

Fall
2012



Mount Sinai School of Medicine

Alzheimer's Disease Research Center



Mary Sano, Ph.D.

Director, ADRC

Hillel Grossman, M.D.

Medical Director, Clinical Core

Margaret Sewell, Ph.D.

Editor, Director Educational Core



Medical Food and Nutraceuticals



Mary Sano, Ph.D.

The notion of using food to treat or prevent disease dates to ancient times of more than 5,000 years ago in Indian traditions and can be traced through the writings of Hippocrates, the father of Western medicine. The interest remains strong, with evidence that more than a third of adults in the U.S.

are using some form of alternative treatments for health problems.

Medical Foods are a modern example of products intended for the specific dietary management of a disease or condition that has distinctive nutritional requirements. In 1988, Medical Foods were regulated by the FDA as part of the Orphan Drug Act. Unlike FDA-approved drugs, which undergo testing in patients to assure they are effective, these products submit health claims to the FDA based on a theory of how the food works. The manufacturer does not have to prove that there is a benefit in patients, however the food must be made of ingredients that are "generally regarded as safe" (GRAS), and the food must be prepared under "good manufacturing practice."

There are two medical foods that are currently targeted toward Alzheimer disease (AD). One, Axona, became available as a prescription supplement in 2009, claiming to target the nutritional needs of people with AD. Specifically, it has been proposed that AD hinders the brain's ability to break down glucose, and Axona may provide an alternative source of glu-

cose that the brain can use for energy.

Another Medical Food, Souvenaid, which is not currently marketed, is now in clinical trials. A single trial reported in 2010 describes small positive effects on memory testing but not on other traditional measures of cognition, daily function or quality of life. This was replicated in another international study, but a large trial in the U.S. with patients who have AD did not show any benefits.

"Nutraceutical" is a term that combines the idea of nutrition and pharmaceutical or drug. The term is used for products that are also GRAS and are used to treat or prevent disease. Though this term is not formally recognized by the FDA, many of these products are developed the same way drugs are developed, with clinical trials that demonstrate their efficacy. Unlike medical foods, these products can be formulated as pills or other medicinal formulations.

The Mount Sinai Alzheimer's Disease Research Center (ADRC) is currently conducting rigorous studies to assess the effectiveness of several nutraceuticals including resveratrol (an anti-oxidant found in red grapeskins), NIC5-15 (a soy-based product) and grapeseed extract. When these products are used in clinical trials there is careful control of the dose and preparation, something that is not guaranteed when purchased on the commercial market.

The decision to use any of these products is best done with a full discussion with your health care provider and a review of the ingredients contained in the product.

Clinical Amyloid Scanning Comes to Mount Sinai



Mary Sano, Ph.D.

We are proud to announce that Mount Sinai Medical Center is the first in the tri-state area to use the newly approved imaging technique to detect Alzheimer's disease (AD) pathology in people who are cognitively impaired. This new technique uses a radioactive agent called florbetapir (trade name Amyvid), which can be administered through injection in the arm. Florbetapir binds to amyloid plaques in the brain that are highlighted so they can be seen in a positron emission tomography (PET) scan. Amyloid plaques are the hallmark pathology in the brains of those with AD. The scan can be used in two ways. A negative scan indicates the absence of plaques and a low likelihood of AD. In those who have cognitive problems, a positive scan indicates plaques are likely to be present and the diagnosis may include AD. However, other conditions may also be present. The scan is not currently covered by health insurance but over time if it proves to be useful in diagnosis, it may become part of reimbursed services.

Cross-Cultural Research

We are pleased to introduce to you Dr. Jesús de Felipe, PhD, who is a Visiting Scholar here at the ADRC. Dr. de Felipe received a PhD in Psychology from University Complutense of Madrid and was awarded a grant from the Conchita Rabago Foundation to work with our team from March until September of 2012. He is currently collaborating with our director, Dr. Mary Sano, PhD, on a project examining the differences between native English and Spanish speakers on neuropsychological testing. From these data, they hope to create a new normative standard for the Spanish speaking population. Dr. Felipe plans to develop similar lines of research upon his return to Spain.



Jesús de Felipe, Ph.D.

