

The National Cell Repository for Alzheimer's Disease

(NCRAD) is a data and specimen collection source for families with Alzheimer disease (AD) or serious memory loss. Families having two or more living individuals with memory loss are encouraged to participate. We would like to thank the hundreds of families nationwide who are already participating in the National Cell Repository. Many family members have provided blood samples, which researchers use to study Alzheimer's disease (AD) and other related diseases. Our hope is that, through the efforts of our participants, we will one day unravel the mystery of devastating diseases, like AD. We are always eager to accept new families to help us move toward this goal.



INDIANA UNIVERSITY
SCHOOL OF MEDICINE

National Cell Repository for Alzheimer's Disease

Health Information and
Translational Sciences Bldg. -HS4000
410 West 10th Street
Indianapolis, IN 46202-3002
Phone: 1-800-526-2839
E-mail: alzstudy@iupui.edu
Website: www.ncrad.org

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NCRAD Update

Newsletter of the National Cell Repository for Alzheimer's Disease

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THE ALZHEIMER'S PROJECT

A Four-Part HBO Documentary Series

Adapted from the Alzheimer's Disease Education and Referral Center, a service of the National Institute on Aging web-site.

Many of you may have seen or heard about the recently distributed HBO documentary film entitled, 'THE ALZHEIMER'S PROJECT'. This project is the result of a collaboration between the National Institute on Aging and HBO Documentary Films. The series is a multi-platform (television, web, DVD, and print) public health series which takes a look at groundbreaking scientific discoveries and seeks to bring a wider public understanding of Alzheimer's disease research and care.

THE ALZHEIMER'S PROJECT is centered on a four-part documentary film series on science and research, children touched by Alzheimer's, and two films focused on people with the disease and their caregivers. The series debuted May 10-12, 2009 on HBO. All films are available to view free at: www.hbo.com/alzheimers

The four documentaries are:

- **THE ALZHEIMER'S PROJECT: THE MEMORY LOSS TAPES*** - provides an up-close and personal look at seven individuals living with Alzheimer's.
- **THE ALZHEIMER'S PROJECT: MOMENTUM IN SCIENCE*** - a two-part state-of-the-science film takes viewers inside the laboratories and clinics of 24 leading scientists and physicians, revealing some of the most cutting-edge research advances.
- **THE ALZHEIMER'S PROJECT: 'GRANDPA, DO YOU KNOW WHO I AM?' WITH MARIA SHRIVER*** - captures what it means to be a child or grandchild of one who suffers.
- **THE ALZHEIMER'S PROJECT: CAREGIVERS** - highlights the sacrifices and successes of the people who experience their loved ones' descent into dementia.
** Has been nominated for an Emmy award.*

The Project also includes 15 short films featuring interviews with scientists involved in research:

1. Understanding and Attacking Alzheimer's
2. How Far We Have Come in Alzheimer's Research
3. Identifying Mild Cognitive Impairment (MCI)
4. The Role of Genetics in Alzheimer's
5. Advances in Brain Imaging
6. Looking Into the Future of Alzheimer's
7. The Connection Between Insulin and Alzheimer's
8. Inflammation, the Immune System, and Alzheimer's
9. The Benefit of Diet and Exercise in Alzheimer's
10. Cognitive Reserve: What the Religious Orders Study is Revealing about Alzheimer's
11. Searching for an Alzheimer's Cure: The Story of Flurizan
12. The Pulse of Drug Development
13. The DeMoe Family: Early-Onset Alzheimer's Genetics > continued on page 6

All films are available
to view free at:
www.hbo.com/alzheimers

Ginkgo Study Fails to Show Benefit in Preventing Dementia



By Mary Guerriero Austrom, PhD
Wesley P. Martin Professor
of AD Education, Department
of Psychiatry Director,
Education Core Indiana
Alzheimer Disease Center

