

Ten Novel Targets Discovered

The ultimate measure of MRF's success will be defined (1) by the number of therapeutic targets that are discovered and validated in a five-year time period and (2) by the treatments that emerge from the subsequent clinical trials which provide benefit to those suffering from MS. To monitor its progress, the MRF business plan requires regular review meetings each year.

Since the scientific team began its research in July of 2004, ten targets and three therapeutic candidates have been identified. This rate of progress and the results achieved are unparalleled and support the value of the ARC™ model for speeding the time to discovery. MRF has filed nine patent applications to date and anticipates the filing of at least two more before the first quarter of 2007.

Therapeutic targets are biological processes that may be involved in controlling myelin repair. Once a potential therapeutic target is identified, the search begins for therapeutic candidates that will control the underlying biological processes. Each target and candidate are then validated through painstaking testing to demonstrate effectiveness in multiple disease models.

Target Identification and Validation					
Target	Fall 2004	Spring 2005	Fall 2005	Winter 2006	Fall 2006
1	I,C	V1		V2	
2	I				
3	I			C	
4		I			
5			I,C		
6			I		
7				I	
8				I	
9				I	
10					I

I = Target Identified C = Therapeutic Candidate V = Target Validation

Description of Identified Targets

1. Target for stimulation of myelin formation and a therapeutic candidate
2. Targeting developmental inhibitor of myelination to stimulate repair
3. Targets for protection of myelin-producing cells from inflammation-induced stress
4. Targeting antigen-presenting dendritic cells to control immune response
5. Target and therapeutic candidate for driving proliferation of precursors to myelin-producing cells
6. Targets for repairing the blood brain barrier
7. New genetic target for control of normal myelin protein expression
8. Second target for control of proliferation of precursors to myelin-producing cells
9. Target for driving proliferation of myelin-producing cells to promote repair
10. Target for controlling myelin protein gene expression

Eleven Research Tools Developed

One of the factors that has limited this area of research has been the absence of fundamental tools for the study of myelin and myelin repair. To that end, an additional measure of significance will be the number of research tools, or enabling technologies, which will have been developed to accomplish complex research of this nature.

New Research Tools					
Tool	Fall 2004	Spring 2005	Fall 2005	Winter 2006	Fall 2006
A	A1		A2		
B	B1				B2
C	C				
D		D			
E			E		
F			F		
G			G1	G2	
H			H		
I				I	
J				J	
K					K

Note: Numbers indicate additional development of the tool

Description of Research Tools

- A. Identification of low-abundance proteins unique to myelin
- B. B2– Method for selective elimination of specific neural cells. (Original approach [B1] identified in Fall 2004 did not provide consistent results and was abandoned.)
- C. Culture system for controlled stimulation of myelination
- D. Profile of gene expression during developmental myelination
- E. Culture systems for extended observation of myelin formation
- F. Purification method for adult oligodendrocyte precursor cells
- G. Profile of myelin gene expression in immune-demyelinating disease models
- H. Method for imaging cells surrounding the nodes of Ranvier
- I. Method for observing myelin formation process in situ
- J. Method for disrupting the blood brain barrier in new animal models
- K. Method for stimulating Blood Brain Barrier formation in culture



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