## **Nancy Davis Foundation for Multiple Sclerosis**

We are dedicated to the treatment and ultimate cure of MS. Funding research is the core focus of the Foundation and all funds raised support our Center Without Walls program, a selected network of the nation's top MS research centers. This nationwide collaboration of physicians and scientists are on the cutting-edge of innovative research programs, working as a team on therapeutic approaches to eradicate MS. In addition to combating MS through research in a clinical environment, we hope to increase awareness by educating the public about this mystifying disease.

#### **Winter 2010**

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Nancy Davis Foundation for Multiple Sclerosis

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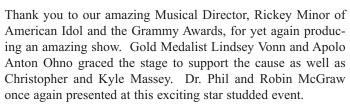
Phone: 310.440.4842 Fax: 310.471.4975 www.erasems.org

## May 7, 2010 Annual Race to Erase MS



Co-Chairs Nancy Davis and Tommy Hilfiger welcomed guests to the 17th Race to Erase MS at the Hyatt Regency Century Plaza on May 7, 2010. The evening kicked off with a high energy celebrity fashion show featuring the Spring 2010 collection by Tommy Hilfiger. Entertainment included rock stop-

ping ballads by legendary Heart, an amazing show by Dr. Hollywood, and a stand up and dance performance by Avril Lavigne. The event raised \$2 million for MS research thanks to a most generous group of supporters. Tommy Hilfiger, EMD Serono, Associated Television International, American Airlines, Lamborghini, and the Hyatt Regency Century Plaza all contributed to the incredible funds raised. A special thank you to the Brass Family Foundation and The Crazy Merchant, Inc.



Our event sponsors were truly instrumental in making the Race to Erase MS an electrifying evening. The extraordinary orange floral arrangements were generously donated by Marks Garden. Mindy Weiss, well known event designer, decorated the ball-

makeup for our celebrity presenters and fashion show participants.

room in vibrant orange to reflect the theme of the Nancy Davis Foundation "Orange You Happy to Erase MS" Month of May campaign. Thank you to Absolut, FIJI Water, POM Wonderful, and Cristophe Salon and MAC, who created the amazing hair and

Nancy O'Dell and Tom Arnold were our celebrity live auctioneers and did an amazing job in helping to raise the stakes high. The high-energy live auction featured a spectacular list of luxury items including a Lamborghini Gallardo LP 560-4 Coupe, and the most incredible vacation



Ken Rickel, Nancy Davis, Tommy and Dee Hilfiger



Avril Lavigne Live Performance



generously donated by the St. Regis Resorts including Asia, Italy and Hawaii. Among the guests were such superstars as Brooke Burke, Paris and Nicky Hilton, Anne Heche, James Tupper, Sophia Bush, and Kelly Rutherford.

Thank you to everyone for your infinite generosity and help in finding a cure for multiple sclerosis. Save the date April 29, 2011 for our 18th Annual Race to Erase MS at the Hyatt Regency Century Plaza!

## Message from **Nancy Davis**

**President and Founder** 



'It has been an exciting vear as we move closer to the finish line in our Race to Erase MS! I am honored to welcome Avril Lavigne to our

Board of Directors. She is an extraordinary and talented young woman who is so deeply passionate about helping others and we are thrilled to have her support.

2010 marked the 3rd anniversary of our month of May campaign, "Orange You Happy to Erase MS", and I am so grateful for the incredible response from so many who shopped to Erase MS! Thank you to all of our Orange Campaign Partners, Celebrity Supporters and Media who helped us raise important funds for MS research. This year we also expanded our annual MS Forum with a health and wellness EXPO. It was a great success and resource for all those that attended this event. Save the date for this amazing morning which is free and open to the public, April 30, 2011.

We are also so honored that Katie Brass, an incredible woman, tremendous supporter and member of our Board, has agreed to be honored for her generous and charitable work at our 2011 Race to Erase MS event along with Bill Perkins, a true pioneer and generous soul who has impacted the face of MS research.

Our Center Without Walls program continues to shine as a glowing example of what can be accomplished as a team! Together we will find a cure for MS and I am so grateful for the diligent work of the brilliant MS scientists that are dedicated to finding a cure.

Hany Sains

#### 2011 Race to Erase MS: Medal of Hope Award Honorees **Katie Mattingly Brass and** William O. "Bill" Perkins III

We are thrilled to announce Katie Mattingly Brass and William O. "Bill" Perkins III as our honorees at our 18th Annual Race to Erase MS event on April 29, 2011. Katie and Bill have been instrumental in the support of the Nancy Davis Foundation for MS. They will be awarded our Medal of Hope for their tremendous impact they have made in the community by educating the public, raising awareness, and funding vitally important multiple sclerosis research.

Our 2011 honorees are both active philanthropists, leaders in their community and forerunner's in supporting research to find a cure for MS. Just this past year, the Brass Family Foundation, together with William O. "Bill" Perkins III and Small Ventures USA, underwrote a genetic research study in conjunction with Dr. Stephen Hauser, Chairman of UCSF Neurology Department. The study, resulting from the most advanced genomic analysis ever conducted on identical twins with MS, suggests a key role of environmental factors in the disease. The study received worldwide attention from the science and medical fields and was featured on the cover of Nature Magazine. See page 5 of our newsletter for details on the study.



Our first co-honoree, Katie Mattingly Brass, is from Houston, Texas and is the mother of two glowing daughters, Hallie age 7 and Joycie age 6, and the wife of longtime love, A.J. Brass. Katie and her family reside in Houston, Texas and she enjoys spending time in Hermosa Beach, CA. Diagnosed with MS in 2006, Katie immediately became a strong advocate of MS related medical research projects to help make the future brighter for those diagnosed with multiple sclerosis.

Katie has been an active board member of the Nancy Davis Foundation for Multiple Sclerosis for over three years and is proud to be a leader in their "Race to Erase MS".