ADRC Summer Internship Program

Thanks to ADRC supporter Robert Kahen, we at the ADRC were pleased to have established our first formal summer research internship program in memory of Mrs. Moussa Kahen. Mr. Kahen's support towards future aging and memory researchers allowed our interns to attend educational lectures and outreach activities and get hands-on experience with clinical and basic science research methods. All four interns were supervised by senior ADRC faculty on a variety of research projects that included neuropsychological testing and education, our ADRC Brain Tissue Donation Program, our ongoing neuroimaging studies, our Spanish cohort and a basic science presentation on gamma-secretase and Alcadein culminating in a presentation on August 1st to an audience of students and faculty. We welcome these young academics to the field!
Not pictured: ADRC Intern Michael Kahen and volunteer Julia Strauss



L-R: Interns Alexandra Fradin, Katherine O'Laary, Kelly Pun; donor Robert Kahen; Emily Exter; Director Dr. Mary Sano

Non-Pharmacological Treatments for Alzheimer's Disease



Mary Sano, Ph.D. & Margaret Sewell, Ph.D.

Non-pharmacological therapy (NPT) is a term that encompasses a wide variety of non-drug interventions for Alzheimer's disease (AD) patients and their care-

givers. Many NPT's are intended to complement the use of standard dementia medications.

Like pharmacological therapies, NPTs for Alzheimer's disease can focus on behavioral or cognitive outcomes as well as economic or quality of life effects. NPT may be conducted in the community or in residences and nursing homes. NPTs often use person-centered approaches that focus on understanding the patient's experience of dementia and dementia-related symptoms. NPTs may also be aimed at caregivers and include caregiver education, skills training, counseling, respite care, and social support. While these may reduce caregiver burden, many also improve outcomes for the patient. A comprehensive list is beyond the scope of this article, but commonly described therapies include behavioral therapy, art and music therapy, spaced-retrieval training (where patients are trained to remember simple tasks over longer periods of time), cognitive stimulation and training, reality orientation therapy, pet therapy, and physical exercise programs.

Determining if NPTs work is confusing and made more difficult by the limited amount of well-conducted research. Compared to medication therapies, there is less research for NPTs. A review of AD/MCI studies listed on the website ClinicalTrials.gov indicated only 24 of 256 studies were specifically non-pharmacologic. Probably less research funding is possible for the lack of high quality randomized controlled trials of NPTs. Many NPT studies have significant limitations including: small sample sizes, positive findings that have not been replicated, small magnitudes of change that do not generalize to daily life, and results that do not last over time. These limitations make it difficult to interpret the results.

Even among well-conducted studies that assess substantial or sustained memory improvement, results are disappointing. In a review of the effectiveness of NPTs in AD, Resiberg et al. described research on behavioral interventions, cognitive stimulation, music and art programs and physical exercise.

While no single cognitive domain could be identified as showing benefit across all therapies, many randomized controlled trials reported positive benefits in areas such as alertness, attention, orientation, mood and self-esteem as well as decreased behavioral difficulties, apathy and social withdrawal.

Several well studied interventions focusing on support for caregivers demonstrate benefits to both the patient and the caregiver. An intervention developed and evaluated by Mary Mittleman, Dr.P.H., focuses on ensuring that the caregiver receives structured support and respite through education and telephone support and identification of other resources. Outcomes include not only benefits to the caregiver such as reduced depression and burden, but also benefits to the patient including reduced behavioral disturbance and delay in the need for nursing home placement. Laura Gitlin, Ph.D., found that in-home training for the caregiver which concentrated on preserving the patient's strengths through teaching communication skills, stress reduction, home safety and delivery of stimulating activities, was associated with an increase in the caregiver's confidence and a decrease in problem behaviors of the patient.

Choosing an NPT for someone with AD can be challenging. Weighing costs and benefits might include deciding what is needed and what expectations are present versus what the therapy costs monetarily as well as in effort and resources. Those who deliver therapies or interventions should be quite clear about expected benefits. While behavioral management or improved cognition may not be guaranteed, it would be valuable to know if others were satisfied with the program or enjoyed the activity. It would be helpful to know how much time it would take to participate or the likelihood of fatigue or frustration on the part of the patient. The local Alzheimer's Association may provide information to help in this evaluation and provide knowledge about specific community resources.

