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Letter to the Editor

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Should We Embrace Vaccines for Treating Substance-Related Disorder, A Subset of Reward Deficiency Syndrome (RDS)?

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To the Editor,

Undoubtedly substance-related disorder is a chronically relapsing problem worldwide, the question is; should anti-drug vaccines be embraced for treatment of this enormous problem?. The Federal Drug Administration (FDA) in the United States has approved a number of Medical Assisted Treatments (MAT) for alcohol, opiates and even Nicotine abuse, while, other abusable drugs like cocaine and cannabis have not been addressed [1]. Estimates place lifetime risks of transitioning from drug use to dependence from 8.9% to 67.5% [2]. Certainly there is strong evidence for inheritability of both substance and non-substance related seeking behaviors now under the Reward Deficiency Syndrome (RDS) rubric [3]. In fact using Bayesian theorem modeling, carriers born with a variant in the dopamine D2 receptor gene have a 74% predictive value to abuse drugs, food, and other process addictions close to the above estimate. However, Kendler et al. [4] suggested it to be somewhat lower at 50%. According to Belcher et al. [1] it is noteworthy that a number of studies have shown that striatal D2 receptor availability inversely correlates with measures of impulsive response in both animals and addicted humans [5].

Understanding the powerful role of dopamine in pleasure induction at mesolimbic and pre-frontal cortex loci, instead of embracing long-term homeostatic activation of dopaminergic function [6, 7] –MAT approval from the FDA has favored blocking dopamine release. Although it is understood that all drugs of abuse preferentially stimulate neuronal dopamine in important brain regions, because powerful D2 stimulation causes chronic D2 down-regulation there are no approved dopaminergic agonists [8]. In an attempt to overcome abuse of these dopaminergic activators, world class scientists have engaged in the development of potential antidrug vaccines [9] and have been quite successful in this important new research.

Vaccines work by inducing drug-specific antibodies in the bloodstream that prevent drug entry into the brain. The antibodies bind to the drug of abuse to create a molecule too large to enter the blood-brain barrier [10]. Many prominent laboratories, especially from Kosten's group, have now developed vaccines with antibodies directed against cocaine [11], methamphetamine [12], and possibly phencyclidine. The anti-cocaine vaccine is now in clinical trials with limited success [13]. Others have pursued similar heroin hapten-BSA conjugated vaccines [14]. Importantly, Schlosburg et al. [15] found that an anti-heroin "Dynamic"

vaccine blocks relapse to compulsive intake of heroin in rats. Unlike other types of vaccines, this "Dynamic" vaccine creates antibodies against heroin and its psychoactive metabolites by the presentation of multihaptenic structures that match heroin's metabolism to the immune system. In addition, anti-nicotine vaccines have been developed recently [16]. Anti-nicotine vaccines showed promise in animal models [17], however when administered to human smokers did not lead to changes in brain activity during smoking cue exposure [18].

An underlying issue in all of this research is to deliver high concentrations of circulating drug-specific antibodies to attenuate drug-seeking and drug-taking behavior when the drug is repeatedly available, especially in high doses. The promise of the presentation of multihaptenic structures to potentially block even drug metabolites seems quite prudent, but must await human clinical trials. This accomplishment, likened in disruptive technology to the Polio vaccine from the early 1950s, could not have been achieved without advancements in immunology and increased knowledge of the molecular biology of substance abuse acquired through progress in neuro-imaging techniques. In fact, unpublished work, from one of us (KB) with Peter Sheridan at the University of Texas Health Science Center, in the mid 80's attempted to utilize known haptens and available adjuncts to develop an anti-ethanol vaccine. While they found significant antibodies, it was not sufficient to block ethanol sleep time in mice.

The questions that remain amongst continued excitement and commitment to this endeavor as a viable treatment option for hardcore addicts that want to quit must be considered and vetted by the scientific community. Accordingly, Kantak [9] pointed out a number of potential problems.

1. There is no protection against drugs that are structurally dissimilar but produce the same effects as the drug of choice;
2. Antibody formation is tremendously variable;
3. Drug cravings that predispose addicts to relapse are not effected;
4. There are serious legal and ethical concerns related to forced or coerced vaccination; and
5. Vaccines are unsuitable for women of childbearing age.

We encourage the further development of this promising treatment option and applaud scientific exploration and the tremendous efforts made toward the advancement of anti-drug abuse vaccines. We are, however, concerned that simply blocking the effects of the drug of choice, would fail to treat poly-drug abuse. It would also leave the hypodopaminergic trait (genetic) or state (epigenetic) untreated resulting in addiction transfer or other RDS behaviors such as food and process addictions as suggested by Blum et al. [19].

Scientists must initiate more clinical research into many options, especially for the long-term dopamine agonistic rather than antagonistic therapy [20-26]. Further research is required, and this worthwhile exploration must continue before we can embrace the use of anti-drug abuse vaccines in chemical dependency programs for the treatment of RDS.

The important work from NIDA and NIAAA and other addiction research institutions across the globe must be given very high priority if we are to combat addiction. RDS effects millions if not billions, like other chronic relapsing diseases that plague humans worldwide.

In summary, we are poised for major breakthroughs regarding potential anti-drug vaccines, however, unlike the poliomyelitis virus a singular disease antigen, the target of these vaccines is the specific molecular structures of the current drug of choice. The widespread utilization of anti-drug vaccines will be limited but may be a valuable adjunct to the treatment of RDS a complex disease subject to associated polygenetic and epigenetic interactions.

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Conflict of Interest

Kenneth Blum, PhD holds US and Foreign patents issued and pending on KB220Z and receives royalties based on its commercialization from various sources. Dr. Blum is also an officer and stock holder of IGENE, LLC, Victory Nutrition, RDSolutions, Inc. and is a paid consultant of Dominion Diagnostics, LLC, and Malibu Recovery Center. Dr. Blum is a member of the scientific advisory board of Dominion Diagnostics, LLC and a member of the Board of Directors of RDSolutions Inc. He also serves as Chief Scientific Advisor to Dominion Diagnostics, LLC and is currently the Chief Scientific Officer of RDSolutions, Inc. and Victory Nutrition International, LLC. DRs Gold and Anges are paid consultants of Rivermend Health, Atlanta Ga. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript part from those disclosed.

Authors Contribution

All the authors contributed equally.

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