



Alzheimer's Disease Research Center Newsletter

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The Alzheimer's Disease Genetics Study:

Mount Sinai has joined Columbia in a nationwide effort to identify 1,000 families with 2 or more siblings with late-life Alzheimer's disease (AD) to participate in a major research study about the genetics of AD. The goal of the study is to speed up the search for risk-factor genes that increase the risk of developing AD later in life.

The AD Genetics Study is sponsored by the National Institute on Aging (NIA), part of the National Institutes of Health in the U.S. Department of Health & Human Services, and is supported by the Alzheimer's Association, the nation's largest private health organization dedicated to advancing AD research and providing information and support to those affected by the disease. The

Study will be conducted by NIA-funded research centers around the country, including Mount Sinai Medical Center.

Researchers will create a large bank of genetic material, cell lines, and data from families with multiple members with late-onset AD, which scientists can then use in their quest to discover the risk-factor genes that contribute to late-onset AD, the most common form of the disease.

Locating one risk-factor gene out of the 30,000 or so genes that are contained within the human cell is no easy task. One of the most effective ways of locating disease risk-factor genes is to study families with multiple members affected with the condition, such as the case in AD. In fact, the

known AD genes as well many of the genes for other human diseases have been located by studying families with multiple members affected with the disease in question.

About 90% of people with AD have the late-onset variety, which strikes people aged 65 or older.

There is no obvious inheritance pattern with late-onset AD, but researchers have identified one "risk-factor" gene, the 4 variant of apolipoprotein E (apoE). This discovery has opened up many important avenues of understanding the biological and environmental interactions that may be important to the development of late-onset AD. While scientists have drawn significantly closer to identifying at least four regions of the chromosomes where



"Genes will help illuminate the underlying disease processes"



Hillel T. Grossman, M.D.

Ask The Expert: Hillel Grossman, M.D. Medical Director, Clinical Core

Q: What about Memantine? Should I take it?

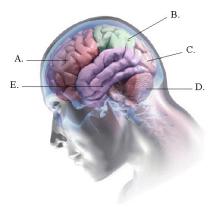
A: Memantine was approved a year ago for *moderate stage* AD and is a new class of drug which may show benefit when used alone or in conjunction with donepezil. Patients at the moderate stage may evidence more difficulties with daily activities such as routine tasks and chores. Memantine, which seems to work through a new mechanism or pathway in the brain, attaches to NMDA receptors in the brain and regulates the activity of the chemical transmitter, glutamate. Dysregulation of glutamate can destroy cells and is thought to contribute to the disease process in AD. This might be the beginning of "cocktail" approach to treating AD—coming at the disease with medications that work in different ways to block or perhaps even reverse the symptoms of this disease. Whether Memantine is right for you or a family member is something to discuss with your physician.

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SPECIAL POINTS OF INTEREST:

- Need a support group?** Call Mari Umpierre at 212-241-6197. We have groups in English and Spanish for both caregivers and those with memory problems.
- Caregivers Program:** Call Elizabeth Fine at 212-241-5673 for information about this series of workshops for caregivers.
- Resources:** ADEAR (www.alzheimers.org or 800-438-4380). Seniors website: <http://nihseniorhealth.gov>



The Alzheimer's Disease Genetics Study: (*continued from headline*)

other risk-factor genes might be, researchers have strongly recommended that further collection and analysis of larger sample sets are needed to root out these genes. Researchers are extremely appreciative of the families that devote their time to research and families often believe that they have contributed to a better understanding of what causes the disease.

Dr. Mary Sano, director of the Mount Sinai ADRC noted, "Families who have been affected by this devastating disease understand the importance of finding the causes of AD, and how to cure it". Discovery of risk-factor genes is essential for getting to the bottom of late-onset AD, and for creating effective treatments and preventive strategies.

To be eligible to participate in the study, families must have at least 3 members who can donate blood, including:

- *2 siblings (brothers or sisters) who developed AD after age 60, AND*
- *Another family member over age 50 who may have memory loss OR a family member over age 60 who does NOT have any memory loss.*

Participation involves a neurological examination or collection of medical records and the donation of a blood sample, which will be made into a cell line (a family of cells grown in the laboratory) that will enable the participant's DNA to be available to qualified scientists over many years. Medical, demographic, and family history information will also be collected. Unaffected family members may also be asked to participate. The cell lines and DNA will be stored at a centralized repository at Indiana University—the National Cell Repository for AD (NCRAD).

There is no cost for those who join the study. To ensure broad participation, both the Mount Sinai and Columbia sites will travel to people's homes to enroll participants. Alternative arrangements can also be made for those people who are eligible to take part in the study but are not located near a designated study site.