The Journal of the American Medical Association has recently published the findings on ginkgo biloba. Dr. Stephen DeKosky (formerly of the University of Pittsburg), vice president and dean of the School of Medicine at the University of Virginia in Charlottesville, conducted the trial known as the Ginkgo Evaluation of Memory or the GEM Study. GEM is the largest clinical trial ever with 3,069 participants aged 75 or older with normal cognition or mild cognitive impairment at 4 clinical sites and followed for 8 years. People with dementia were excluded from the study. The study was conducted primarily to see if ginkgo would decrease the incidence of all types of dementia and to evaluate the overall effects of ginkgo on cognitive decline, functional disability, incidence of cardiovascular disease and stroke, and total mortality. Extensive medical and neuropsychological screening was done and participants were randomly assigned to receive twice-daily doses of either 120 milligrams of ginkgo extract or a placebo (looked the same but did not contain ginkgo). The 240 milligrams

daily dose of ginkgo was used based on the current recommended dose and prior clinical studies that showed some possible effectiveness at this dose.

The results indicated that ginkgo had no effect on reducing dementia or Alzheimer's disease. If older people are thinking of using ginkgo to prevent dementia they are urged to speak to their health care providers so that the best treatment plan can be designed. Dr. Martin Farlow, the Indiana Alzheimer's Disease Center (IADC) Clinical Core Director who has conducted over 100 clinical trials comments that: "No drug or herb has been demonstrated in placebo-controlled double-blind trials to delay or reduce risk of AD. However, most physicians would agree that exercise and reducing body weight towards ideal standards are good bets for improving general and cognitive health."

Dr. Richard Hodes, director of the National Institute on Aging, said, "We have made enormous progress in understanding the basic mechanisms involved in Alzheimer disease (AD) and we continue to pursue a vigorous program to translate what we know into the development and testing of new potential therapies for this devastating disease. However, it is disappointing that the dietary supplement tested in this study



had no effect in preventing the disease". While this study showed that ginkgo does not have an effect on reducing dementia, it did, however, provide important information about how to design and conduct large dementia prevention trials for older adults. Future analyses will also provide additional information on ginkgo's possible effects on cardiovascular disease, cancer, depression and other age-related conditions.

Adapted from the NIA-sponsored ADEAR announcement

10 SIGNS OF AD

1. Memory loss.
2. Difficulty performing familiar tasks.
3. Problems with language.
4. Disorientation to time and place.
5. Poor or decreased judgment.
6. Problems with abstract thinking.
7. Misplacing things.
8. Changes in mood or behavior.
9. Changes in personality.
10. Loss of initiative.

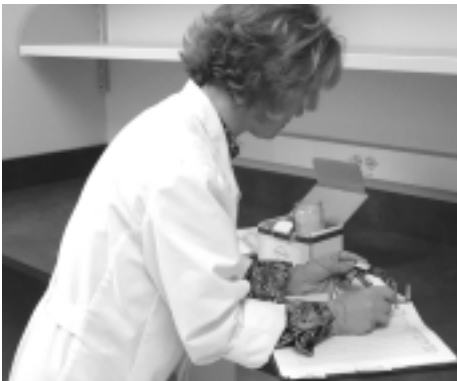
If you recognize several of these warning signs in yourself or a loved one, the Alzheimer's Association recommends consulting a physician. Early diagnosis of Alzheimer's disease or other disorders causing dementia is an important step in getting appropriate treatment, care, and support services.

For more information, call the Alzheimer's Association at (800) 272-3900.

Banking at the National Cell Repository for Alzheimer's Disease



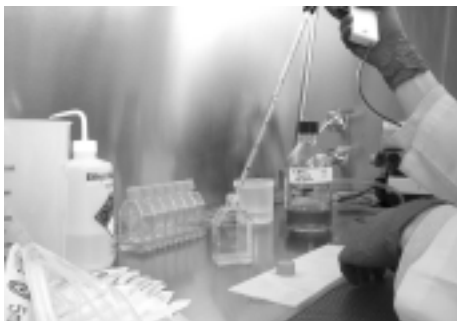
The Banking Center for NCRAD is located at Indiana University, Department of Medical and Molecular Genetics