William O. "Bill" Perkins III, our second co-honoree, is the founder and president of Small Ventures USA, LP (SMV), a private equity and venture capital firm based in Houston, Texas, and founded in 1997. Mr. Perkins has more than a decade of experience in energy derivatives trading and is currently a significant market participant for Centaurus Energy. Mr. Perkins has produced a number of films under his production company, Lleju Productions and Films, includ-

ing After Life, The Chameleon and Road Kill. He currently resides in Houston with his wife and three children.

We look forward to honoring these two generous individuals who have a made a significant mark in the field of MS research, bringing us one step closer to finding a cure for multiple sclerosis. Visit www.erasems.org for more information on the event and full biographies on our honorees.



## **RACE** SAVE THE DATE! 18th Race to Erase MS Gala

Friday, April 29, 2011

For Tickets and Sponsorship Opportunities please call 310-440-4842 or visit www.erasems.org.

## **Avril Lavigne Joins Board**

We are pleased to announce award-winning singer/songwriter Avril Lavigne has agreed to serve on the Nancy Davis Foundation for MS Board of Directors, effective January 1, 2010.

Avril has been a long-time supporter of the Race to Erase MS and performed at this year's event which took place this past May, in addition to contributing a number of auction items.

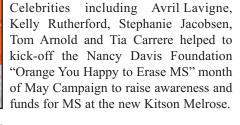
Avril recently created her own foundation, The Avril Lavigne Foundation, to support children and youth with lifethreatening illnesses or disabilities. The Avril Lavigne Foundation partners with leading charitable organizations to design and deliver programs, raise awareness and mobilize support for children and youth who are sick or who have disabilities. More information can be found at www.theavrillavignefoundation.org.

## **Kitson Melrose "Orange You Happy** to Erase MS" Kick-Off May 1, 2010



Nancy Davis, Avril Lavigne

Kitson Display



Throughout the month, Kitson generously

supported the cause and sold a variety of

orange products in their stores including Peace & Love by Nancy Davis products,



Kelly Rutherford

Stephanie Jacobsen



Brandon Davis, Nancy Davis

Celebrity Designed T-Shirts and Jewelry by Avril Lavigne, Paris Hilton and Ziggy Marley, Donni Charm scarf, Simon G jewelry and more, with 100% of the sales going to benefit the foundation. In addition, Kitson donated 1% of all Kitson store sales for the month of May to the Nancy Davis Foundation in their Race to Erase MS. We thank Kitson for their incredible, amazing contribution! Inspired by Nancy's dedication to finding a cure, a group of high school students



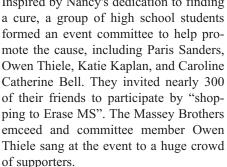
Barbara, Isabella, Alexander, Mariella Davis, Lindsay Schoneweis, Nancy Davis



Avril Lavigne



Tawny Sanders, Dean Keihl, Nancy Davis, Mariella Davis Rickel



Thank you to Crumbs Bakeshop and FIJI for sponsoring the event with delicious mini cupcakes designed in white and orange and mini bottles of FIJI water.

Shop year round at www.erasems.org and keep a look out for new products in 2011!





Crumbs Cupcakes FIJI Water



Massey Brothers with Paris Sanders, Owen Thiele, Katie Kaplan, and Caroline Catherine Bell











Nancy Davis, Ken Rickel

Tia Carrere

Steven Cojocaru, Nancy Davis

Owen Thiele sings

Kathy Hilton, Nancy Davis Display

> Hosted by WebMD, research scientists from the Nancy Davis Center Without

> Walls program shared the latest advances

in ground breaking research along with

## **MS Forum and Expo**

May 8, 2010



with Guests

Bill Perkins, Dr. Christian von Budingen, Dr. Stephen Hauser



Cast of "The Doctors



Ron Husman, Nancy Davis, AJ Brass



Expo Vendors & Guests

Dr. Michelle Cameron and Claudia Curry Hill



Mary Ellen Mitchell. Dr. Emmanuelle Waubant, Nicole Whitmore



David Osmond Performs





Expo and Forum Guests



Expo and Forum Guests

guest panelists who spoke about their personal experience with MS. This annual event is free and open to the public and attendees have the unique opportunity to ask questions and to speak directly to top MS neurologists. The cast of "The Doctors" emceed the mornings activities and David Osmond inspired the audience with an incredible musical performance. WebMD hosted clips from the forum as well as interviews with some of the CWW doctors. Please

This was the first year we integrated a health and wellness EXPO into the morning's events and we thank all of our resourceful EXPO Partners for their valuable participation. We would also like to thank Hyatt Regency Century Plaza, FIJI water, POM Wonderful, and Clementine's for their invaluable donations to this very important educational opportunity.

visit WebMD.com or our website for a

live podcast of this special forum.

Save the date for next year: April 30, 2011 at the Hyatt Regency Century Plaza. For more pictures and details on the event visit www.erasems.org.



Nancy Davis, Loni Anderson, Debbie Eaton, Deidra Hoffman and Lynn Palmer

**Nancy Davis Foundation** for Multiple Sclerosis

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Leslie Weiner, M.D. University of Southern California

Emmanuelle Waubant, M.D., **CWW Medical Director** University of California, San Francisco

## **Ampyra FDA Approval for MS**

Patients with advanced forms of MS often develop difficulty walking as a result of scars on their spinal cord. Some of them experience a lot of fluctuations in how they can move around from one day to the next, and often within the same day, thereby greatly limiting activities. Over the past 20 years, it was found that a chemical compound called 4-aminopyridine (aka as fampridine) could help ambulation in some patients with substantial leg fatigability. This compound was available until last year only through compounding pharmacies as a three to four times a day administration. A novel formulation (i.e. time-release formulation, twice a day) of 4-aminopyridine, also call dalfampridine (AmpyraTM, made by Acorda Therapeutics), was recently shown to marginally improve speed of ambulation in patients with disability due to MS. Improvement was seen in approximately 1/3 of the patients. This new formulation is overall more reliable than compound pharmacy products as there is much less variability from one batch to the next, thus decreasing the risk of side effects.

