



MULTIPLE SCLEROSIS update

(VOL. 4 : SPRING 2005)

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Five dedicated runners took to the road on Monday, April 18th to raise money for the Accelerated Cure Project in the 109th annual Boston Marathon. This was possible thanks to the marathon numbers given to Accelerated Cure Project by John Hancock, a major sponsor of the marathon. The marathon is 26 miles, 385 yards, running from the rural outskirts of Boston to the heart of the city. The course record is just over two hours for women and men, but most runners expect to take somewhere between four and five hours.

At the time of this writing the marathon had not yet been run, but you can see how our runners did at the official Boston Marathon web site, www.baa.org, or in the Events section of the Accelerated Cure Project website, www.acceleratedcure.org. This year the team was composed of three women and two men, some who were old friends of the Accelerated Cure Project and others who were new arrivals eager to show their support for the first time. Here's a little information about the runners:

Carol Rose of Connecticut started running six years ago to keep in shape after having children. She has since taken up running for many deserving causes through the Pfizer Corporate Running Club. Her running is a collaborative affair with her family, who help her write letters to encourage sponsors, train with her, and

support her the whole way. Carol says, "My husband and I had the privilege of meeting Art Mellor and were inspired by his passion, focus, and drive for finding a cure for MS. With two close members of our family and a couple of friends who were recently diagnosed with MS, we wanted to be part of his process." She had her first opportunity to support the Accelerated Cure Project last year, running her first marathon, Mystic Places, and raising over \$7,000.

John Gannon, now living in Texas, was a long-time resident of New England and is an avid marathon runner. He has consistently finished marathons around the 4 hour 30 minute mark. John had wanted to run the Boston Marathon since high school so as a Valentine's Day gift his wife and running partner Mary contacted the Accelerated Cure Project and arranged for John to run for us. The family has a close friend with MS, which only strengthened John's dedication to making his first Boston Marathon something special. Before running, he said, "I love to run, but it is a purely selfish act. Running for a cause and raising money will allow me to connect my passion with a greater goal. If I do this right I can raise money for MS research and break my 4:30 time."

Boston Public School teacher and technology coordinator **Kelly Corrigan** is a new but enthusiastic runner. In her five

Letter from the President



Welcome to this edition of our newsletter! Inside, you'll read about where we stand with our sample collection and our Cure Map, and find out how scientists are studying the role of pathogens in MS. We are also pleased to report on the matching challenge that Water Cove Charitable Foundation has once again put forth to help us raise the funds necessary to do our work.

On the events side we tell you about our Boston Marathon team and a new fundraising initiative that we think lots of people will enjoy since it involves cooking and eating with friends.

Of course the big news in MS this past quarter has been that the most recently approved MS drug, Tysabri, has been suspended from sale by its manufacturer. Inside we provide an update on this unfortunate turn of events.

If you'd like to get monthly updates via email on what we are doing, you can receive them by clicking on the "Sign Up" button at the top of every page of our web site at www.acceleratedcure.org.

Regards,

Art Mellor President & CEO
Accelerated Cure Project

Calendar of Upcoming Events

We hope you can join us for some of these events!

For more information, go to www.acceleratedcure.org.

- Support a team for our **Fourth Annual Hunt to Cure MS**, a scavenger hunt on **May 21st** starting at the Skellig in **Waltham, MA**.
- Keep an eye out for our annual **Cuts to Cure MS** salon-a-thon, to be held in **Norfolk, VA** this **July**.
- Dust off the tees for the **Third Annual Tee-Off to Cure MS** golf tournament at the prestigious Charter Oak Country Club in **Hudson, MA**, fast approaching on **September 26th**.
- The spooky annual **Sing to Cure MS** Halloween concert is coming to **Lexington, MA** this **October**.
- Save the date of **October 29th** for the **Fifth Annual Boston Cure Party**, our fabulous annual event in **Cambridge, MA** that features a silent auction, guest speakers, and live entertainment.

Boston Marathon Team Runs for Accelerated Cure Project

(continued from page 1)

years of dedicated running she has run the Dublin City Marathon in 2002, and a prior Boston Marathon in 2003. Kelly's teaching experience has involved teaching students with special needs, including several with MS. Because she is familiar with this devastating disease, Kelly was especially honored to be able to do something she loves while helping such a good cause.

