Myelin Repair Foundation

Discovery through Collaboration

Summary of the Myelin Repair Foundation Research Plan

The Myelin Repair Foundation (MRF) research plan is a roadmap that guides the identification, execution and coordination of projects necessary to achieve myelin repair via these four objectives

1. Understand the basic mechanisms of myelination in the central nervous system, how these mechanisms are disrupted by Multiple Sclerosis (MS) and how to induce myelin repair
2. Identify therapeutic targets that effectively restore remyelination, rational drug targets that are effective in animal models and test these targets on human cells in vitro
3. Develop these targets to the point where they can be transferred, within 5 years, to commercial partners for rapid development and clinical trials
4. Document and protect our discoveries to ensure rapid development and commercialization and to fund future MRF research

The MRF uses a research planning and funding process that allows investigators flexibility in the design and execution of their research, within this well-defined and structured framework.

Problem definition:
Understanding the systems biology of myelination

The MRF research planning process began with the selection of Principle Investigators (PI) knowledgeable in neurobiology, with experience and expertise with myelin, and a broad, complimentary range of scientific backgrounds and specialties. Working with MRF, they developed a map of the biological interactions likely to play key a role in the myelination process. In addition, as a team they catalogued unanswered questions that must be resolved in order to understand how MS disrupts myelination and how the repair process can be stimulated. The scope of the project was defined from these critical questions and the associated map of biological interactions.

Myelin Repair—Key Biological Interactions

Six Areas of Investigation

Research projects in these six key areas of investigation are focused on identifying novel therapeutic targets to arrest the MS process and/or promote remyelination.

1. Understanding how oligodendrocytes are normally generated from neural stem cells and how MS perturbs this process

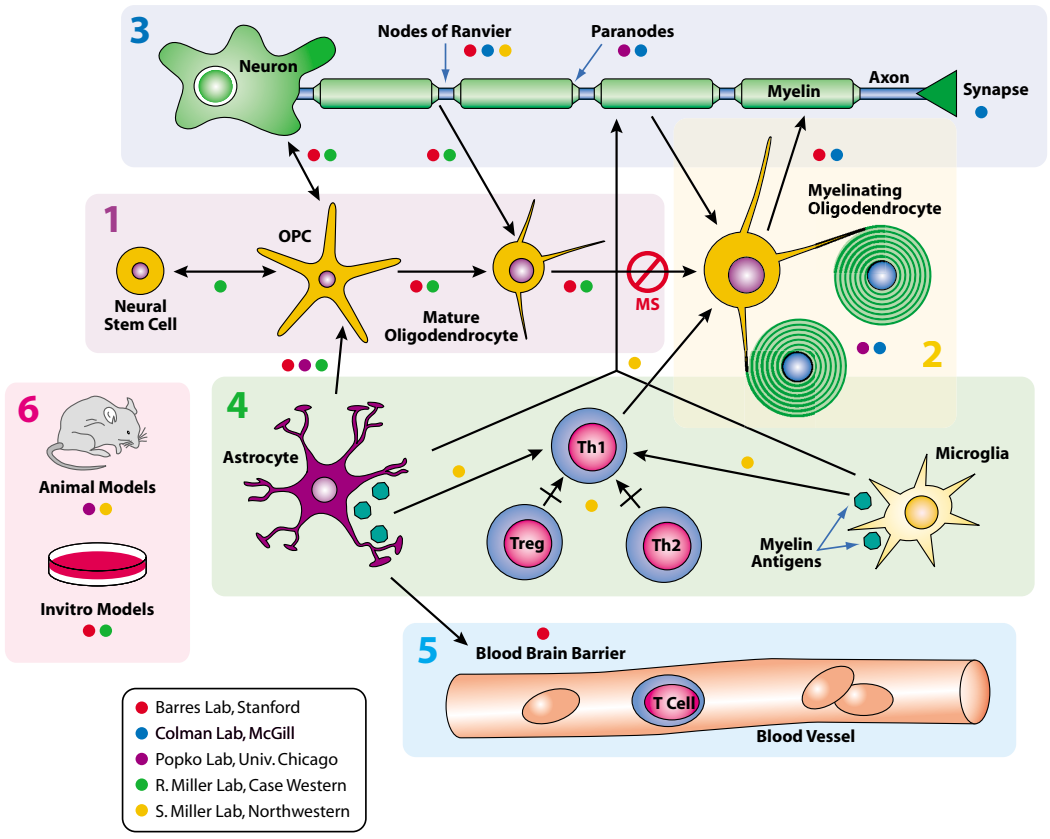
2. Understanding the underlying mechanism of myelination and how it is perturbed in MS

