



Friday, 12 October 2007  
Epidemiology (Poster topic 4)  
15:30 – 17:00

## **[P315] Establishment of a large-scale, multidisciplinary sample and data repository for determining genetic and environmental causes of multiple sclerosis**

B. Greenberg, J. Goins, E. Frohman, G. Remington, S. Sadiq, B. Thrower, E. Iski, P. Riskind, J. Weaver, T. Vollmer, B. Bullock, S. Loud, A. Mellor, H. Schmidt (Baltimore, Dallas, New York, Atlanta, Worcester, Phoenix, Waltham, USA)

A large-scale MS Sample and Data Repository is being established to collect biological samples and extensive medical, clinical, and epidemiological data from MS cases and controls. The purpose of this repository is to support the growing need for well-characterized biological samples in MS research and in particular to promote the understanding of how genetic and environmental factors interact to cause MS. A variety of sample types are being banked in order to facilitate research in multiple fields (genetics, virology, etc.). Samples and data from the Repository are available to scientists from any institution who are working to determine the causes of MS, with the stipulation that data from their experiments be returned to the Repository database. Data analysis techniques will be applied to the Repository database to find correlations across studies that reveal how various factors interact to cause MS. Participants will be followed longitudinally so that changes in status can be recorded and so that additional samples and data can be obtained.

As of May 2007, the Repository has enrolled 472 participants from five MS clinics across the United States; by the end of the year we project that 1,000 participants will have enrolled. Further recruitment will take place so that the repository can support much-needed large-scale studies. The Repository has to date provided samples and data to three research teams (one of which has presented its results) and has approved the proposals of two others. Our participant base consists of 328 cases with MS or a clinically isolated syndrome (CIS), 23 cases with other demyelinating diseases, and 121 unaffected controls. Of the MS cases, 72% are relapsing-remitting, 19% are secondary progressive, and 9% are primary progressive. 76% are female, and the average age is 46.5 years (range 19-77). The average disease duration is 8.6 years (range 0-38). Of the 78% who are on a disease-modifying drug, 23% are taking Avonex, 13% Betaseron, 13% Rebif, 34% Copaxone, 4% Tysabri, and 13% another drug. 44% of our MS participants have at some time smoked more frequently than once per month.

We will present further characterization of the participant base as well as more information about the operation of the Repository. The availability of this Repository will enable the discovery and/or confirmation of MS etiological factors and contribute to the body of knowledge about how diverse factors interact to cause MS.

# Establishment of a large-scale, multidisciplinary sample and data repository for determining genetic and environmental causes of MS

B. Greenberg<sup>1</sup>, J. Goins<sup>1</sup>, E. Frohman<sup>2</sup>, G. Remington<sup>2</sup>, S. Sadiq<sup>3</sup>, B. Thrower<sup>4</sup>, E. Iski<sup>4</sup>, P. Riskind<sup>5</sup>, J. Weaver<sup>5</sup>, T. Vollmer<sup>6</sup>, B. Bullock<sup>6</sup>, S. Loud<sup>7</sup>, A. Mellor<sup>7</sup>, H. Schmidt<sup>7</sup>

<sup>1</sup>Johns Hopkins School of Medicine (Baltimore, MD, USA); <sup>2</sup>University of Texas Southwestern (Dallas, TX, USA); <sup>3</sup>Multiple Sclerosis Research Center of New York (New York, NY, USA); <sup>4</sup>Shepherd Center (Atlanta, GA, USA); <sup>5</sup>University of Massachusetts Medical School (Worcester, MA, USA); <sup>6</sup>Barrow Neurological Institute (Phoenix, AZ, USA); <sup>7</sup>Accelerated Cure Project for MS (Waltham, MA, USA)

## Overview

We are establishing a large-scale MS Sample and Data Repository to collect biological samples and extensive medical, clinical, and epidemiological data from MS cases and controls. The purpose of this repository is to support the growing need for well-characterized biological samples in MS research and in particular to promote the understanding of how genetic and environmental factors interact to cause MS.

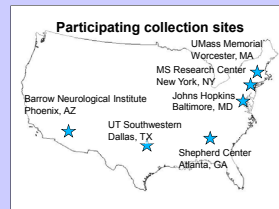
This repository is being made available to the MS research community through a partnership between Accelerated Cure Project for Multiple Sclerosis, a nonprofit organization, and leading MS clinics located throughout the United States.