An important part of the study is the confidential treatment of the genetic information collected from participants. Researchers will not be able to identify samples on an individual level. While clinical, demographic and family history information about the participants will be available to researchers, this information will also be free of unique identifiers. Coded data on the blood sample will be stored in a secure computer at the NCRAD. Detailed discussion of informed consent documents will outline for participants how the study will be conducted

and how data will be protected at each site and at the cell repository.

To participate in the study, families can call Mount Sinai: Rachel Lally coordinates this study from our Bronx VA site. You may reach her at 718-584-9000, ext. 2784 or her email Rachel.lally@mssm.edu. You may also contact the Columbia University site through Jennifer Williamson (212-305-4655) or her email jlw61@columbia.edu. Finally information may also be found through NCRAD toll-free at 1-800-526-2839 or through their email, alzstudy@iupui.edu.

"Families who have been affected by this devastating disease understand the importance of finding the causes of AD, and how to cure it"

How can I get a memory evaluation?

To make an appointment with one of our physicians for a memory evaluation, or to find out more about clinical research opportunities, please call our coordinator, Ms. Norma O'Neill at 212-241-1844.

In addition to the Mount Sinai site, all clinical services and research programs are available at our three other locations:

Elmhurst Hospital, Queens
Tel: (718) 334-3983

Bronx VA Medical Center
Tel: (718) 584-9000 x5199

Phelps Memorial Hospital, Westchester
Tel: (914) 366-3669



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What's new in the ADRC?

Homocysteine (HC) Study

The purpose of this randomized, placebo-controlled study is to determine whether reduction of homocysteine levels with high dose folate/B6/B12 supplementation will slow the rate of cognitive decline in subjects with Alzheimer's disease. Homocysteine is an amino acid (a building block of proteins) found in the bloodstream.

Blood levels of homocysteine are elevated in AD, and these high levels may contribute to the disease. Patients over the age of 54 with Alzheimer's disease are eligible. All study medications are free of charge. For more information, please contact our research coordinator at (212) 241-8329. GCO#91-208(11), Principal Investigator: Dr. Hillel Grossman, MSSM IRB approved through 2/17/05.

The ADRC is committed to developing new treatments for AD and memory loss. We are recruiting for many studies sponsored by the National Institute of Aging and by Industry, which will provide answers about new drugs and better ways to assess treatment effects. The below list is always changing and new studies are always in the planning process. Please call us for more information.

A Trial of an Insulin-Sensitivity Enhancing Agent to Improve Cognition in Alzheimer's Disease

This study uses an insulin-regulating medication to enhance the activity of insulin degrading enzyme so that it can break down β -amyloid proteins. People with Alzheimer's disease cannot properly break down β -amyloid proteins, which accumulate to form plaques in the brain. This medication could interfere directly with the disease process by blocking the formation of plaques and hopefully prevent the development and progression of the disease. Patients with Alzheimer's disease are eligible. For more information, please call our ADRC research coordinator at (212) 241-8329. GCO #01-1223, Principal Investigator: Dr. Hillel Grossman, MSSM IRB approved through 1/14/05.

Statin Study

We are seeking patients with Alzheimer's disease to participate in this multi-center, randomized, double-blind, placebo-controlled trial of simvastatin, a cholesterol-lowering drug. This study will test whether this drug can slow the progression of symptoms in AD. For more information, contact our ADRC research coordinator at (212) 241-8329. GCO #91-208(10), Principal Investigator: Dr. Hillel Grossman, MSSM IRB approved through 11/14/04.

A Multi-Center, Double Blind, Placebo-Controlled Therapeutic Trial To Determine Whether Natural Huperzine-A Improves Cognitive Function

The objective of this research study is to determine whether natural Huperzine-A improves cognitive (thinking/memory) function of patients diagnosed with Alzheimer's disease (AD). Huperzine-A is a natural cholinesterase inhibitor (stops the breakdown of helpful chemicals in the brain) and is extracted from the Chinese herb Huperzia serrata. There is evidence which suggests that Huperzine-A may be as effective as the medications currently approved by the FDA for the treatment of AD. Patients over the age of 55 who have a diagnosis of Alzheimer's disease and who are not currently taking one of the FDA approved medications for AD (except namenda) are eligible to participate. For more information, please call our ADRC research coordinator at (212) 241-8329. GCO #04-0418, Principal Investigator: Dr. Hillel Grossman, MSSM IRB approved through 8/31/04.

