August 25, 2004

Review Committee
2136 Gallows Road, Suite E
Dunn Loring, VA 22027

Attention: Mr. R. Erikson, Review Committee

Subject: Project #172-716-ARF

To keep up with the growing interest in myelin research, “A Proposal for Myelin Growth and Transplantation” is being submitted.

As you are aware, no cure and very limited treatment options currently exist for demyelinating diseases such as multiple sclerosis. Our research teams are interested in deriving oligodendrocyte precursor cells from stem cells and Schwann cells to transplant onto nerve cells that have been damaged by demyelinating diseases.

If you have any questions, please do not hesitate to call our office.

Sincerely,

[Signature]

Research and Development, NIND
MYELIN GROWTH AND TRANSPLANTATION RESEARCH:
A PROPOSAL

Prepared for:  Richard Erikson, Review Committee
              The Myelin Project

Prepared by:  , Research and Development
              National Institute of Neurological Disorders

August 25, 2004

NIND
National Institute of Neurological Disorders
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Summary: A Proposal for Myelin Growth and Transplantation Research

Remyelination is the key to treating and one day possibly curing demyelinating diseases such as multiple sclerosis or leukodystrophies. The National Institute of Neurological Disorders (NIND) would like to contribute to new discoveries and potential treatments. Our research teams are interested in deriving oligodendrocyte precursor cells from stem cells and Schwann cells. Upon successful transplant onto human nerve cells, oligodendrocyte precursor cells could remyelinate the damaged nerve cells, thus halting the degradation of myelin and even repair the myelin covering that had already been lost. We are requesting a grant of $125,000 to cover a facility large enough to house five research teams and equipment costs to continue research on this topic. Research is expected to begin early December of 2004 and a detailed progress report will be sent to The Myelin Project after the first six months of research. The NIND is proud to be a leader in remyelination research, and with the help of The Myelin Project, we hope to find a successful treatment and potentially a cure for demyelinating diseases.
The Problem: No Cure Available

Remyelination is the key to treating and possibly curing demyelinating diseases, which comprise of many neurological disorders. Demyelinating diseases affect more than two million people worldwide. These diseases which target myelin fall into two main categories: acquired diseases such as multiple sclerosis (MS), and hereditary neurodegenerative disorders such as leukodystrophies. Without myelin, nerve impulses are slowed or stopped, leading to a collection of neurological symptoms. Since research has only begun a mere 20 years ago, there is still much to discover about myelin and the potential for remyelination. Current estimates are that approximately 2.5 million people worldwide have MS, with between 250,000 and 350,000 cases in the United States. Each day new discoveries are being made towards remyelination, which is the main goal of The Myelin Project. The National Institute of Neurological Disorders (NIND) would like to contribute to new discoveries and potential treatments.

Figure 1. (Left) Normal myelin is the substance that insulates nerve cells, much like the insulation around a wire. (Right) Stripped of myelin, nerve signals cannot be transmitted from the brain and spinal cord to other parts of the body.
Our Proposal & Research Focus:

This proposal is brought to your intention in hopes of receiving funds for a new research project the NIND hopes to have initiated by early December of 2004. The project will focus on identifying a method for cell therapy that will coax human stem cells along the neural cell pathway, with the ultimate goal of having them become myelin-producing oligodendrocyte precursors (Ops). Past NIND research has shown that at least three factors are involved in failing remyelination:

- Loss of oligodendrocytes and oligodendrocyte precursors
- Inhibitory signals produced from inflammatory processes
- Reduced receptiveness of injured nerve fibers to remyelination

In order to combat these factors, the NIND believes the following possible therapeutic strategies have potential and would like to apply research teams to these options:

- Protecting oligodendrocytes from immune attack
- Recruiting oligodendrocytes into lesions and stimulating myelination
- Removing signals which inhibit myelin production
- Increasing the receptiveness of nerve axons to being remyelinated
- Replacing dead oligodendrocytes through transplantation of oligodendrocyte precursors, Schwann cells or stem cells

Figure 2. An overview of the stages of transplanting oligodendrocytes grown from stem cells into a human brain. This is the procedure that our research is working to make a treatment for demyelination caused by various neurological disorders.
The research project we are asking The Myelin Project to fund will consist of small teams, each headed by a distinguished research team member, working in collaboration because each therapeutic strategy is closely related. We feel that by approaching the research in this manner, more will be accomplished in a shorter time frame. Thus, less money will have to be spent for a large amount of research to be carried out.

