THE MICHAEL J. FOX FOUNDATION
FOR PARKINSON'S RESEARCH

Fall 2022 Request for Applications
Translational Pipeline Program

PRE-PROPOSAL TEMPLATE

Principal Investigator: Kirsten Lykkegaard DVM, PhD
Institution/Company: Institute for the Study of Peak States
Project Title: Treatment of PD prionoids using psycho-immunology

THERAPEUTIC	We will be using a non-drug, completely new psycho-immunology (PI) approach to eliminate symptoms of Parkinson's disease (PD). PI is a 'disruptive technology' and will be unfamiliar to most biomedical research staff *and difficult to evaluate using standard biometrics.* The concept of PI is not new; interaction between emotional experience and the immune system has been researched since Dr. Ader's 1970's breakthrough work on conditioning the immune system using taste aversion in rats (R Ader and N Cohen, *Psychosom Med*, Vol 37:4 333-340, 1975). However, practical application remained elusive. Three years ago, we made a breakthrough in this field when we realized how pathogen glycans inhibit the immune system (see also the work of Dr. Carolyn Bertozzi of Stanford University). Specific generational epigenetic damage is at the root of this susceptibility, and can be repaired with standard trauma-healing techniques used in a novel way (see *Frontiers in Psychiatry*, July 2014, article 93). Fortunately, only one PI protocol needs to be derived per pathogen (ameba, bacteria, fungi, virus, or prion), making treatment simple and efficient. Although our model remains to be confirmed using standard lab tools, we've successfully demonstrated this approach on a number of pathogens. Existing PI treatments have about a 70-80% success rate; surprisingly, symptoms generally disappear within hours. We've also found experientially that many chronic diseases are directly or indirectly caused by unrecognized pathogen infections. For example, our PI approach has led to successful treatments for obsessive-compulsive disorder and schizophrenic voices; these 'diseases of unknown etiology' were both indirectly caused by fungal infections.
TARGET	We have performed a pilot survey in humans with (N=5) or without PD (N=5). All our PD group had basal ganglia damage in the brain with corresponding damage linked to a prionoid infection at the cellular nuclear membrane level. In healthy controls, the prionoids were not present. Thus, we consider the prionoid infection as both a marker for the disease and its primary cause. Eliminating this prionoid infection with PI psychological techniques, and observing symptom change would allow us to quickly verify or disprove this hypothesis. Diagnostically, all PD patients in our sample had a consistent initiating event for PD - a sudden and permanent loss of a feeling of exceptional clarity in perceiving the world; symptoms appeared 10-15 years later. How likely is this PD prionoid hypothesis? There is a growing body of evidence that prionoids play a key role in neurodegenerative diseases (see *Frontiers Molecular Neurosci*, Nov 2019, Vol 12, Article 271). In fact, we *have* seen several other diseases of unknown etiology caused by prionoid infections (e.g., some types of chronic pain, certain types of cancers, multiple sclerosis, adolescent-onset schizophrenia, and as a co-factor in autism), so it is not unreasonable to suspect that a prionoid infection could also be causal for PD.

DEVELOPMENT PLAN	Proof of concept (PoC) will be achieved by developing a PI psychological treatment process that specifically targets the marker prionoid found in PD. Symptom elimination (or consistent and permanent symptom reduction) in 2 (out of 2) patients is considered PoC. If PD turns out to be caused by more than a direct effect of the marker prionoid, the development plan will become more complex, and getting to PoC can take longer. We have seen this with other diseases and it may be due to either of three problems. 1) The marker prionoid is only an opportunistic infection, in which case we start an iterative process of elimination and uncovering the 'next' causal layer (type-1 diabetes in our pipeline is an example of this). 2) Different pathogens can cause different groups of symptoms, all lumped under the PD name. In this case, treatment would involve deriving different PI processes and eliminating each pathogen as needed (we have seen this in our successful process for OCD, where there are three distinctly different symptom sets – patients can have one, two, or all three of the pathogens). 3) Similar PD symptoms have completely different causes in which case part of the research process then becomes figuring out ways to do differential diagnosis in order to apply the appropriate PI treatment.
IP/PATENT LANDSCAPE	PI techniques are not patentable (which we think is a very good thing). However, the process steps can be copyrighted.
IMPACT	If the proposed PI treatment approach targeting PD prionoids is successful, the next step would be to do efficacy, safety and stability testing. For this, we would require funding, as it involves using paid staff. (We already have an international network of trained therapists who test our PI processes for other diseases, and we'd be happy to also train MJFF staff.) Our request for this stage is negotiable, but in the range of $100,000.00. This stage would probably take about 6-12 months. If a PI PoC demonstrates prionoids as causal for PD, we strongly recommend following up with established drug companies to develop a biomarker blood test and drug treatment (e.g. antibodies against prionoid glycans). We have no estimate of cost or length of time. We would be happy to consult, but this is outside our core PI research mission.
SAMPLE SIZE AND RECRUITMENT	For the PoC, we would only need a couple of PD patients. If we successfully demonstrate PoC, it would take a total of about 100 PD patients for the follow-up efficacy and safety studies. Since we're using a psychological treatment approach, we assume MJFF would have many PD sufferers who would be interested in being treated. We do exclude any patients who have been suicidal in the last 5 years. There are no other patient population restrictions that we know of at this time. We won't need a control group. Note that we do not use medical tools such as double-blind studies or statistical techniques such as p-values, where the underlying assumption is that biology is too complex to fully predict. Instead, we treat this like an engineering product with performance specs; we design for elimination of all symptoms in all patients. If we fall short of that, we do the additional research to find out why.
DIVERSITY, EQUITY, INCLUSION	From a technical viewpoint, anyone with a diagnosis of PD would be acceptable. PI psychological treatments can be provided face to face via an online video media, so there is no limitation in nationality, ethnicity and location.