3. Understanding how nodes of Ranvier and paranodes are normally formed and how they are perturbed in MS

4. Understanding the immune response in MS and how inflammation affects myelin repair.

5. Understanding how the blood-brain barrier is effected in MS and its role in the disease.

6. Development of better animal models for study of MS and remyelination



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Developing a collaborative research plan

Once the scope of the research plan was defined, each investigator outlined a sequence of research projects based on their areas of expertise, to be led by their laboratory. These projects were sequenced to identify projects that must be started immediately, in Phase I, to facilitate the achievement of the overall plan. Once the team agreed on the research projects and the selection was reviewed and approved by the Scientific Advisory Board, the team leader for each project identified the collaboration support required from other laboratories.

In some cases the initial projects will provide critical research tools that do not exist commercially. This includes new animal models that more closely mimic human MS, methods to measure and monitor myelination in vivo, and novel cellular co-culture systems that allow the study of binary interactions to evaluate drug targets.

Throughout the research process, the team evaluates each research project to ensure maximum contribution to achieving project objectives, against both the overall roadmap and the key unanswered questions. It is the responsibility of MRF management to provide the tools, support and accounting to ensure that these collaborations run smoothly and that effective coordination between labs is achieved.

A flexible process with clear objectives

Because this effort involves basic discovery research it is difficult if not impossible to predict an exact timeframe for individual projects. Furthermore, the MRF encourages its investigators to try high-risk experiments, since more is often learned by failure than by success. Since relative priorities and future investigative sequences will be in large part determined by the results of current investigations, the MRF planning process is flexible by design. The research plan will be reviewed and adjusted based on results, every 4 months by the Principle Investigators. Proposed modifications will be reviewed and approved by the Scientific Advisory Board.

Since understanding the sequence requirements and interdependencies of these projects is critical to effective coordination and resource utilization, progress will be tracked via a project table rather than a timetable. In this manner, rate limiting steps can be identified early in the process and additional resources focused on timely completion of experiments or projects that are key to the next project in sequence. It will be the responsibility of the Principal Investigators, SAB and MRF management to evaluate the performance of each participating laboratory during the 4-month review process.

Principal Investigator Institution Laboratory Staff	**Ben Barres Stanford 16**	**David Colman MNI-McGill 40**	**Brian Popko Univ. of Chicago 13**	**Robert Miller Case Western 15**	**Steve Miller Northwestern 15**
Areas of Expertise					
Cellular Migration	✖			✖	✖
Cellular Maturation	✖		✖	✖	
Cellular Differentiation	✖		✖	✖	
Cellular Survival	✖			✖	
Cellular Proliferation	✖			✖	✖
Myelin Structure		✖	✖		
Myelination–Mechanisms	✖	✖	✖		
Myelination–Inhibition	✖	✖	✖		✖
Myelination–Activation		✖	✖		✖
Animal Models–Genetic			✖		
Animal Models–Disease					✖
Cell Culture Models	✖	✖		✖	
Human Tissue Testing				✖	
Immune Response					✖

Please visit our web site
www.myelinrepair.org

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18809 Cox Avenue, Suite 190
Saratoga, CA 95070
T 408.871.2410
F 408.871.2409
www.myelinrepair.org