## Repository Design and Operation

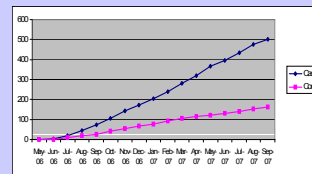
- Case subjects: People with MS, clinically isolated syndromes (CIS), and other demyelinating diseases (ADEM, TM, ON, and NMO)
- Controls: First-degree relatives and unrelated gender-, age-, ethnicity-, and geography-matched controls
- Large-scale: Up to 10,000 cases and controls
- Pediatric subjects included (minimum weight: 37 pounds)
- Longitudinal
  - Cases will return for a study visit (new interview, examination, sample collection) approximately once a year
  - Controls will return for a study visit up to once a year
- Following participants over time allows us to document the clinical course of cases, ask new questions (e.g., diet and trauma), and obtain new types of samples and replenish existing ones
- Samples collected: DNA, RNA, serum, plasma, lymphocytes (for EBV transformation)
- Data collected:
  - Extensive case report form covers clinical status, ethnicity, family and personal medical history, exposure to toxic agents, exposure to sunlight, and other factors
  - Disease ascertainment form allows enrolling physician to document the results of examinations and medical tests that supported the case's diagnosis

## Collection Status

We are currently enrolling cases and controls from six sites in the US:



As of September 21, 2007, 665 participants have enrolled:

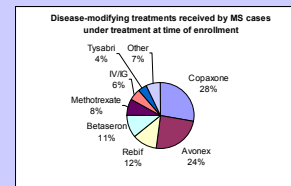
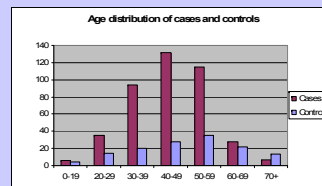


## Characterization of Cases and Controls

Subjects: 665	Treatment Status						Time Since Diagnosis			
	Tx+	Tx-	Tx Naive	TBD	< 5 yrs	5-10 yrs	> 10 yrs	TBD		
MS: 441	RRMS: 336	217	32	11	78	137	100	61	38	
	SPMS: 74	46	17	3	8	7	23	44	0	
	PPMS: 31	16	11	2	2	12	12	7	0	
Cases: 500	CIS: 10	3	1	5	1	8	1	1	0	
	TM: 32	1	2	28	1	20	6	6	0	
	NMO: 8	5	0	0	3	7	0	0	1	
	ON: 4	1	0	3	0	4	0	0	0	
	ADEM: 5	0	0	4	1	4	1	0	0	
Controls: 165										

TBD = to be determined (pending complete data)

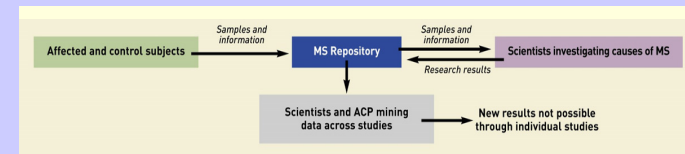
Participant Demographics		
Ethnicity	Race	Gender
Hispanic or Latino 12	American Indian or Alaska Native 1	Male 28%
Non Hispanic or Latino 567	Middle Eastern 2	Female 72%
Don't know 1	South Asian 2	
TBD 85	Black or African American 42	
	Native Hawaiian or Pacific Islander 1	
	White 531	
	Don't know 1	
	TBD 85	



## Distribution of Samples and Data

The repository is open-access – any scientist from any institution can request samples or data for projects that meet certain criteria. These criteria include scientific merit, potential benefit to people with MS or related diseases, and scale of project. A scientific oversight committee reviews all requests for samples and data.

Data generated from use of the samples are returned to the repository database to allow analysis across studies and identification of combinations of factors that interact in MS.



## Projects supported to date:

- Stanford University: Detection of anti-blood brain barrier antibodies in serum
- Beth Israel Deaconess: Genetic analysis of mitochondrial DNA
- Montreal Neurological Institute: Detection of myelin damage biomarkers
- State University of New York: Analysis of genes involved in inflammation and neurodegeneration
- Gene Logic: Whole-genome gene expression screen
- Oklahoma Medical Research Foundation: Analysis of serum antibodies to EBV

## For more information

The Accelerated Cure Project is a national nonprofit dedicated to curing MS by determining its causes.

VP of Scientific Operations:  
Hollie Schmidt [hollie@acceleratedcure.org](mailto:hollie@acceleratedcure.org)

MS Repository Director:  
Sara Loud [sara.loud@acceleratedcure.org](mailto:sara.loud@acceleratedcure.org)

Web: [www.acceleratedcure.org/repository](http://www.acceleratedcure.org/repository)  
Phone: +1-781-487-0008