Local runner **Mark Aher** of Needham, MA, is a longtime friend of the Accelerated Cure Project. He said, "Not long after my wife Jacqui was diagnosed with MS in 2001 we read an article about Art and Accelerated Cure Project and were impressed by their approach and commitment to finding a cure. Jacqui is now on the board of the Accelerated Cure Project, and we are both actively involved with fundraising and bringing new people into the fold." Because he lives near Boston, Mark has had the luxury of training on the Marathon course itself. Although Mark has been a runner for many years, this was his first marathon.

Lifelong athlete and mother of four **Angela Robinson** grew up playing tennis in Texas. She attended college on a tennis scholarship, but took up running after she married, completing her first marathon in 1986. Angela lived in China starting in 1994 and ran for charity in the 100 kilometer MacLehose Trailwalker annual fundraiser organized by Oxfam Hong Kong. She recently ran the Disney Marathon, and her experience there has made her really excited to run for us. As she said, "I was amazed and inspired to observe so many physically-challenged runners pressing on. I remarked to my partners how great it would be to run on behalf of others who could not run themselves."

In addition to these dedicated team members, scores of Accelerated Cure Project volunteers were gathered to support the team on the day of the marathon, cheering them on through this grueling race.

This was the first year the Accelerated Cure Project received numbers to run in the Boston Marathon. We were moved by the dedication of the athletes who generously gave their time and energy to running this difficult race to raise money to cure MS.

WHAT'S COOKING?

Dine to Cure MS Coming Soon to a Kitchen Near You!

From June 18th to June 26th, the Accelerated Cure Project is offering supporters around the world a way to run an easy, fun event to raise money and awareness for the Project's mission.

We are asking volunteers to organize a dinner party with their friends on one day during this nine-day period. As part of the event, volunteers may choose to discuss Accelerated Cure Project with their guests, and they will collect contributions towards our efforts. We are especially hoping that volunteers will find this a great time to share their reasons for supporting the Accelerated Cure Project.

The Dine to Cure MS event was designed and spearheaded by volunteer Debbie Mellor. The idea appealed to Debbie partially because she loves an excuse to hold a dinner party, but as she says,

"I liked the concept of everyone gathering together in unison for a cause they believe in. I also like the concept because dining with friends is something that appeals to a wide variety of people. It's also a fundraiser that supporters throughout the country can be a part of. I also like the idea because I know we have a lot of supporters who want to introduce the Accelerated Cure Project to friends but could use a formal event or reason to do so."

There is still plenty of time to plan a party of your own to promote the Project among your circle of friends. Whatever your budget, available time, or location, we have designed this event so that everyone can participate in it. You'll have a great time with your friends for a great cause, so be sure to get in touch with us about hosting a party!

Contact Melissa at 781-487-0011 or melissa@acceleratedcure.org, or go to www.acceleratedcure.org/dine.

Cure Map Update

The Cure Map is well underway, with Phase 1 almost complete! MIT student Nina Mann's internship this January gave us a great start on the Phase 1 trauma track and we are now considering our options for finishing this up. Vice President of Scientific Operations Hollie Schmidt is working on infectious agents Phase 2, currently reviewing evidence accumulated on the many individual pathogens that have been investigated for a causal role in MS. She is also updating the Phase 2 genetics spreadsheet with studies published in the past year and flagging areas in the Phase 2 genetics documents that need to be updated. This summer we plan to hire two college interns to perform the Phase 2 analyses on nutrition and toxic agents. Interviews are currently underway.

	GENETICS	PATHOGENS	NUTRITION	TOXIC AGENTS	TRAUMA
Phase 1	COMPLETE	COMPLETE	COMPLETE	COMPLETE	In Progress
Phase 2	COMPLETE	In Progress	Pending	Pending	
Phase 3	In Progress	Pending			
Phase 4	In Progress: Blood and Tissue Bank				

VOLUNTEERS

Our volunteers are a precious resource! These generous folks have been giving their time to Accelerated Cure Project in recent months:

VOLUNTEER STAFF

Susan Mellor –
Administrative Assistant

ANNUAL REPORT

Ann Embrescia
Sue Flynn
Dave Henderson
Rip Kinkel
Eric Langlois

BOOK REVIEWS

Crystal Diemert
Martha Garrett

BOSTON MARATHON FUND RAISERS

Mark Aher
Kelly Corrigan
John Gannon
Greg Higgins
Jacqui McCoy
Angela Robinson
Carol Rose