More research is needed to further understand which NPTs are most effective. However, considering the profound emotional and economic costs of caregiving as well as the modest benefit of medication, NPTs represent important, cost effective, and easy to implement strategies that may dramatically improve the quality of life of families living with Alzheimer's disease.

If you have any further questions regarding non-pharmacological therapies (NPTs), please feel free to contact the ADRC at (212) 241-8329.

ADRC Studies Currently Enrolling

Alzheimer's Disease Neuroimaging Initiative-2 (ADNI-2)

In this study, we hope to determine whether imaging of the brain through MRI, PET and amyloid imaging scans can help predict and monitor the onset and progression of Alzheimer's disease. In addition to neuroimaging, the study will collect and test blood and cerebral spinal fluid to determine if biomarkers can predict and monitor the disease. This study is sponsored by the National Institutes of Health and will take place at about 50 major universities across the US and Canada. No study drug is used in this research. Participants cannot be involved in other clinical trials while in this study. This is a longitudinal study which will span several years. We are looking for volunteers who can participate for the full duration. The study needs volunteers who: are between 55 and 90 years of age, are fluent in English or Spanish, are willing and able to undergo the test procedures, and have a study partner – a friend or relative who can accompany the volunteer to all clinic visits. Participants with and without cognitive or memory complaints are welcome. Participants' health will be closely monitored by a team of doctors and nurses. Participants will receive compensation for their time and costs incurred for travel, parking and meals. For more information, please contact **Helene Geramian at (212) 659-8885**, or via email at helene.geramian@mssm.edu. MSSM #IF1245934; Principal Investigator: Hillel Grossman, M.D. MSSM approved through 10/31/12.

Alzheimer's Disease Research Center Longitudinal Study

This is a national study of healthy elders and those with memory problems that examines how memory disorders affect cognitive abilities and daily functioning over time. For those willing to be followed on a yearly basis, free memory and medical evaluations are available to two groups: healthy elders over 74 years old who may or may not be concerned about memory changes and those of any age who have a diagnosis of Alzheimer's disease and related diseases including Mild Cognitive Impairment. Participation in this research study does not include treatment; however doctors and psychologists will review test results, and provide a letter with a diagnostic impressions and recommendations. Participants will also be given information about other research opportunities as they become available, such as clinical trials, brain imaging studies, and surveys. For more information or to schedule an appointment, please contact **Gloria Benson at (212) 241-0438** or email at Gloria.benson@mssm.edu. MSSM #84-119; MSSM approved through 4/1/13.

Alzheimer's Disease Research Center Resveratrol Study

The Resveratrol study looks to evaluate the safety, tolerability and effectiveness of Resveratrol when given to people with Alzheimer's disease (AD). Resveratrol is a substance found in red wine and in the skins of certain red grapes. We will be studying the effect of Resveratrol on memory and thinking as well as cerebrospinal fluid (CSF) and blood biomarkers. In this study, individuals with Alzheimer's disease will be given either Resveratrol or placebo (sugar pill) for 12 months. The study needs volunteers who are 50 years of age or older, have mild to moderate Alzheimer's disease, are fluent in English or Spanish, can undergo testing procedures, and have a study partner. Participants will receive compensation for procedures and will be provided lunch during study visits at Mount Sinai Hospital. For more information regarding this study, please contact **Helene Geramian at (212) 659-8885**, or email at helene.geramian@mssm.edu. Principal Investigator: Judith Neugroschl, MD GCO: 91-208 (0015)(01) PS, HSM: 12-00068. MSSM IRB approved through 3/5/13.

Trial of NIC5-15, a natural product in subjects with Alzheimer's disease

We are seeking Veterans and non-Veterans with Alzheimer's disease to participate in a research study of a natural product, NIC5-15 at the Bronx James J. Peters Veterans Medical Center. NIC5-15 is a natural product found in legumes and soybeans. In laboratory studies it interferes with the accumulation of a protein in the brain that is involved in the development of Alzheimer's disease. Researchers hypothesize that this may slow down the progression of the disease. Some study participants will receive NIC5-15 and some will receive a placebo (sugar pill). Participation in the study includes physical exams, neurological exams, blood tests, and tests of memory and thinking skills. Participation of 8 months is necessary. For more information please contact **Sabrina Lopez at (718) 584-9000 ext 5179**, or email at Sabrina.lopez@mssm.edu. Principal Investigator: Hillel Grossman, M.D. VA GRO#10-029 approved through 5/2/13.