AmpyraTM blocks tiny pores, aka potassium channels, on the surface of nerve fibers. This can improve the conduction of nerve signals in nerve fibers with damaged insulation. This medication is overall well tolerated except for some dizziness, insomnia and a very small risk of seizures. The FDA approved AmpyraTM at the beginning of 2010 for improved walking. Because of cost, specific paperwork is necessary to obtain authorization from the health insurance and in some cases insurances may deny use of this drug. AmpyraTM is a symptomatic medication, i.e. it can help with symptoms of limited ambulation and possibly leg strength. It does not slow down progression of MS, i.e. does not limit the damage caused by the disease.

Information Provided By: Emmanuelle Waubant, MD, PhD, UCSF Director, Center Without Walls Program

## **Twin Genomic Study**

**University California, San Francisco** 

The study was conceived of by Stephen L. Hauser, MD, chairman of the Department of Neurology at UCSF, in collaboration with Jorge Oksenberg, PhD, UCSF professor of neurology and was funded by Bill Perkins of Small Ventures USA Inc., Katie and AJ Brass of the A. J. Brass Foundation. Scientists are reporting what they say is compelling evidence that some powerful non-heritable, environmental factor likely plays a key role in the development of multiple sclerosis. Their finding, the cover article in the April 29, 2010 issue of Nature, results from the most advanced genomic analysis ever conducted on identical, or "monozygote," twins where one sibling has multiple sclerosis and the other does not. The study was the first to examine all three levels of a human genome at the same time, giving the first full picture of a living genome. As a probe of a human genome, the study was a tour de force. The MS genome was explored at a depth of 20-fold coverage. By comparison, the first two single human genomes ever published -those of biologist and entrepreneur Craig Venter, PhD, followed by Nobel laureate James Watson, PhD - were sequenced at a depth of 7 to 8 fold coverage. In addition, the study investigated the first female genomes, the first genomes of twins and the first autoimmune disease individual genome sequences.

For the full article visit http://news.ucsf.edu/releases/ms-study-suggests-key-role-ofenvironmental-factor-in-the-disease

### **Stem Cells from Skin Cells**

Update from Dr. von Budingen's Laboratory **University California, San Francisco** 

Work currently going on in Dr. von Büdingen's laboratory at UCSF includes the generation of induced pluripotent stem (iPS) cells from skin cells from patients with multiple sclerosis (MS), neuromyelitis optica (NMO) and healthy donors (HD). iPS cells hold tremendous promise, on the one hand to more faithfully reproduce human disease in the laboratory, and on the other hand in regenerative medicine. Like embryonic stem cells, iPS cells have been differentiated into cells of numerous tissues, including brain cells, which in turn are expected to carry disease-specific determinants as they can be derived from patients with established disease. We have collected skin biopsy samples from 2 patients with retroviral transfection with 4 transcription MS, 4 patients with NMO and 2 HD and have successfully grown and multiplied their skin cells (dermal fibroblasts) in cell culture.

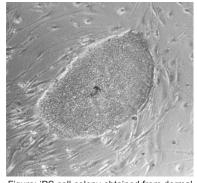


Figure: iPS cell colony obtained from dermal fibroblasts of a patient with neuromyelitis optica. Dermal fibroblasts were subjected to factors (KI44, Sox2, Oct4, c-Myc) and grown on a layer of feeder cells

Additional patients and HD are scheduled to have skin biopsies performed in the near future. In collaboration with the Stem Cell Research Institute at UCSF we have so far successfully obtained iPS cells from one NMO patient (Figure) - skin cells from 3 more study participants are lined up to be turned into iPS cells. We are currently in the process of expanding our first iPS cell line and have set up collaborations at UCSF to begin turning iPS cells into brain cells (oligodendrocytes, neurons, astrocytes). The goal is to study the influence of immune system cells and antibodies on brain cells that were generated from patients' skin cells. We expect to learn more about mechanisms leading to tissue damage in MS and about ways to prevent and possibly revert such damage.

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#### photo gallery: 17th Annual Race to Erase MS



Nancy O'Dell and Tony Dovolani



Nancy Davis Rickel, Mariella, Isabella and Ken Rickel



Tommy Hilfiger Fashion Show Finale



Avril Lavigne



Dee and Tommy Hilfiger



Nancy Davis, Avril Lavigne and Tommy Hilfiger



Bill Perkins and Skye Perkins



Marcy Taub, Katie Brass and Nancy Davis



Markie Post, Debbie Eaton, Sherry Corday and Sheri Disney



Paul and Lynn Palmer



Julie Chrystyn-Opperman and Diana Jimenez



Tawny and Jerry Sanders



Rickey and Karen Minor



James Tupper, Nancy Davis and Anne Heche



Ann and Nancy Wilson



David Horowitz and Guests



Paris Hilton, Brandon Davis and Nicky Hilton



Jimmy and Debbie Lustig



Drew Anderson, Kiki MacMillan, Bill MacMillan and Nancy Davis



Alexander Davis, Lindsay Schoneweis and Barbara Davis



Gary Stevens, Darrell and Debbie Patillo



Robert Knepper



Paris Sanders, Owen Thiele and Katie Kaplan



Apolo Anton Ohno and Nancy Davis



Victoria Page and Benjamin Sinclair



Brooke Burke



Brody Jenner and Linda Thompson



Ben and Ellen Rose, Bill and Alexis MacMillan Jr.



