof;
 - b) one or more probes that hybridize to SEQ ID NOs:1, 2, 3, 4, or 5, over a region of nucleotides comprising the polymorphic site, wherein said probe hybridizes to a particular variant of the polymorphism at the polymorphic site—₁;
 - c) one or more reagents and/or products comprising buffers, nucleotides, DNA amplifying enzymes, or any combination thereof₁;
 - d) one or more reagents, components and/or products for genotyping the polymorphisms of SEQ ID NO:1, 2, 3, 4, 5, or a combination thereof₁;
 - e) one or more reagents, components and/or products for performing a DNA sequencing reaction that determines the sequence of SEQ ID NO: 1, 2, 3, 4, 5, or a combination thereof,
 - f) a gene chip or nucleotide sequence array comprising a plurality of nucleotide sequences comprising or consisting of SEQ ID NOs:1-5, and₁;
 - g) one or more instructions for using the components as described herein, practicing the methods as described herein, interpreting the data obtained from practicing the methods, or any combination thereof₁;
 - h) a scale, reference or the like that may be used to test, diagnose, monitor or determine symptoms of the a subject;
- or any combination or sub-combination of a) through h).