Neuropore Therapies Inc.
Lead PI: Douglas W. Bonhaus

Organization and Team Overview
Neuropore Therapies is focused on discovering and developing novel therapeutics for the treatment of Parkinson’s disease and related disorders. Working in close collaboration with preeminent academic groups at the University of California, the scientists at Neuropore Therapies are targeting the pathologic processes believed to underlie these disorders. Their hope and expectation is that this work will lead to new break-through therapies that not only improve the symptoms of Parkinson’s disease but also stop or slow its progression.

Opportunity Overview
Neuropore Therapies is taking several different approaches towards targeting one of the key underlying causes of Parkinson’s disease - the accumulation of pathological forms of the protein alpha synuclein in cellular membranes. The most advanced of these programs has yielded a promising lead compound called NPT200-11. This novel small molecule has been shown to reduce the accumulation of toxic oligomeric forms of alpha synuclein in lipid membranes and to reduce alpha synuclein accumulation in brains of animals over expressing the human form of this protein. The beneficial consequences of targeting alpha synuclein with NPT200-11 in these animals has been shown to include: reducing neuroinflammation, reducing neurodegeneration and improving motor function. Moreover, in all other respects NPT200-11 is, so far, proving to be a promising clinical candidate. The compound, has an excellent in vitro safety profile, is CNS penetrating and is orally bioavailable. The compound has also been shown to be well tolerated in both rodent and non-rodent animal species at doses well above those required for beneficial activities. NPT200-11 is currently in preclinical development.

Details of MJFF Grant
The overall goal of the MJFF-awarded grant is to further characterize the activity of NPT200-11 in animal models and to facilitate its advancement through early preclinical safety, pharmacokinetic and toxicology studies.

Work supported by this grant includes:
1) characterizing the relationship between dose, drug levels (in the periphery and in the brain) and, beneficial activities in animals models;
2) conducting mechanistic studies, using transcranial calcium imaging to further characterize the relationship between drug levels in the brain and acute beneficial actions on neuronal function;
3) evaluating NPT200-11 in early exploratory safety and toxicology studies to further assess its potential as a candidate for clinical trials.

For additional information, please contact: ResearchPartnerships@michaeljfox.org
Results and Potential Next Steps

Results:
We have evaluated NPT200-11 in multiple animal models with multiple endpoints measured so as to characterize the dose and drug levels required for therapeutic-like activities. By identifying the lowest effective dose in animals we have now identified a target concentration and pharmacokinetic profile that we believe will be required in order for the compound to produce beneficial actions in humans. This is of course a critical piece of information for any drug-development program.

We have also completed transcranial calcium imaging studies in animals over expressing alpha synuclein. These studies revealed that NPT200-11 could, upon a single administration, reverse alpha-synuclein mediated dysregulation of calcium dynamics. These effects lasted for at least three hours. The rapid beneficial effect on calcium signaling dynamics raises that possibility that, in addition to slowing the progressive neurodegeneration in Parkinson’s disease, NPT200-11 may also have relatively rapid beneficial effects in reducing untoward effects of pathological forms of alpha synuclein on neuronal physiology.

We have also completed dose range-finding toxicology studies in two species. The goals of these toxicology studies were to identify potential target organs of toxicity and to identify the appropriate doses for the subsequent definitive, IND enabling toxicology studies.

Additional work completed:
Using these MJFF funded activities as a spring-board Neuropore Therapies has further advanced the development of NPT200-11 by initiating all safety and toxicology studies required for IND submission. These studies will be fully completed in the coming months. In addition, several kg of NPT200-11 have been produced under GMP conditions in order to support initial clinical trials.

Next steps
The next steps in the development of NPT200-11 will be to complete and submit the IND application and then initiate clinical trials to evaluate the safety, tolerability and pharmacokinetics of NPT200-11 in humans.

Intellectual Property Status
Neuropore Therapies has numerous patent applications in different stages of prosecution protecting the composition and use of NPT200-11 in the treatment of neurodegenerative disorders.