DONOR DATABASE PROJECT

Joan Coyne
David Kaffine

GOLF TOURNAMENT

Mark Aher
Jayne Casey
Jacqui McCoy

LDN PROJECT

Dr. Yash Agrawal
Rob Lester

LETTER WRITING CAMPAIGNS

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Phyllis Baron
Linda Falcone
Mike Yashko

MSNEWS UPGRADE

Dave Baker
Brian Del Vecchio

NEWSLETTER

Joyce Ananian
Lisa Desautels
Barbara Morgenlender

OPERATION MISSING LINK

Debbie Mellor
Katherine Mosley
Lily Towers

SCAVENGER HUNT TO CURE MS

Kevin Abramson
Nancy Costello
Nancy Medeiros
Debbie Mellor
Bill Meyers
Debi Robison
Stephanie Sisto
Amanda Song
Lily Towers

On the Trail of MS Pathogens

By Hollie Schmidt

Trying to find out what causes MS is like being in a complicated detective novel. The story includes a crime scene (demyelinating lesions), clues (scientific and medical evidence), and detectives (scientists all over the world working to analyze these clues). And there are lots of suspects – potential causes that must be identified, followed, and interrogated so their connection to the disease can be revealed. Among the most intriguing suspects are infectious agents like viruses and bacteria, some of which are familiar characters and some of which are relatively new to the scene. Could viruses or other pathogens trigger MS, and if so, how can we tell which ones are involved? Read on to find out how scientists track down infectious culprits and what is happening in the search for MS pathogens.

Clues and Suspicions

There are a number of reasons why infectious agents are considered likely suspects as triggers of MS. For one thing, a number of similar diseases are already believed to be caused by viruses. These include human demyelinating diseases such as HAM/TSP which is caused by the HTLV-I retrovirus, and progressive multifocal leukoencephalopathy which is caused by the JC virus (and is the reason for the recent suspension of the MS drug Tysabri). We also know of animal viruses that cause demyelination and these are often used as models of MS. Suspected outbreaks or epidemics of MS, such as those reported in the Faroe Islands beginning in the 1940's, also

suggest that MS may have an infectious basis. Finally, although genetic factors are known to play a role in MS, family studies indicate that they are not sufficient on their own to cause the disease, and therefore environmental factors (such as pathogens) must also be involved.

So there is certainly plenty of circumstantial evidence pointing toward the involvement of pathogens in MS, but anyone familiar with courtroom dramas knows that circumstantial evidence is not enough to secure a conviction. We also need physical evidence that links a particular pathogen with MS.

Building the Case

What types of evidence are needed to prove that a pathogen is involved in causing or triggering a disease, and how is this evidence gathered? For diseases that are suspected to be directly caused by a single pathogen, there is a simple list of rules called Koch's postulates that are used to demonstrate causality. These postulates, published in 1884, state that the organism must be found in sick animals but not in healthy ones, that the organism must be isolated and cultured, that when the organism is introduced into a healthy animal the healthy animal also develops the disease, and that the organism must be reisolated from the experimentally infected animal.

Although these postulates seem logical and can be satisfied for some diseases, they don't apply in every situation. For instance, not all human

pathogens can be isolated and cultured, and not all human pathogens cause disease when transferred to an animal. However, for many diseases, the most difficult point may be the first requirement, that the organism must be found in all people with the disease but not in healthy people. It is quite possible that any pathogens involved in MS are common and even perhaps normally harmless, only triggering MS when other factors are present. It is also possible that a variety of pathogens are involved in MS, perhaps different ones in different people. Therefore, to demonstrate an association between a pathogen and a disease like MS, we need a more flexible set of criteria than Koch's postulates. Here are a few of the criteria we use when analyzing the MS literature on different pathogens:

- Is the pathogen more commonly found in people with MS compared with others?
- Is the presence of cell death, tissue injury or another characteristic of pathogenic activity more common in people with MS than in others?
- Does the immune response to the pathogen (e.g., antibody or T cell response) differ between people with and without MS?
- For common pathogens, does the age at which people are infected or another characteristic of the infection differ significantly between people with and without MS? (Age of infection may influence the development of a person's immune system.)