Lindsey Vonn and Becky Hernreich



Paris Sanders, Barbara Davis, Linda Thompson, Tom Arnold, Lindsey Vonn, Nancy Davis, Avril Lavigne, Lynn Palmer, Tawny Sanders



Jessica Lowndes



Laura and David McKenzie



Steven Cojocaru



Marcy Taub, Elizabeth and Gary Petersen, Nancy Davis, Anna Burns, Wes Welker, Katie Brass



Louis Van Amstel and Nancy Davis



Harriet Sternberg, Lyndi Hirsch, Vivan Fernandez, Dawne Davis



Dana Davis and Shane Henderson



Dr. Andrew Ordon, Dr. Lisa Masterson, Nancy Davis, Dr. Jim Sears



Lilia and Ed Ponce and Cammy MacMillan



Nicole Perna and Tina Kennedy



Rick and Kathy Hilton



Rosemarie and Matt Johnson



Lauren King, Kathy Hilton and Kathryn Belton



Gilles Marini



Sean Corcoran, Kim Kemper, Michael Utz



Austin Nichols, Sophia Bush, Marcy Taub and Elizabeth Petersen



Suzanne, Alexis and Sari Berman



Debbie and Jimmy Lustig (center) with Guests



Ryan and Carmel Geise Erin and Travis Holowach



Stephanie and Lilly Grace Cleveland



Ann Wilson, Nancy Davis and Nancy Wilson

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#### ms health tips and resources

#### **Improving Fatigue**

Some research suggests that acetyl-L-carnitine can improve fatigue associated with MS, although more study is needed. Acetyl-L-carnitine is a form of L-carnitine, an amino acid that is found in nearly all cells of the body. L-carnitine plays a critical role in the production of energy from long-chain fatty acids. In addition, it increases the activity of certain nerve cells in the central nervous system.

Fatigue is a common symptom in people with multiple sclerosis. A study published in 2006 evaluated the benefit of supplementation with L-carnitine in people with MS-related fatigue who had low blood levels of L-carnitine. Study participants were given 3 to 6 grams of oral Lcarnitine daily. Researchers reported a decrease in fatigue intensity in 63 percent of participants treated with immunosuppressive drugs, especially in those treated with cyclophosphamide and interferon beta. However, problems with the design of these studies make it unclear whether acetyl-L-carnitine is truly effective at reducing MS-related fatigue, and more study is needed.

Although acetyl-L-carnitine generally has only few or mild side effects, it can interfere with several medications, including anticoagulants, anticonvulsants, cephalosporins, penicillin derivatives, zidovudine and valproic acid. So talk to your doctor before starting acetyl-L-carnitine or any dietary supplement.

For more tips and and read the entire artcile VISIT: Source MayoClinic http://www.mayoclinic.com/health/acetyl-lcarnitine/AN01838

#### **Managing Your Weight**

When you have an autoimmune disorder, it may feel like there is already enough to deal with without worrying about whether you can still fit into your jeans. But weight management may have more to do with your long-term health than you think. Even people who do not have an autoimmune disorder experience the effects of excess weight gain or loss - so

it's not surprising that those effects, such as joint pain, fatigue, sleep problems, and long-term chronic disorders, may be multiplied if you also have an autoimmune disorder.

"Get out there and do as much as you can," advises Dr. Shaffer. Diagnosed in 2002 with multiple sclerosis, Shaffer knows the barriers to being physically active, both personally and professionally. If it is appropriate for the patient, he recommends flexibility exercises, such as yoga, Pilates, and stretching (modified as needed) in addition to whatever level of cardio exercise you can manage whether it's swimming, walking, biking, or dancing. As your autoimmune disorder progresses, you may find that you need to work with a physical therapist to learn how to move and exercise comfortably. Unfortunately, as autoimmune disorders progress, patients face a loss of mobility due to pain or muscle spasms. That's when changing your diet becomes a high priority, says Shaffer - although you should already be eating a nutritious, balanced diet.

For more tips and and read the entire article VISIT: Source: WebMd http://www.everydayhealth.com/autoimmune-disorders/managing-your-weight-with-an-autoimmune-disorder.aspx

## Alternative Symptom Remedies

Acupuncture. This ancient Chinese practice that uses hair-thin needles to stimulate the body's energy may be helpful in treating autoimmune disorders because of its effect on inflammation. There are numerous theories on how acupuncture works, but one explanation is that the needles trigger the body to produce hormones that suppress inflammation and pain.

Supplements. Like acupuncture, supplements that have an effect on inflammation may be helpful for patients with autoimmune disorders. These include vitamins E and A, fish oil, primrose oil, flaxseed oil, and SAMe (S-adenosylmethionine).

Massage. For autoimmune disorders that cause pain, massage therapy can be useful. It's a good idea to find a massage therapist who has experience working with autoimmune patients, however, because massage is sometimes contraindicated for acutely inflamed areas. Talk to your doctor about alternative therapies. One or more of these options may give you added pain and symptom relief without interacting with the medications you are already taking.

Source: Web MD Alternative http://www.webmd.com/multiple-sclerosis/guide/multiple-sclerosis-alternative-therapies?page=2

#### How to Get a Good Night's Sleep With MS

If you have multiple sclerosis, one of the most important ways to ensure a good night's sleep is to create a consistent bed-time routine. Here are some tips to get you sleeping soundly:

- Relax in the evening before going to bed. Try to not rehash the day's problems or worry about tomorrow's schedule.
- Go to bed when you're tired. Try to be consistent about the time you go to bed.
- Prepare yourself for bed by wearing comfortable nightclothes, adjust your bed pillows in a comfortable position, turn off the lights, adjust the temperature in your bedroom, and position yourself comfortably in your bed.
- If you do not fall asleep after 10-15 minutes -- get up! Do not lie in bed and watch the clock or count the cracks in the wall. Find something to do that is relaxing to you, such as putting together a puzzle, reading, or writing a letter to a friend. Rather than watching TV, which is a passive activity, do something active so that natural tiredness can build up.

Remember your bed is only for sleeping. Any of the above activities should be done out of bed. Return to the bed only when you feel tired.

