

[0005] NMDA-modulating small molecule agonist and antagonist compounds have been developed for potential therapeutic use. However, many of these are associated with very narrow therapeutic indices and undesirable side effects including hallucinations, ataxia, irrational behavior, and significant toxicity, all of which limit their effectiveness and/or safety. Further, 50% or more of patients with depression do not experience an adequate therapeutic response to known administered drugs. There currently is no single effective treatment for depression, anxiety, and other related diseases.

[0006] Thus, there remains a need for improved treatments of depression, anxiety and/or other related diseases with compounds that provide increased efficacy and reduced undesirable side effects.

SUMMARY

[0007] The present disclosure relates in part to methods of identifying a candidate compound suitable for treatment of depression. In some embodiments, a candidate compound may be a NMDAR partial agonist.

[0008] In one aspect, a method for identifying a candidate compound suitable for treatment of depression is provided. The method comprises exposing a cell to a potential compound in a culture medium, or administering a potential compound to an animal; retrieving a sample from the cell and/or culture medium, or from brain or neural tissue of the animal, at one or more predetermined time points; analyzing the sample for increased or decreased expression levels of Wnt1 and /or identifying the candidate compound as suitable for treatment of depression based on the increased expression level of Wnt1.

[0008a] In one aspect, there is provided a method for identifying a candidate compound suitable for treatment of depression, comprising:

exposing a cell to a potential compound in a culture medium and retrieving a sample from the cell and/or culture medium at one or more predetermined time points; or

providing a sample that was retrieved from brain or neural tissue of an animal, at one or more predetermined time points, wherein the animal was previously administered a potential compound; and

analyzing the sample for increased expression levels of Wnt1, and
identifying the candidate compound as suitable for treatment of depression based on the increased expression level of Wnt1.

[0009] In another aspect, a method for identifying a candidate compound suitable for treatment of depression is provided. The method comprises exposing a cell to a potential compound in a culture medium, or administering a potential compound to an animal; retrieving a sample from the cell and/or culture medium, or from brain or neural tissue of the animal, at one or more predetermined time points; analyzing the sample for increased expression levels of at least one of the genes listed in Table 1 or 2 indicated with a G, or decreased expression levels or at least one of the genes listed in Table 1 or 2 indicated with a K, and identifying the compound as suitable for treatment of depression based on the increased expression level or decreased expression level.

CLAIMS

1. A method for identifying a candidate compound suitable for treatment of depression, comprising:

exposing a cell to a potential compound in a culture medium and retrieving a sample from the cell and/or culture medium at one or more predetermined time points; or

providing a sample that was retrieved from brain or neural tissue of an animal, at one or more predetermined time points, wherein the animal was previously administered a potential compound; and

(a) analyzing the sample for increased expression levels of Wnt1, and

identifying the candidate compound as suitable for treatment of depression based on the increased expression level of Wnt1, or

(b) analyzing the sample for increased expression levels of at least one of the genes listed in Table 1 or 2 indicated with a G, or decreased expression levels or at least one of the genes listed in Table 1 or 2 indicated with a K, and

identifying the compound as suitable for treatment of depression based on the increased expression level or decreased expression level, or

(c) analyzing the sample for NMDA receptor NR2B subunit plasticity, and

identifying the compound as suitable for treatment of depression based on inducing the NR2B plasticity.

2. The method of claim 1 when comprising step (b), wherein the sample has a gene expression pattern as provided in Table 1 or 2 with the indication "G" and the identifying is based on increased expression of those genes.
3. The method of claim 1 when comprising step (a) or step (b), further comprising analyzing the candidate compound for NDMA subunit NR2B synaptic plasticity.

4. The method of claim 1 when comprising step (c), wherein a candidate compound suitable for treating depression significantly induces NR2B dependent synaptic plasticity as compared to ketamine.
5. The method of any one of claims 1-4, wherein the tissue is medial prefrontal cortex.
6. The method of any one of claims 1-5, wherein the animal is a rodent or human, and the cell is a human or rodent cell.
7. The method of any one of claims 1-6, wherein the compound modulates the NMDA receptor.
8. The method of any one of claims 1-7, wherein the compound suitable for treating depression has fewer side effects as compared to ketamine.
9. The method of claim 8, wherein the compound does not have substantial addictive sensory motor grating and/or sedative effect.
10. The method of any one of claims 1-9, wherein the cell is a eukaryotic cell.
11. The method of any one of claims 1-10, further comprising selecting the candidate compound from a library of compounds.

CLAIMS

1. A method for identifying a candidate compound suitable for treatment of depression, comprising:

exposing a cell to a potential compound in a culture medium and retrieving a sample from the cell and/or culture medium at one or more predetermined time points; or

providing a sample that was retrieved from brain or neural tissue of an animal, at one or more predetermined time points, wherein the animal was previously administered a potential compound; and

analyzing the sample for increased expression levels of Wnt1, and

identifying the candidate compound as suitable for treatment of depression based on the increased expression level of Wnt1.
2. The method of claim 1, further comprising analyzing the candidate compound for NMDA subunit NR2B synaptic plasticity.
3. The method of any one of claims 1 or 2, wherein the tissue is medial prefrontal cortex.
4. The method of any one of claims 1 to 3, wherein the animal is a rodent or human, and the cell is a human or rodent cell.
5. The method of any one of claims 1-4, wherein the compound modulates the NMDA receptor.
6. The method of any one of claims 1-5, wherein the compound suitable for treating depression has fewer side effects as compared to ketamine.
7. The method of claim 6, wherein the compound does not have substantial addictive sensory motor grating and/or sedative effect.
8. The method of any one of claims 1-7, wherein the cell is a eukaryotic cell.
9. The method of any one of claims 1-8, further comprising selecting the candidate compound from a library of compounds.