- Have any therapies aimed at controlling or eliminating the pathogen been shown to alter the risk or clinical features of MS?

If the answer to any of these questions is yes, have cause-effect relationships been established to explain and validate the findings? For instance, scientists often look for similarities between viral proteins and human proteins, which might be the basis of a harmful autoimmune reaction.

Note that unlike Koch's postulates, these criteria don't imply the existence of a clear-cut situation where something is present in MS subjects but not in anyone else. Instead, they presume that whatever is found in people with MS will also be found in people without MS, but perhaps to a different degree.

The Body of Evidence Today

The types of investigations listed above have been used to analyze a long list of infectious agents considered to be possible triggers of MS. Pathogens that have been investigated over the years include animal viruses known to affect the nervous system and common "childhood" viruses like measles. More recently, herpesviruses such as Epstein-Barr virus (EBV) and human herpesvirus 6 (HHV-6) have come under close scrutiny. The study of retroviruses in MS is also a currently active field, particularly the investigation of endogenous retroviruses which are virus-like genetic sequences that long ago integrated into human DNA. And while most of the attention has focused on viruses, other types of pathogens such as the bacteria *Chlamydia pneumoniae* (Cpn) have also been analyzed for a role in MS.

Despite all of these investigations, however, no infectious agent has been confirmed as a trigger of MS. Many of the findings linking a particular pathogen to MS have been non-specific – that is, they also have been found when studying other pathogens or when studying other diseases. Furthermore, for any given study showing that a relationship exists between a given pathogen and MS, other studies almost always exist that also tried but failed to detect that relationship. The

possibility that MS may be multiple diseases could contribute to the lack of clear signals, as different study populations may produce divergent results. Differences in methodologies or study design can also produce mixed signals, as highlighted by a recent study on the detection of Cpn¹.

The Search Goes On

Clearly, the hunt for infectious triggers of MS poses many challenges that must be addressed before success can be claimed. One major challenge is that there may be a significant time lapse between the initial infection and onset of MS, so any evidence implicating the pathogen may be disappearing by the time MS becomes clinically apparent. One way to address this challenge is to study people with MS as close to the onset of the disease as possible. Scientists are also increasingly studying children with MS since the time lapse between infection and onset could conceivably be much shorter than in adults. At one center performing this type of study (The Hospital for Sick Children in Toronto, Ontario), a team recently made the interesting discovery that 83% of children

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OTHER

Joyce Ananian - User Quotes Project
 Joel Baron - Research Paper Access
 Ashley Brody - FitSense Fundraising
 Mike Gonnerman - Accounting Advice
 Marion Leeds Carroll - Sing to Cure MS
 Philip Luongo - NYC Event
 Nina Mann - Cure Map
 Asha Mellor - FitSense Fundraising
 Debbie Mellor - Dine to Cure MS
 Barbara Morgenlender - Admin
 Peter Schmidt - Volunteer Intro Document
 Jane Shapiro - Winter Appeal, Auction and Sponsor Requests
 Jen Tobin - Neuroanatomy Paper
 Leslie Wolf - Boston Cure Party for MS

CONTRIBUTED GOODS AND SERVICES

Mark Aher and Jacqui McCoy
 Clockwork Design Group, Inc.
 Clock Tower Law Group
 Lisa Desautels
 Debbie Frattaroli
 Philip Luongo
 Mail Perfect, Inc.
 Jill McGaffigan
 Frank and Stephanie Sisto

If for any reason you've been left off this list in error, please let us know so we can include you in our next issue!

TISSUE BANK UPDATE

Since our pilot study started collecting samples in September we have successfully recruited about 20 people. The rate of collection is slower than we would like due to some regulatory hiccups at one site and some personnel changes at the other, but the pilot is serving its purpose. We're learning quite a bit about what works, what doesn't, and how we can improve things before launching our main study.

The main study will involve the collection of many more samples. Our initial goal will be to enroll 1,000 participants, but we intend to collect far more than that as we go forward. We are almost done with the first draft of the design for that study and we are talking with another major MS clinic (outside of Massachusetts) to be our next site. We will need to negotiate a contract and get IRB approval before beginning, but we'll announce the progress toward launching there as we proceed. Things are really starting to take off!

