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Niculescu

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(54) **METHODS FOR OBJECTIVE ASSESSMENT OF STRESS, EARLY DETECTION OF RISK FOR STRESS DISORDERS, MATCHING INDIVIDUALS WITH TREATMENTS, MONITORING RESPONSE TO TREATMENT, AND NEW METHODS OF USE FOR DRUGS**

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See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

2011/0045998 A1* 2/2011 Niculescu C12N 15/8509 506/7
2014/0073524 A1* 3/2014 Hood G01N 33/6896 506/18
2016/0158213 A1 6/2016 Mouston et al.
2017/0029892 A1* 2/2017 Lombard A61K 31/197

FOREIGN PATENT DOCUMENTS

WO 2010/029176 A1 3/2010
WO 2013/102116 A1 7/2013
WO 2016201299 A1 12/2016

OTHER PUBLICATIONS

Le-Niculescu H. Identifying blood biomarkers for mood disorders using convergent functional genomics. *Molecular Psychiatry* 14: 156-174. (Year: 2009).*

International Search Report and Written Opinion issued by the ISA/US, Commissioner for Patents, dated Oct. 4, 2019, for International Application No. PCT/US2019/035513; 9 pages.

Savitz David A et al: "Atovaquone/Proguanil" In: "Assessment of Long-Term Health Effects of Antimalarial Drugs When Used for Prophylaxis", Mar. 24, 2020 (Mar. 24, 2020), National Academies Press, Washington, D.C., XP055934385, ISBN: 978-0-309-67210-8 pp. 217-246.

* cited by examiner

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(57) **ABSTRACT**

Disclosed are methods for assessing severity, determining future risk, matching with a drug treatment, and measuring response to treatment, for stress disorders. Also disclosed are new methods for use for drugs and natural compounds repurposed for use in reducing stress severity, as well as for preventing and treating stress disorders. All the above mentioned methods are computer assisted methods analyzing the expression of panels of genes, clinical measures, and drug databases. A universal approach in everybody, as well as a personalized approaches by gender, and by diagnosis, are disclosed.

5 Claims, 10 Drawing Sheets

Specification includes a Sequence Listing.