

Can We Change the Current Landscape of All Addictive Behaviors by Adopting a Personalized Genetic Guided Approach to Help Epigenetically Induce Dopamine Homeostasis at the Brain Reward Circuit?

Kenneth Blum^{1-7*} and Rajendra D Badgaiyan^{8,9}

¹Department of Nutrigenomics, Geneus Health, LLC, San Antonio, TX, USA

²Department of Psychiatry, University of Vermont, Burlington, VT, USA

³Western University Health Science Centers, Graduate College, Pompano, CA, USA

⁴Institute of Psychology, Eotvos Loránd University, Budapest, Hungary

⁵Department of Psychiatry, Wright University Boonshoft School of Medicine, Dayton, OH, USA

⁶The Kenneth Blum Behavioral and Neurogenetic Institute, (Division of Ivitalize Inc), Austin, TX, USA

⁷Division of Nutrigenomics, Victory Nutrition International, LLC, Lederoch, PA, USA

⁸Department of Psychiatry, South Texas Veteran Health Care System, Audie L. Murphy Memorial VA Hospital and Long School of Medicine, University of Texas Health Science Center, San Antonio, TX, USA

⁹Department of Psychiatry, MT. Sinai School of Medicine, New York, NY, USA

***Corresponding Author:** Kenneth Blum, Department of Nutrigenomics, Geneus Health, LLC, San Antonio, TX, USA.

Currently planet earth is in deep trouble housing not only the Covid pandemic with new strains like delta and lamda and many people not willing to get vaccinated thereby spreading the virus globally, but our drug and non-drug addiction pandemic as well. Nora Volkow director of the National Institute on Drug Abuse (NIDA) estimated that opioid induced overdoses increased to 30 - 40 percent post COVID. In fact, in 2020, 93,000 people died from narcotic overdoses. In the face of the current Opioid crisis in America killing close to 1,000,000 people since 2004, and even more when we consider tobacco smoking, we are hereby proposing a novel approach to assist in at least attenuating these unwanted premature deaths. The current approach is failing, and other alternative approaches should at least be tested [1].

The current DSM-5 does not actually accurately display the natural brain reward process. The human brain has not been designed to carve out specific drugs like opioids, alcohol, nicotine, cocaine, benzodiazepines or cannabis and process addictions such as gambling as distinct endophenotypes [2]. It is noteworthy that

our brain consists of natural ligands for cannabinoids, endorphins, or even benzodiazepines but not alcohol or cocaine [3].

Indeed, the most accurate endophenotype is reward dysfunction (e.g. hypodopaminergic or hyperdopaminergic). To reduce stigma related to the field of addictive behaviors including alcoholism (termed "Isoquinolism") [4], we are encouraging the term "Hypodopamineinism" instead.

While we applaud the enormous efforts of NIDA and NIAAA and other societies dedicated to the field of Addiction Medicine like ASAM, the current Medication Assisted Treatment (i.e. 'MAT') that has expanded to needed individuals as an initial "-temporary aid -" to reduce societal harm, in the minds of some is the standard "treatment" [5]. However, by only substituting opioids for opioids without the long-term goal of prophylaxis seems minimalistic.

So, to be clear, there may be other promising modalities other than MAT such as repetitive transcranial magnetic stimulation (rTMS) [6], exercise [7] and even new medications with positive

Received: July 28, 2021

Published: August 19, 2021

© All rights are reserved by **Kenneth Blum and Rajendra D Badgaiyan.**

allosteric modulators of GABA-A receptors [8]. Our proposal to change the current landscape of treatment and relapse prevention, resides in early identification of vulnerability or risk for all Reward Deficiency Syndrome (RDS) addictive behaviors [9]. This concept involves the highly researched Genetic Addiction Risk severity (GARS) coupled [10] with precision KB220Z [11] with at least 50 human clinical trials and genetically bred animals including self-administration studies [12].

Based on human evidence in both abstinent Psychostimulant [13] and Heroin misusers [14], utilization of genetic guided precision KB220 [15], as observed in a generational family study [16], induced “dopamine homeostasis” to effectively rebalance and restore healthier brain function by promoting the cross talk between various brain regions (e.g. Nucleus accumbens, cingulate gyrus, hippocampus etc.) by enhancing resting state functional connectivity [17]. Certainly, the measurement of tonic and phasic tone of dopamine in the brain as accomplished by Badgaiyan’s group [18] with ADHD and similar findings in cocaine abuse [19] provides molecular evidence for the fact that low brain tonic dopamine leads to increased intake of psychoactive drugs.

While we are encouraging neurologists to consider these salient points, our laudable goal is to not only save lives, but to redeem joy and improve the quality of life in the recovery community through scientifically sound natural non-addicting alternatives. We are also encouraging scientists across multi-disciplines, but especially genetic investigators to include ethnic groups in their cohorts for better representation.¹⁹ Our team believes that the future is now.