On the Trail of MS Pathogens

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with MS had a previous Epstein-Barr infection compared with 42% of their peersⁱⁱ.

Another challenge is that MS might be multiple diseases involving multiple pathogens, making any particular relationship between a virus and MS much harder to detect. The key to solving this challenge is to study large numbers of subjects, and gather as much information from the subjects as possible, so that even subtle or occasional associations can be extracted from the data. This is the strategy that we at the Accelerated Cure Project are taking with our large-scale, multidisciplinary blood, tissue and data bank for MS research.

With any disease of the central nervous system, a huge challenge is that it is hard to obtain affected tissue such as brain tissue or cerebrospinal fluid. The best solution currently to the scarcity of CNS material is for more people with MS to seek out tissue banks and sign up with them.

Finally, there are often difficulties in interpreting promising scientific evidence linking a pathogen with MS. An increased presence of a virus in MS brain tissue samples may mean that the virus is an active factor in the disease, possibly a key trigger. Or it might just mean that the breakdown in the

blood-brain barrier that occurs in MS lets more of the virus into the MS brain. A higher level of antibodies against a particular pathogen in MS subjects may indicate that the virus is active in MS and the body is trying to fight it with antibodies. Or it might be part of an overall immune system response that has ramped up production of other antibodies as well. This is why scientists tend to be on the cautious side when discussing positive results and why promising pathogens have to be investigated from many different angles.

What lies ahead in the search for the elusive MS pathogen? In the near term, scientists will continue to study the leading candidates such as HHV-6, EBV, Cpn, and endogenous retroviruses. Some researchers are interested in conducting additional clinical trials of antiviral and antibacterial therapies to see what effect they may have on people with MS. New techniques such as analyzing brain tissue for nonhuman genetic sequences may reveal the presence of pathogens not previously detected or studied in MS. There is much work to be done, but if it reveals one or more MS triggers, the rewards will be great indeed.

References: ⁱ Kaufman M, et al. "Is Chlamydia pneumoniae found in spinal fluid samples from multiple sclerosis patients? Conflicting results." *Mult Scler*. 2002 Aug;8(4):289-94.
ⁱⁱ Alotaibi S, et al. "Epstein-Barr virus in pediatric multiple sclerosis." *JAMA*. 2004 Apr 21;291(15):1875-9.

Tysabri Update

In our last newsletter we presented a feature article on a new drug, Tysabri, which had been recently approved by the FDA for the treatment of relapsing-remitting MS. Since that article there has been an unfortunate and tragic turn of events.

At the time of writing it was known that three people who were taking Tysabri contracted a very rare disease called progressive multifocal leukoencephalopathy or PML. The disease is usually fatal and at the time of writing two of

these people have already died. Because the disease is so rare, there was significant concern that their medications played a role.

All three people had been taking Tysabri for more than two years and two were also on Avonex. Biogen Idec voluntarily pulled Tysabri from the market in response to these events. An extensive investigation is currently being conducted to see if these cases of PML can be understood and to see what, if any, role Tysabri and/or Avonex played in its development.

PML is caused by a virus that is present in approximately 80% of the adult population, but does not cause disease unless a person becomes immunocompromised through a disease such as AIDS or via drugs used in organ transplantation to reduce rejection rates.

[MORE DETAILS ON THIS SITUATION AND RELATED DEVELOPMENTS WILL BE POSTED TO OUR NEWS SITE, MSNEWS.ACCELERATEDCURE.ORG.](http://MSNEWS.ACCELERATEDCURE.ORG)

Water Cove Matching Program

How it Works and What it's all About

It goes without saying that when an individual makes a gift to a charitable cause, they want to see it used as productively as possible. Some donors restrict their gifts to specific programs. Others look for creative ways to leverage them to ensure additional progress and support for the organization.

One such donor is the Water Cove Charitable Foundation. The foundation has been Accelerated Cure Project's largest contributor annually since its inception in 2001, and for three of those four years its gifts have been offered specifically through a matching program. The foundation matches, up to a specific amount and through a certain timeframe, gifts that other donors make to the organization.

The program is designed to motivate new and existing donors to support the Accelerated Cure Project and to do so with larger than average gifts. By speeding up funding it is speeding up progress on critical programs such as the Cure Map and the Tissue Bank.