Markers of Transition to Alzheimer Disease in Veterans with MCI

This is a longitudinal study of aging veterans that will compare the results of memory and thinking tests as well as biological tests to see which are best at identifying who is at risk for developing Alzheimer's disease and their rate of cognitive, functional and global decline. To learn more about this project, please call **Jimmy Akrivos at (718) 784-9000 ext 1705**.

Upcoming Studies

Phase 2 GrapeSeed Extract as an Anti-Oligomerization Agent in Alzheimer's Disease
More information to come...

Ask the Expert: Samuel Gandy, Ph.D., M.D., ADRC Associate Director



Samuel Gandy, PhD, M.D.

Q: I have heard there's a new cancer drug that might work for Alzheimer's disease – is this a new cure?

The cancer drug you may have heard about in the news is called Bexarotene and indeed, it is US Federal Drug Administration (FDA)-approved to treat certain cancers. However, as with all new drugs, the FDA needs more information about the safety of this drug – for example, what are the side effects? Does it actually work? There are currently a few different research groups looking into Bexarotene as a treatment for AD. So far, nobody has been able to confirm that this drug is safe and effective in treating Alzheimer's disease. In fact, even the effectiveness in mouse models of AD has not yet been confirmed. Until this is done, no doctors should be prescribing this drug "off label" for treatment of AD. We'll be sure to keep you posted if there is news about this!

Among off label drugs, the one in widest use (which amounts to a few dozen patients who have the resources to afford it) is IVIg, which costs \$4,000-\$5,000 each month. A study with 300 subjects is underway and the results will be available next year. If that study confirms the benefit of IVIg and the FDA approves its use for AD, then Medicare and insurance is likely to begin reimbursing so that everyone can gain access to the drug.

Q: There was a lot of media coverage in July, 2012, concerning off label use of IVIg for Alzheimer's. How can I learn more about this therapy?

Among off label drugs, the one in widest use (which amounts to a few dozen patients who have the resources to afford it) is IVIg, which costs \$4,000-\$5,000 each month. A study with 300 subjects is underway and the results will be available next year. If that study confirms the benefit of IVIg and the FDA approves its use for AD, then Medicare and insurance is likely to begin reimbursing so that everyone can gain access to the drug.

Q: Does the generic version of Aricept work as well as the regular one?

The active ingredient in the generic version of Aricept, known as donepezil, is identical to the active ingredient in the trademarked version. Some differences in formulation can sometimes change effects of generic medications, but, so far, no problems with generic donepezil have been reported. This is something that has doctors on the alert and we will let our readers know if any reports appear that suggest any problems with generic donepezil.

2012 Walk to End Alzheimer's



Sponsored by the Alzheimer's Association, the

2012 Walk to End Alzheimer's

will be held on Sunday, October 21, 2012, at Riverside Park.

Last year our team raised over \$10,000, and we hope to do even better this year but we need your help! We invite you to join our

2012 Mount Sinai ADRC team and spend a great day with us at Riverside Park. If you are interested and would like more information, please contact

Dr. Margaret Sewell at (212) 241-0188
or by email at margaret.sewell@mssm.edu

Caregiver's Corner

Resources for Patients and Caregivers (ENGLISH)

- **Alzheimer's Disease Education and Referral (ADEAR)** — A comprehensive website with AD information and resources from the National Institute on Aging. <http://www.nia.nih.gov/Alzheimers/>
- **AARP Caregiving Resource Center** — Sponsored by the AARP, this website provides helpful information for caregivers and their families. <http://www.aarp.org/relationships/caregiving>
- **Family Caregiver Alliance** — Sponsored by the National Center on Caregiving, this website provides both caretakers and their loved ones with access to helpful information and resources. <http://www.caregiver.org>
- **Mount Sinai ADRC** — Our website contains information about AD and our research programs, as well as resources for caregivers. You can also find previous editions of our newsletter here. <http://www.mssm.edu/adrc>
- **Strength for Caring** — An online community providing important information while allowing caretakers to interact with and learn from one another. <http://www.strengthforcaring.com>
- **This Caring Home** — An interactive website with information and tips to make the home safer for individuals with Alzheimer's disease. <http://www.thiscaringhome.org/>
- **VA Caregiver Support**— An informative website providing support and resources for caretakers of veterans provided by the U.S. Department of Veterans Affairs. <http://www.caregiver.va.gov>