For more tips and and read the entire article VISIT: Source: WebMd http://www.webmd.com/multiple-sclerosis/guide/taking-control-sleep

# Thank you to our 2010 Major Sponsors

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LOS ANGELES

## **Gilenya Receives FDA Approval**

First Oral Pill for Relapsing Multiple Sclerosis

The FDA approved Novartis' Gilenya this past June, the first oral drug that treats the relapsing form of MS and significantly reduces MS attacks. In MS, white blood cells attack the myelin sheaths that protect nerve cells. Gilenya, the first drug in its class, keeps white blood cells penned up in lymph nodes by taking away the chemical key they need to unlock the lymph node door. Fewer white blood cells mean fewer MS attacks. But it also means less protection against infections. Novartis will set up a careful program for educating and monitoring patients taking the drug. Moreover, the company will continue long-term studies to look for side effects that may occur with longer-term use. Side effects can include possible heart, lung, and eye toxicity and increased risk of infection. Patients must be closely monitored, and regular eye exams are advised. For more info see full article at www.webmd.com.

## **Genes, Environment and MS**

David A. Hafler, M.D. Chairman, Dept of Neurology, Yale School of Medicine

Multiple sclerosis is a complex genetic disease mediated by self-reactive immune CD4 cells that attack the myelin in the brain and spinal cord. The sequencing of the human genome in 2003, perhaps the creation of mankind's most important library, has finally allowed an intense investigation to identify the genes that cause MS. An international effort led by a number of members of the Nancy Davis Center Without Walls program have just been successful in creating a list of approximately 50 genes that are associated with MS risk. Over the next months, this list will be expanded to about 150 genes that are associated with the disease of the over 20,000 genes in humans. This genetic road map will be used by the next generation of MS researchers in understanding the cause of the disease allowing the development of new therapeutic approaches that may finally allow a cure for the disease.

However, it is not just the genes; instead, it can be viewed that these are good genes that have become disconnected from the environment. Here is a theoretical example: Eskimo populations evolved a genetic state such that because of their environment, they are very efficient in holding on to calories. That polar bear they may capture in the harsh winters need to last a long time. They do fine in this setting, as their genes were selected for their environment. However, if you take that same Eskimo matched for their environment and put them into, let's say the "golden arches" found in Florida with constant availability of high fat diets, the incidence of type 2 diabetes and obesity are rampant. It's not that the genes are bad - it is just those genes become disconnected with the environment. What is the environmental disconnect in MS? While we don't know, there are a number of interesting ideas. Something has changed in the environment such that the incidence of autoimmune diseases, such as MS and autoimmune diabetes have markedly increased. My guess is the bacteria in the gut, the so called "microbiome", has changed. We know that over 90% of the immune system focuses on the gut intestine keeping the bacteria we have co-opted for digesting food out of our bodies and in the gut. The rampant use of antibiotics, changes in diet, increased use of cesarean section for childbirth may all have possibly contributed to changes in the types of bacteria in the gut. Our immune systems so carefully co-evolved with the gut bacteria selected over the millennium, may lead to the heightened immune responses seen in autoimmune diseases such as MS. Ideas are easy; scientific proof is hard. We have begun experiments at Yale where we are using new technologies to deeply interrogate the gut bacteria in relationship to genetics and immune system to determine if this hypothesis in MS patients is at work.

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#### highlights from the lab

## **Center Without Walls Program Multiple Sclerosis Research Update**

The Nancy Davis Center Without Walls (NDCWW) is currently made up of seven groups with complementary expertise in multiple sclerosis (MS) research. The NDCWW exchanges scientific information and collaborates at multiple levels. Several new and exciting scientific achievements in the past year have continued to fuel the NDCWW's commitment to find a cure for MS. Scientific meetings provide an open forum for discussion and presentation of novel ideas and findings. Centers with specific expertise provide valuable support to others, with each having a unique background. This constant exchange process is nurturing an outstandingly rich research activity. The specific scientific accomplishments of individual centers are contained in the individual reports. The highlights are presented below and details on the research summaries can be found on our website at http://www.erasems.org/center-without-walls/.

## HARVARD MEDICAL SCHOOL:

In the past year we have made important advances in both animal and human studies in MS. We are trying to understand secondary progressive MS and have discovered a new pathway that can be used for drug discovery and as a blood test for relapsing remitting vs progressive MS. We have made new insights into the effect of treatment with the drug Tysabri on the immune system in MS patients. We are also developing a new oral treatment for MS and for the first time tested

the effect of oral anti-CD3 in humans. Our MRI studies investigated changes in normal white matter and regional white matter which has given us a better understanding of the disease. As part of our genetic studies we have helped to replicate and identify new genetic factors that are associated with the disease. Finally, in our CLIMB natural history study, we have investigated factors associated with treatment failure and the association between cognitive impairment and quality of life in early MS.

## JOHNS HOPKINS MULTIPLE SCLEROSIS PROGRAM:

During the 2009-2010 year for the Johns Hopkins MS Center in the Center Without Walls program, we have continued to enhance our understanding of the mechanisms underlying damage to the brain and are developing strategies aimed at arresting disease progression and improving quality of life in multiple sclerosis by the following three studies:

(1) Understanding how MS causes clini-

cal depression and cognitive impairment. (2) Uncovering the ability of combinations of antidepressants to potentially protect neurons and treat the immune dysregulation of MS.And (3) Visualize axons and myelin with magnetic resonance imaging. Details on these studies can be found at www.erasems.org.

#### YALE MULTIPLE SCLEROSIS PROGRAM:

Our laboratory is interested in preservation and restoration of function in MS, via prevention of axonal degeneration and restoration of conduction in emyelinated axons. Voltage-gated sodium (Na) channels play pivotal roles in MS not only in restoration of conduction following demyelination, but also in a degenerative cascade that leads to axonal death. We have demonstrated Na channel plasticity in axons within acute MS plaques, and have identified Na channel isoforms associated with injury of demyelinated axons within acute MS lesions. Our recent work also demonstrates that Na channels contribute to the regulation of function of microglia and macrophages in neuroinflammatory disorders, and suggests that microglia/macrophages play an important role in axonal degeneration in MS. Clinical studies of several Na channel blockers (including lamotrigine, topiramate, and phenytoin) as potential neuroprotective agents in MS have been planned and/or launched. However, we have demonstrated that withdrawal of phenytoin and carbamazepine from mice with MOG-induced EAE results in acute exacerbation and inflammatory rebound

associated with significant mortality. Thus, it is critically important to more fully understand the roles of Na channels, of Na channel block, and of withdrawal of Na channel block in neuro-inflammatory disorders.