This year the Water Cove Charitable Foundation's matching gift program will again match, one to one, any gift of \$1,000 or more made by July 1, 2005. Pledges will qualify as long as they are made by July 1, 2005 and paid in full by December 31, 2005. Matching gifts from employers can be counted as part of an individual's total contribution in order

to qualify for matching. This means that if you contribute \$500 and your company matches it, the combined gift of \$1000 will qualify. Similarly, if you organize an event and the total collected is over \$1000, that amount will be matched.

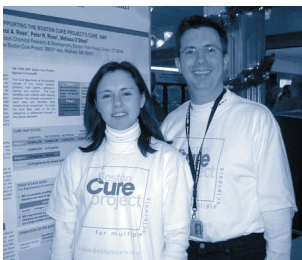
Last year, the Water Cove Charitable Foundation offered to match up to \$75,000 through their matching gift program. This year, however, the foundation is significantly raising the bar. It will match up to \$150,000 in total gifts.

It's a big goal for the organization. Should we meet the challenge of raising \$150,000 in qualifying gifts, we will receive \$150,000 from the Water Cove Charitable Foundation for a total of \$300,000. This will account for nearly forty percent of our overall 2005 budget, going a long way toward supporting our scheduled programs for the remainder of the year.

You can help by making a qualifying gift or pledge, by putting us in touch with others who can do the same, or by putting your own matching program in place. If you have the interest and ability to do any of these three things, please don't delay. Get in touch and help us determine the causes of MS as fast as we possibly can. Contact Melissa at 781-487-0011 or melissa@acceleratedcure.org.

Boston Cure Project T-Shirt Pictures

WANT A NEW ACCELERATED CURE PROJECT T-SHIRT? VISITING AN EXOTIC (OR NOT SO EXOTIC) LOCALE? If you offer to take a picture at your destination with an Accelerated Cure Project T-shirt on, we'll send you one for free!



Peter and Carol Rose at Pfizer, where Carol works, giving a presentation on the Cure Map and Tissue Bank and her fundraising efforts through our Sense of Purpose program.

Photo by Jodi Gaynor



Barbara Morgenlender and Max and Charlotte Nelson in Pompano Beach, Florida

Photo by Julie Morgenlender



Hollie and Peter Schmidt in Paris, France



Lisa Sargeant and Debbie Mellor at the Aquarium on the banks of the Mississippi River in New Orleans

Photo by Art Mellor



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Change Service Requested

ABOUT MULTIPLE SCLEROSIS

Multiple Sclerosis is a chronic demyelinating disorder of the central nervous system that often results in severe disability including the inability to walk, blindness, cognitive dysfunction, extreme fatigue and other serious effects. MS affects over 400,000 people in the US and 2 million individuals worldwide. The disorder occurs twice as often in women as in men. The cause is not known and there is no known cure.

CONTRIBUTE TO ACCELERATED CURE PROJECT:

By Check: make checks payable to Accelerated Cure Project and mail to:

Accelerated Cure Project
300 Fifth Avenue
Waltham, MA 02451

By Credit Card: On www.acceleratedcure.org, click on the "Contribute" box at the top of the page and follow instructions under the heading "Contributions by Credit Card."

Volunteer Today: See www.acceleratedcure.org for volunteer opportunities. On the left click "About," then click "Volunteer," then click on any of the volunteer opportunities for more details. You may also call 781-487-0008 or email info@acceleratedcure.org.

Want an Accelerated Cure Project T-Shirt? For any donation of \$25 or more, we will send you a t-shirt upon request. If you offer to send us a picture of yourself in one of our t-shirts, we'll send you one for free! Please remember to indicate t-shirt size when making your request. Call 781-487-0008 or email info@acceleratedcure.org

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MS NEWS WEB SITE: PRODUCED BY ACCELERATED CURE PROJECT

MS News is the first interactive online source of MS-related news and research updates. MSNews provides a place for the MS community – individuals with Multiple Sclerosis, family members, clinicians, scientists and others – to read and submit the latest news and research updates, participate in discussions on MS topics, and stay up-to-date on the issues that affect them most. Access to the site is available free of charge by visiting msnews.acceleratedcure.org.

Have you moved? Changed your email address? Let us know! Send changes in contact information to newsletter@acceleratedcure.org or call 781-487-0008!

ACCELERATED CURE PROJECT UPDATE

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