Personally I will head the research team on replacing dead oligodendrocytes through transplantation of oligodendrocyte precursors, Schwann cells, and stem cells. My research team and I have been working together for 8 years; 5 of these years spent at the NIND on MS and remyelination. Our research has brought us far already, but we have run out of funding and are unable to continue the projects we have outlined.

**Budget: Remyelination Research Expense Distribution**

The funds are needed for various aspects of the remyelination research. Since we are hoping to have a collaboration of five research teams, a larger facility is required. Purchasing a used facility and stocking it with new equipment required to run tests and store data is the cheapest option. An estimated cost of $75,000-$82,000 is given for the facility and $26,000 for new equipment such as cell storage and culture equipment, computers, various lab supplies, and chemicals. Purchasing of stem cells will total $6,000. Lab rats will cost about $250 to purchase and maintain. Since the staff’s salary is being paid for by various universities and institutes, this will not be an expense drawing from the fund.

![Remyelination Expense Distribution](image)

Figure 3. The forecasted expenses that funding through The Myelin Project will cover. The estimated total being requested is $125,000.
These expenses total $114,250; we are submitting the request for $125,000 to cover any unexpected developments or expenses that are associated with biological research. The research is anticipated to begin early December of 2004 and will continue up to and through the first progress report that will be sent out to all interested parties six months into the research. During the first six months we hope to secure new ground breaking information about oligodendrocytes and demyelination and potentially a method for remyelination, though this will most likely require at least eight months.

Remyelination Research Schedule:

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<td>Stem Cell Differentiation into OPs</td>
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<td>Transplant OPs into Rats</td>
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Figure 4. A proposed outline of the timeframe the research teams will be working under. Most aspects of the research progress take up to a month. After the six month period, a progress report will be sent to The Myelin Project describing what was done and the results of the experiment. At this time, it will be decided if transplantation of OP cells has a chance of being successful. After that, the Committee can decide whether or not to further fund NIND’s research on remyelination.

The National Institute of Neurological Disorders is proud to be a leader in the ongoing research of myelin disorders and potential treatment options. With future funding from The Myelin Project, experiments in stem cells and Schwann cells will
continue and progress will be recorded. Without continued funding, years of previous research and collected data will go to waste and more time will pass before a treatment is found. Time, as we all know, is not an option with demyelinating diseases.

**Our Qualifications:**

Since MS is the most common of the demyelinating disorders, the NIND has focused on this neurological disease for the past 11 years, making more than seven of the most important medical advances in this field of study. My research team, under the NIND, is credited for the recent discovery and transplant of Schwann cells into rat brains. This is the first step in the direction of transplanting Schwann cells and stem cells in humans. Schwann cells are myelin producing cells from other parts of the nerve system. Also, the NIND currently has two research teams making progress on experiments with stem cells.

**Conclusion:**

My research staff has been working with the development of a successful remyelination procedure and after five years we are making huge advances towards our goal. We feel that oligodendrocyte precursor cells are the key to remyelination in a precise transplantation procedure. The oligodendrocyte precursor cells can be produced from stem cells. Funding this project will bring us to the discovery of a new life-saving procedure that has been the dream of The Myelin Project since it was founded. Allow my research teams and myself to make that dream come true. Patients of demyelination diseases have very little hope in a cure or advanced treatment and it is our goal to change their perspective. The cost of $150,000 is a small budget for such an overwhelming opportunity that The Myelin Project has a chance to be a part of.
Works Referenced