## UNIVERSITY OF SOUTHERN CALIFORNIA (USC):

The team at the USC Center remains engaged in the study of stem cells and their ability to participate in brain repair and regeneration. Our efforts in this project involve new strategies to control the development of stem cells into the specialized brain cells needed to repair damage to myelin and promote healthy brain function. We have successfully transplanted stem cells into the brains of mice with MS-like disease and shown that these cells remain alive for over two months. Our current strategies are to enhance the function of these transplanted cells so that they can facilitate repair and recovery. The study of pregnancy in MS also remains a primary focus of USC investigators, with a goal of understanding the protective effect of pregnancy on MS, and what might be responsible for the increased risk for relapse that occurs after delivery. Recent data suggest an indirect neuroprotective function in immune cells isolated from pregnancy, and that the balance in the immune response is dramatically changed during and after pregnancy. We continue our efforts to develop a successful vaccine for the treatment of MS using heat shock protein, myelin complexes. We will test these complexes to see if they can treat animal

models of MS. Finally, the USC team is continuing to study both endogenous viruses (HERV) and viral infections such as Epstein-Barr Virus.

## UNIVERSITY OF CALIFORNIA, SAN FRANCISCO:

Genes, the fundamental hereditary units, are likely to play a role in determining who is at risk for developing multiple sclerosis, how the disease progresses, and how someone responds to therapy. Understanding these genetic events is key to define the basic underlying etiology of this disease. Our strategy for gene discovery relies on the meticulous scanning of the entire genome of patients and their relatives in order to identify DNA variants linked to the disease. To achieve our research objectives, we collect blood samples to extract genetic material from a large number of families with one or more affected individuals. These individuals are recruited from different ethnic groups, at high, intermediate and low MS risk. Since the initiation of this effort, we have completed the ascertainment and collection of biological specimens from over 9,000 individuals, including 4,750 affected with MS. This resource has been made available to investigators worldwide. By analyzing their genetic makeup, we will be able to understand the rules of MS inheritance, and consequently define the basic etiology of MS, improve risk assessment, and influence therapeutics.

## CLEVELAND CLINIC FOUNDATION:

Key issues in MS treatment include the underlying mechanisms causing disease, and the related issue of how to repair damaged brain tissue in MS patients. We believe that chemokines may be important in the MS disease process - both inflammation mediated tissue damage, and the repair process. Dr. Richard Ransohoff and colleagues are using sophisticated gene-targeted mice to determine which model system will permit the most powerful insights into the function of individual chemokines and receptors. It has become clear that certain chemokine

receptors are essential to development of brain inflammation in the animal model of MS. This information will identify which of the chemokine receptors should be targeted for novel treatments. The information from these studies will also provide valuable information needed to track inflammation in MS patients. The studies supported by the NDCWW address the role of CXCR2 in the disease. These studies are directed at testing the hypothesis that the chemokine receptor CXCR2, which is expressed both by infiltrating white blood cells, and by myelinating cells in EAE lesions, carries out two deleterious functions during demyelination. First, CXCR2 helps white blood cells enter lesions. Second, CXCR2 stops remyelinating cells from entering lesions to carry out repair. Dr. Ransohoff is studying both effects, which can be separated by sophisticated gene knock out mice and radiation chimeras.

#### OREGON HEALTH SCIENCE UNI-VERSITY:

The highlights of 2009-2010 are as follows: 1. Continued research on how blocking a protein in mitochondria protects nerve fibers. 2. Started the first study on how inflammation can disrupt axonal transport. 3. Continued to develop lipoic acid as a treatment for multiple sclerosis. And 4. Continued to study whether energy production in the brains of people with MS is impaired. We believe that the mitochondria in the brain in MS does not produce normal amounts of ATP, the energy "packets" of all cells. We have continued to pursue testing this idea using a high field (7T) MRI scanner. Measuring ATP levels in the brain is technically challenging but this year we established the technique to do so. We have begun measuring ATP in the brains of people with MS and in healthy age and sex matched controls. Our early results suggest that the ATP is abnormally low in the grey matter of people with MS. If confirmed, this finding would suggest that ATP depletion may cause progressive grey matter atrophy and point to the need to develop treatments that enhance ATP production.

## Center Without Walls Collaborating Physicians

Dr. Lilyana Amezcua, University of Southern California Dr Rob Bakshi Brigham & Women's Hospital Dr. Robert Bernel, Cleveland Clinic Dr. Guy Buckle, Harvard Brigham & Women's Hospital Dr. Tanuia Chitnis, Harvard Brigham & Women's Hospital Dr. Jeffrey Cohen, Cleveland Clinic Dr. Kathy Conant, Johns Hopkins Dr. George Eisenbarth, University of Colorado, Health Sciences Center Dr. Elizabeth Fisher, Cleveland Clinic Dr. Bob Fox. Cleveland Clinic Dr. Suzanne Gauthier, Harvard Brigham & Women's Hospital Dr. Wendy Gilmore, University of Southern California Dr. Ari Green, University of California, San Francisco Dr. Charles Guttman, Harvard Brigham & Women's Hospital Dr. Halina Hoffner. Oregon Health Sciences Dr. Norman Kachuck, University of Southern California Dr. Adam Kaplin, Johns Hopkins Dr. Samia Khoury, Harvard Brigham & Women's Hospital Dr. Jeff Kocsis, Yale University Dr. Brian Kotzin, Amgen Dr. Brett Lund, University of Southern California Dr. Ellen Mowry, University of California, San Francisco Dr. Jorge Oksenberg, University of California, San Francisco Dr. Daniel Pelletier, University of California, San Francisco Dr. Richard Ransohoff, Cleveland Clinic Dr. Jack Ratchford, Johns Hopkins Dr. William Rooney, Oregon Health Sciences Dr. Jamie Stankiewicz Brigham & Women's Hospital Dr. Bruce Trapp, Cleveland Clinic Dr. VJ Yadav, Oregon Health Sciences Dr. Arthur Vandenbark, Oregon Health Sciences Dr. Arun Venkatesan, Johns Hopkins Dr. Ruth Whitham, **Oregon Health Sciences** Dr. Scott Zamvil, University of California, San Francisco PAGE 12 2010