Author Contribution

KB developed the first draft and RDB commented and help edit and added to the manuscript.

Conflict of Interest

KB is the inventor of a number of USA and Foreign patents related to, genetic testing and Pro-dopamine regulation (KB220) licensed Ivitalize Inc.

Funding Support

KB is the recipient of a NIHD grant with Marjorie Gondre Lewis -R41 MD012318/MD/NIMHD NIH HHS/United States; RDB is the recipient of I01 CX000479/CX/CSRD VA/United States/VA United States.

Bibliography

1. Hall SM, et al. “Cigarette Smoking Cessation Intervention for Buprenorphine Treatment Patients”. *Nicotine and Tobacco Research* 20.5 (2018): 628-635.
2. Casey BJ, et al. “DSM-5 and RDoC: progress in psychiatry research?” *Nature Reviews on Neuroscience* 14.11 (2013): 810-814.
3. Herz A. “Multiple opiate receptors and their functional significance”. *Journal of Neural Transmission* 18 (1983): 227-233.
4. Blum K, et al. “Isoquinoline alkaloids as possible regulators of alcohol addiction”. *Lancet* 1.8015 (1977): 799-800.
5. Downs BW, et al. “Death by Opioids: Are there non-addictive scientific solutions?” *Journal of Systems and Integrative Neuroscience (JSIN)* 5 (2019).
6. Detrick JA, et al. “Motor cortex modulation and reward in children with attention-deficit/hyperactivity disorder”. *Brain Communication* 3.2 (2021): fcab093.
7. Swenson S, et al. “The therapeutic potential of exercise for neuropsychiatric diseases: A review”. *Journal of the Neurological Sciences* 412 (2020): 116763.
8. Olsen RW. “GABAA receptor: Positive and negative allosteric modulators”. *Neuropharmacology* 136 (2018): 10-22.
9. Gondré-Lewis MC, et al. “Pre-clinical models of reward deficiency syndrome: A behavioral octopus”. *Neuroscience and Biobehavioral Reviews* 115 (2020): 164-188.
10. Blum K, et al. “Biotechnical development of genetic addiction risk score (GARS) and selective evidence for inclusion of polymorphic allelic risk in substance use disorder (SUD)”. *Journal of Systems and Integrative Neuroscience* 6.2 (2020): 10.
11. McLaughlin T, et al. “Pro-dopamine regulator, KB220Z, attenuates hoarding and shopping behavior in a female, diagnosed with SUD and ADHD”. *Journal of Behavioral Addictions* 7.1 (2018): 192-203.
12. Blum K, et al. “Pro-Dopamine Regulator (KB220) A Fifty Year Sojourn to Combat Reward Deficiency Syndrome (RDS): Evidence Based Bibliography (Annotated)”. *CPQ Neurology and Psychology* 1.2 (2018).
13. Blum K, et al. “Overcoming qEEG abnormalities and reward gene deficits during protracted abstinence in male psychostimulant and polydrug abusers utilizing putative dopamine D₂ agonist therapy: part 2”. *Postgraduate Medicine* 122.6 (2010): 214-226.

14. Blum K., *et al.* "rsfMRI effects of KB220Z™ on neural pathways in reward circuitry of abstinent genotyped heroin addicts". *Postgraduate Medicine* 127.2 (2015): 232-241.
15. Blum K., *et al.* "A Novel Precision Approach to Overcome the "Addiction Pandemic" by Incorporating Genetic Addiction Risk Severity (GARS) and Dopamine Homeostasis Restoration". *Journal of Personalized Medicine* 11.3 (2021): 212.
16. Fried L., *et al.* "Hypodopaminergia and "Precision Behavioral Management" (PBM): It is a Generational Family Affair". *Current Pharmaceutical Biotechnology* 21.6 (2020): 528-541.
17. Febo M., *et al.* "Enhanced functional connectivity and volume between cognitive and reward centers of naïve rodent brain produced by pro-dopaminergic agent KB220Z". *PLoS One* 12.4 (2017): e0174774.
18. Badgaiyan RD., *et al.* "Attenuated Tonic and Enhanced Phasic Release of Dopamine in Attention Deficit Hyperactivity Disorder". *PLoS One* 10.9 (2015): e0137326.
19. Abijo T., *et al.* "Neuropharmacological and Neurogenetic Correlates of Opioid Use Disorder (OUD) As a Function of Ethnicity: Relevance to Precision Addiction Medicine". *Current Neuropharmacology* 18.7 (2020): 578-595.

Volume 4 Issue 9 September 2021

© All rights are reserved by Kenneth Blum and Rajendra D Badgaiyan.