Note:
Spanish-speaking participants are welcome in all studies. All study participants receive reimbursement for any related expenses. Participants without AD receive monetary compensation for their time.

Alzheimer's Disease Genetics Initiative: A Multiplex Family Study: The Family Studies Research Center, in conjunction with the Department of Psychiatry and the Alzheimer's Disease Research Center, is conducting a study on the genetics of Alzheimer's disease. We are looking for families in which there are two siblings with Alzheimer's disease, as well as a third blood relative (parent, child, sibling, half sibling, aunt, uncle or first cousin) who is 50 years old or above and may or may not have a memory problem. For more information, or to participate in this study, please contact Joy Wang at (718) 584-9000, ext 2784 or (718) 367-5727. GCO#84-119, Principal Investigator: Dr. Jeremy Silverman, MSSM IRB approved through 3/31/05.

Protective/Risk Factors for Alzheimer's Disease in Healthy Adults

This study aims to identify biological factors that might either predispose or protect individuals from developing Alzheimer's disease. The 2-3 hour interview would be completed at the subjects' home. A small blood sample is drawn to allow investigators to examine possible protective factors. Participants will be compensated for their time. Men and women who are 85+ years old with no memory impairment or dementia will be eligible for the study. If interested, please call the Family Studies Office at (718) 584-9000, ext 2713. GCO# 84-119, Principal Investigator: Dr. Jeremy Silverman, MSSM IRB approved through 3/31/05.

Brain Tissue Donation Program

The goal of this program is to improve existing treatments and to develop new treatments for AD, which is not possible without the generosity and altruism of individuals who partner with Mount Sinai by participating in our brain donation program. Therefore, men and women, with and without memory impairment are eligible to provide their "intent" to consent for this program. There are several benefits to participation and we have specially trained staff available to discuss these benefits, the donation process, and any related concerns that you and your family might have. For more information, please contact Dr. Karen Dahlman at (212) 241-2968. GCO #84-119 and #79-141, Principal Investigator: Dr. Vahram Haroutunian, MSSM IRB approved through 3/31/05.



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Email: margaret.sewell@mssm.edu

Join us for the 2004 Memory Walk!
Sunday, October 17th, Riverside Park.

Help raise money for the NYC chapter of the Alzheimer's Association. We'll be part of the NYCARE team—which represents the joint efforts of all 3 NYC Alzheimer's centers. Please contact Dr. Sewell at 212-241-0188 or email margaret.sewell@mssm.edu.

Visit our website:
[www.mssm.edu/
psychiatry/adrc](http://www.mssm.edu/psychiatry/adrc)

Other ADRC News:

Are you getting what you need from your doctors visit?

Join us for a free program sponsored by the NYC chapter of the Alzheimer's Association: "Partnering with your Doctor: A Workshop for Caregivers of Persons with Memory Loss." This free program will be held Wednesday September 29th, 1:30-3:30. Call for reservations, 1-800-272-3900.

Upcoming Project, November 2004: A trial of rasagiline and donepezil (Aricept) in Alzheimer's disease.

(Aricept) in Alzheimer's disease. Rasagiline is a selective and highly potent MAO-B inhibitor. In cell cultures and in animals it has the ability to protect or rescue dying neurons, independent of inhibition of the enzyme activity. With this anti-apoptotic function, rasagiline may rescue or protect declining neurons in Alzheimer's Disease. In animals rasagiline increased the activities of anti-oxidative enzymes, superoxide dismutase and catalase. It has been hypothesized that rasagiline may have a neuroprotective effect through its potential to diminish damage caused by oxidative stress. Rasagiline also has the effect in cell cultures of increasing the activity of an enzyme, gamma secretase, that produces non-toxic amyloid. Patients who are currently taking Aricept are eligible for this study which adds on rasagiline.

Upcoming Project, December 2004: The Alzheimer's Disease Neuroimaging Initiative (ADNI).

The Alzheimer's Disease Neuroimaging Initiative (ADNI). The purpose of this Initiative, being launched by the National Institute on Aging (NIA), is to examine how brains change as mild cognitive impairment (MCI) and Alzheimer's disease (AD) progress. Participants, including people with Alzheimer's, memory disorders without Alzheimer's and normal controls, will receive an imaging study several times over a three year period. All participants will receive magnetic resonance imaging (MRI) and some will receive positron emission tomography (PET) scans as well. Scientists will correlate the imaging information with clinical, neuropsychological, and biological markers from blood, cerebrospinal fluid (CSF), and urine samples. The goal of the study is to identify biomarkers for disease on the brain scans and from these fluids that can aid in early diagnosis and in the evaluation of response to treatment.