#### photo gallery, continued

#### Race to Erase MS



Keith and Kirsten Sarkisian



Aiden Turner



Sean McNabb, Christine Devine and Amy Puente



Debbie Gibson



Ali Landry



Skye Perkins, Bill Perkins, Tama and John Klosek



Tony Williams and Lynn Palmer



Nancy Davis and Nancy O'Dell



Jessica Holmes, Kurt Knutsson, Matt Rosler, Maggie Knutsson, Todd Lieberman, Heather Lieberman



Paris Hilton



Gay Blackstone, Emma Sharratt MacEachern, Sasha Fiebig



Stephanie Jacobsen



Ken Rickel, Tom Arnold and Tony Dovolani



Claudia Curry Hill and Guests



Kelly Rutherford



Mary Milner and Lauren King



Alexander Davis and Nancy Davis



Dr. Phil and Robin McGraw



Heather duBoef, Carla Soloman Tawny and Jerry Sanders



Chelsie Hightower



Lamborghini



Megyn Price



Jami Lea and Austin Winkler



Dina and Noel Cohen



Melissa Rycroft



Jordan Cohen with Guest



Nancy Davis, John Davis, Barbara Davis and Tom Arnold



Ashlan Gorse and James Maslow



Cindy and Nick Locke, Alexa Ernstam and Angelo Ferrara



Kaley Cuoco and Guest



Silvia Baker, Deidra Hoffman, Loni Anderson, Debbie Eaton, Sherry Corday, Robin Correll



Nicole Whitmore and Mary Ellen Mitchell



Debbie Conti and Kimberly Hanapel



Ron Rosen (center) and Guests



Drake Bell



Brenda Richie and Grace Rwaramba



Vanessa and Terry Thanos



Kyle and Chris Massey



Robyn Williams Culver, Paul Culver, Ron and Liz Williams



Dr. Hollywood



Brandon Davis and Nancy Davis



Mariella Rickel, Lindsay Schoneweis, Isabella Rickel



Pamela and Sheri Sussman



Alexander Davis, Lindsay Schoneweis Matt and Karen Winnick



Kathy Hilton, Nancy Davis, Lynn Palmer and Marcy Taub



Masi Oka



Ken Rickel, Joyce Black, Nancy Davis and Stanley Black



Elizabeth Stanton and Jazzlyn Marae



Benjamin Sinclair (center) and "St Regis" Guests



Jeanette Elsner and Guest



Manfried von Imbior



Nancy Davis and Linda Gray



Brett and Ashley Barker



Erik, Nanette and Francesca Estrada, Nikki Haskell



Eva Julfayan and Austin Ryan Feuntes

#### from our supporters

Thank you to our incredible supporters across the country who are raising money for the Nancy Davis Foundation Center Without Walls program! With your generosity and support in our "Race to Erase MS", we will find a cure!



#### **Nicole** Whitmore Salem, MA

Nicole produced her first fundraising event on March 20th at the Kernwood Country Club located in Salem, MA and raised over \$35,000 for the Nancy Davis Foundation to find a cure for MS! The evening kicked off with cocktails and a silent auction and everyone enjoyed festivities.

Congratulations Nicole! And on behalf of everyone who is affected by this disease, we are so grateful for your energy and spirit and to all of Nicole's friends and family who helped make her first event such a huge success! THANK YOU!



Nicole Whitmore (Center) with Family







Display



Dr. Maria Houtchens, Brigham & Women's MS Center



#### Louis nagine Rittberger Cleveland, OH

Louis Rittberger's mother was diagnosed with MS 20 years ago and since that time he has made it his mission to raise money for the cause. He produced his first fundraising event "Imagine" in Mayfield Heights, Ohio on September 11th and we are honored to have been chosen as the beneficiary! The evening was full of wonderful food, amazing entertainment, and beautiful atmosphere including a silent auction and

We are so appreciative of everyone who participated in "Imagine". Each one of you helped to raise over \$60K for MS research! Thank you to Louis for your incredible dedication and enthusiasm to help us get one step closer to winning our Race to Erase MS!



Louis and Betsy Bloch



**Event Venue** 





Louis Speaking



Betsy Bloch Gayle Marks





## **Debbie Conti** Jacksonville,

Debbie, who was diagnosed with MS two years ago, held her first fundraising event last Fall to raise money for the Nancy Davis Foundation. Thank you Debbie for your incredible effort and support to raise much needed funds and awareness for MS! Debbie, a wife and mom of three is a great inspiration to all of those around her and we are thrilled to have her as part of our team in our Race to Erase MS!

Debbie wanted to shout out to her support team a big thanks - Leah Smith, Kelli Morrison and Kim Hanapel - "who are a huge part in helping me with our fundraiser. Couldn't do it without them!"

Debbie and her band of volunteers are preparing for their Second Annual "Dance Your Orange Off" in Jacksonville to benefit the Nancy Davis Foundation for MS. Details of date and location will be posted on www.erasems.org and you can also look out for Facebook and Tweet updates!