Resources for Patients and Caregivers (ESPAÑOL)

- **Sobre el AD:** <http://www.alz.org/espanol/>
- **Centro de asistencia para personas y con AD y desordenes relacionados (ADAC):** 212-659-8872
- **Recursos en español:** http://www.alz.org/espanol/resources/sitios_web.asp#organizaciones

Participant Appreciation Day

This year's 5th annual ADRC Participants' Appreciation Day yielded the highest attendance yet with 81 participants joining us as well as many ADRC staff and students! After a welcome by event organizer and Education Core Director Margaret Sewell, Ph.D., ADRC director Mary Sano, Ph.D. updated the audience with "What we've learned so far: Results from recent studies." The day also included caregiver-oriented break-out sessions including a special Chair Yoga session by Barbara Benedict from the Memory Tree as well as Dr. Sewell's Power Memory Work-Out, and a talk by returning speaker Mari Umpierre, co-director of the Alzheimer's Disease Assistance Center. A new feature of the event was an interview with Clinical Core Director, Hillel Grossman, M.D. and a volunteer research participant, whose comments you can see on page 7.

Finally, Dr. Grossman, Education Core co-director Judith Neugroschl, M.D. and ADRC Associate Director Samuel Gandy, M.D., Ph.D. chaired a panel discussion of "What's next: New and novel ideas in dementia research." Because of the recent press release announcing FDA approval of the new diagnostic PET scan agent Amyvid, there were many audience questions about Amyvid and what its approval means. (Thanks to your feedback on that day, we have expanded on this topic on page 2) We asked the audience to answer this question: "Dr. Sano spoke of the new PET scan that can detect beta-amyloid in the brain. If you could find out if you had beta-amyloid in your brain, would you want to know?" to which 34 of you answered yes and 7 answered no. We offer our heartfelt thanks to all the families who give so much to the fight against Alzheimer's. We look forward to seeing you next year!



L-R: Jimmy Akrivos, Riana Moring-Parris, Helene Geramian, Aliza Romirowsky, Elisheva Bellin, Sabrina Lopez, Gloria Benson, Judy Creighton

Participant Interview: Susan Joseph



Susan Joseph

Q: What led you to choose to participate in research with the Mount Sinai ADRC?

My friend Mitch had been involved in research at the James J. Peter VA Medical Center and found out about the studies being done at Mount Sinai. So we came in as a team and were asked to take part in the program, which includes brain studies and verbal tests for memory, and the idea made a lot of sense to both of us.

Q: Tell us about your experience as a research participant.

I am very impressed by the professionalism and competence of the ADRC staff, as they have been supportive and helpful every step of the way. Staff members have scheduled appointments with our needs in mind and have made reminder calls. Coordinators are knowledgeable, polite, and respectful of our concerns.

Q: You had a spinal tap performed. Were you comfortable having this procedure?

What got me feeling confident was the stated assurance that this procedure poses no risk of paralysis. I understood that the neurologist, Dr. Goldstein, who performed the spinal tap, was a highly qualified and experienced physician. I was further reassured by Mt. Sinai's excellent reputation and by the fact that the hospital would handle any problems that might arise. Additionally, arrangements were made to make the experience as comfortable and convenient as possible.

Q: Was the spinal tap painful?

No. What was unpleasant was the awkward "fetal" position I had to maintain—sitting on the side of the bed, my back stretching forward, my face resting on two pillows in my lap. The procedure took around 45 minutes. Dr. Goldstein explained that he could speed it up by using a bigger needle. But the larger the needle, the more likely I would be to have a headache afterward. Understanding the reason for going slow gave me the patience to remain still for the duration.

Q: Would you recommend research participation to others?

Yes. Taking part in an investigation of the mental and physical factors that may help researchers identify the causes and early symptoms of Alzheimer's, and its treatment, is a way of contributing to society. As Alzheimer's is a dreadful disease, it is important for all of us to help with research, and I would certainly recommend participating with the ADRC to anyone interested in this field of research.