Debbie Conti, Leah Smith, Kelli Morrison, Kim Hanapel

## Targetin B Cells with Rituxim ab

In the past 10 years, a renewed interest has emerged in a specific white blood cell type involved in the immune response, aka B cells. These cells appear now to be key players in the immune chaos occurring during multiple sclerosis. B cells are important as they make antibodies, help prevent some infections, and keep the memory of prior vaccinations. However, some of the B cells appear to promote unwanted inflammation, and thus they might be bad for MS patients.

Only a few drugs target specifically B cells. Rituximab, a drug approved for non-Hodgkin lymphoma since 1997 and rheumatoid arthritis since 2006, has been evaluated as a promising treatment for MS. Rituximab belongs to the drug family called "monoclonal antibodies", i.e. proteins that are manufactured to look like some antibodies we make, with some subtle differences. In 2008 and 2009, rituximab was proven to dramatically improve MS outcomes in patients. During the trials, patients with relapsing-remitting MS had much less MS scar develop in their brain, and also had less relapses than patients who received the sugar pill. The Nancy Davis centers played a key role in these studies. One trial also tested whether rituximab helped to slow down the disease in patients with insidious progression, aka primary progressive MS. This trial showed the drug prevented new MS scars on brain and spinal cord MRIs but its effect on worsening of patient's ambulation was unclear. Thus it was decided the drug should be further evaluated to confirm whether it helped patients with progressive disease or not.

Rituximab is given as an intravenous infusion once or twice a year, making it very interesting for patients. It is overall safe, although some side effects can occur during infusions such as chills, fever and low blood pressure, mostly with the first infusion. The long-term risks of infection are unclear.

The company making the drug has now developed an improved version of rituximab called ocrelizumab. This new drug has been tested last year in a small MS trial and was found to be beneficial and better tolerated than rituximab. It was also found to work better than interferon treatment. Thus, the company is now proceeding with several larger trials so they can obtain FDA approval for MS. These promising trials will start early 2011.

Information Provided By:Emmanuelle Waubant, MD, PhD, UCSF Director, Center Without Walls Program

#### Vitamin D Levels Effect MS?

Emmanuelle Waubant, MD, PhD, UCSF Director, Center Without Walls Program

Vitamin D is actually a hormone that maintains not only normal bone health, but also appears to have a broad impact on the immune response. Several studies have shown that decreased sun exposure early in life and decreased intake of foods rich in vitamin D are associated with a modest increase in the risk of developing MS. Until this year, it was unclear whether vitamin D was also important for MS severity once the disease had started.

One study performed by one of the Nancy Davis centers shows that patients with low vitamin D levels have a higher risk of experiencing MS relapses, regardless of whether patients were also on MS drugs such as interferon or Copaxone. These exciting findings have now been replicated by an Australian team, confirming the strong ties between vitamin D levels in the blood and the risk of relapses in patients already diagnosed with MS. Another Nancy Davis center studied the absorption of several types of vitamin D supplement. This study is important as some types of vitamin D supplements do not result in appropriate increase in blood levels of vitamin D compared to others. This is highly relevant as we are seeking funding to perform a definitive study that will confirm whether vitamin D3 supplementation prevents MS relapses and brain MRI scars. We hope to start this study during the first quarter of 2011.

Our findings, confirmed by the Australian team, have brought hope for the development of a cheap oral treatment for MS. Until our vitamin D trial is completed, the question that a lot of patients with MS will have for their doctors is whether they should take vitamin D supplements or spend more time in the sun. Physicians often recommend measuring a patients serum 25-hydroxyvitamin D3 levels before considering customized oral supplementation, as it is unclear whether vitamin D truly affects the course of MS and also because overdosing on vitamin D can have serious health consequences. Make sure to check with your personal physician before taking any supplements and have your vitamin D levels evaluated.



## **Young Investigator Awards**

Congratulations to our 2010-2011 Grant Recipients!

Our mission is to fund cutting-edge, innovative research programs in our quest to find a cure for multiple sclerosis. We are thrilled to support the best and the brightest young minds in scientific research. Below are the 2010-2011 Young Investigator Awardees. Complete bio sketches on each recipient can be found at EraseMS.org.



Kevin C. O'Connor, PhD, Assistant Professor of Neurology Yale School of Medicine

Antigen-antibody Complexes in MS: In our current work we are evaluating if these newly identified antibody-antigen pairs can be found in the cerebrospinal fluid and blood. If they are, we will correlate their presence with

clinical parameters in an effort to identify new biomarkers for MS. We are equally focused on understanding the role these antibodies play in the destruction of tissue in the MS CNS. The overall study aim is to provide insight into the nature of the autoimmune cell response in MS, which may lead to new ways to prevent or treat the disease.



H.-Christian von Büdingen, MD, Assistant Professor of Neurology University of California-San Francisco

The Role of Antibodies in MS: Several lines of strong evidence ascribe antibodies an important role in the formation of scars in brain tissue of MS patients. The proposed research project will, therefore, study the influence

of MS antibodies on iPS cell-derived brain cells from MS patients. Induced pluripotent stem (iPS) cells, can be derived from patients' skin cells. The overall goal is to unequivocally establish the disease-relevant role played by antibodies in MS. Such knowledge is expected to greatly enhance our understanding of MS and will likely facilitate the development of innovative therapies.



Jack Ratchford, MD, Assistant Professor of Neurology, Johns Hopkins University, Baltimore, MD

Optical Coherence Tomography Biomarker of Axonal Itegrity in MS: Current MS treatments are partially successful at targeting the inflammation that occurs in MS, but it has been difficult to prevent the axonal degen-

eration that causes much of the disability in progressive MS. Identification of neuroprotective treatments is critically important, but testing of potential neuroprotectants has been limited by a lack of biomarkers of axonal integrity. Optical coherence tomography (OCT) may be a good biomarker for measuring axonal damage in MS patients and could help to accelerate testing of neuroprotective compounds. The overall study aim will help establish OCT as a surrogate outcome measure in MS and will lead to a proposal to test several potential neuroprotectants using OCT together with traditional disability outcomes in progressive MS.

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