Memory Enhancement Class

Dr. Margaret Sewell, Director of the Education Core and the Memory Enhancement Program, is very excited to offer a free, three-session Memory Enhancement program this fall. Classes will be held on three consecutive Wednesday mornings, October 3rd, 10th, and 17th, from 11:00am to 12:30pm in the Mount Sinai Goldwurm Auditorium located at 1425 Madison Avenue. The program is targeted to healthy elders over 55 and is not aimed at those with a dementia diagnosis.

If you are interested and would like information about registration, please call **the ADRC at (212)241-8329**. Stay tuned for more up-to-date information, and we look forward to seeing you this fall!



Margaret Sewell, PhD



Have you considered brain donation?

Brain donation is a priceless contribution to knowledge that leads to the development of more effective treatment for Alzheimer's disease. It is also critically important to be able to study brain tissue of individuals with no memory or other cognitive impairments. This allows scientists to compare normal and abnormal brain tissue, which will lead to a greater understanding of factors that may protect the brain from disease in aging.

To update your brain donation registration information, or to learn about becoming a donor, please contact **Dr. Judy Creighton** at (212) 241-1844, or email her at **Judy.Creighton@mssm.edu**.



**ALZHEIMER'S DISEASE
RESEARCH CENTER**
One Gustave L. Levy Place, Box 1230
New York, NY 10029-6574

**MOUNT SINAI
SCHOOL OF
MEDICINE**

Phone: (212) 241-8329
Fax: (212) 996-0987
Email: Margaret.Sewell@mssm.edu

Alzheimer's Association International Conference (AAIC) 2012

From July 14 -19, several ADRC faculty joined the international AD scientific community in Vancouver to discuss new developments in the field at the Alzheimer's Association International Conference (AAIC). Some highlights:

- **Gammagard's IGIV treatment:** One clinician found that his four patients receiving the study drug showed improvement. This information was primary data released of four individuals who demonstrated 3 years of stable cognition during their participation. Nurses' Health Study on sleep disorders and lower cognition: The study explored if sleeping too much or too little could lead to lowered cognition and demonstrated that people whose sleep changed significantly - either increasing or decreasing by 2 hours- had increased risk of cognitive decline.
- **Swiss study on the relationship between stride speed and variability and cognitive impairment:** The study found that in people with worse cognitive decline, gait was slower than in those with less severe cognitive concerns. In addition, specific parts of walking were observed - for example, information processing speed was associated with the rhythm aspect of gait (stride time and cadence).
- **University of California - San Francisco study on alcohol use and MCI:** The study followed elderly women over 20 years who continued to drink 7-14 drinks per week as they aged or those who started later in life. The data indicated possible increased risk of cognitive decline in late-life binge drinkers as well as increased risk of mild cognitive impairment. They also found that sleep apnea was associated with greater risk of MCI.

Donations

Please consider supporting the research and care provided to all of the families within the ADRC

Enclosed is my tax deductible gift of
\$ _____.

Please note that this contribution is:

In Memory of: _____ In honor of: _____

Please make checks payable to:

Alzheimer's Disease Research Center
One Gustave L. Levy Place, Box 1230
New York, NY 10029-6574

Thank you for your contribution!

Contributions

With the help of volunteers like you, scientists and medical educators across the country are making strides against Alzheimer's disease. Unfortunately, there continues to be federal funding cuts to memory and aging research programs- including ours. With your gift, we are better able to serve the growing population of those living with memory disorders and their families. Your contribution supports our scientific research, as well as our education and training programs. We gratefully accept tax-deductible gifts and bequests that help all our scientific and educational endeavors and we can provide information on corporate or matched donations. Contact Jane Martin, PhD at (212) 241-8517 or by email at jane.martin@mssm.edu for more information.

Need a Memory Evaluation?

The ADRC's Memory & Aging Center (MAC) provides comprehensive evaluations for those who have memory complaints:

- **Experts:** Our team includes experts in geriatrics, geriatric psychiatry and neuropsychology, neurology, and radiology.
- **Quick:** The evaluation can be completed in one visit, including evaluation by a geriatric specialist, neuropsychological testing, and neuroimaging.

To make an appointment, please call (212) 241-8329