Step 3



Step 4



Step 6a

1. The main function of the National Cell Repository for Alzheimer's Disease involves collecting, storing and distributing genetic material for Alzheimer's disease research. Our goal is to provide the scientific community with a valuable resource for obtaining the genetic material needed to study families with Alzheimer's disease. Researchers from around the world may request DNA or cell lines, the material that is used in genetic research. All DNA and cell lines are always de-identified (no identifying information such as name or date of birth) before being distributed. Research on these samples does not provide any diagnostic testing information.
2. The process of banking (storing) DNA and cell lines begins when a blood sample is received from a member of a family having Alzheimer's disease or serious memory loss.
3. The sample is taken to the lab and assigned a unique kit number. The kit number and information about the participant is recorded in a secured database.
4. The sample is then assigned a unique bar code. The bar code number is entered into a logbook along with the unique kit number. These numbers are checked by several technicians for accuracy.
5. The blood sample is then placed in a machine and spun to separate the sample into three main layers: the red blood-cell layer, the plasma layer, and the buffy coat, which contains the white-blood cells. The white-blood cells are needed to establish cell lines and obtain DNA.

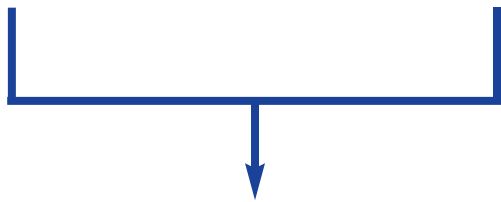


- 6a. To establish cell lines, the white-blood cells are placed into two separate flasks along with a solution that allows permanent cell growth. The cells are incubated at 37°C (body temperature) anywhere from three weeks to three months for continuous cell division.
- 6b. To isolate DNA, the white-blood cells are washed and spun at a high speed, enabling the cells to cluster together.
- 7a. The cell-containing solutions are then transferred into two larger flasks for further cell growth. It takes approximately one week for the cells to divide to the desired number. The cells are checked throughout this process to ensure they are growing properly.
- 7b. The clusters of white blood cells are placed in a solution containing an enzyme that degrades unnecessary cell components. The solution is stored at 98° F overnight. The cells are split open during this time while the DNA stays intact.

> continued on next page

- 8a. The cells are then placed in a plastic cryo-vial along with a cryo-preserved. Each vial holds approximately 1 milliliter of solution containing 1×10^7 (10,000,000) cells.
- 9a. The cells are gradually cooled to freezing temperatures and then placed in a tank of liquid nitrogen. The slow freeze prevents damage to the cell line and takes place in a controlled-rate freezers.
- 10a. The frozen cells are stored in a tank filled with liquid nitrogen at -316°F . Cells can be preserved this way indefinitely and thawed at any time for additional cell growing. This culture and storage process is necessary for immortalizing our participant's cells for ongoing genetic research in Alzheimer's disease.

- 8b. Next, the DNA is separated from the cell components. This is accomplished by adding a salt solution and spinning the DNA and cell components at a high speed.
- 9b. The DNA is isolated and transferred to another tube, which now contains the desired DNA without the unnecessary cell components. A form of alcohol is added to the solution and interacts with the DNA. This allows the DNA to gather together and become visible.
- 10b. The DNA is then transferred to a small tube containing a solution that preserves the genetic material for future studies. In a freezer set at -94°F , the DNA is stored for future use. If a sample did not grow, the individual who provided the sample may be contacted and asked to provide another blood sample.



- 11. Since 1991, NCRAD has collected more than 12,000 samples from individuals and families. These samples and the clinical and family history information from these individuals have been used by researchers to understand the genetics of Alzheimer's disease. Over the past 18 years, over 29,000 samples have been distributed to researchers studying AD. More than 80 different investigators from around the world have requested samples from NCRAD. These researchers have published 164 papers about Alzheimer's disease and dementia. These papers have helped to better understand the genetics of early onset Alzheimer's disease, late onset Alzheimer's disease and other types of dementia.

The cell lines and DNA are extremely valuable for Alzheimer's Disease research. We greatly appreciate all the support from the families who participate in the National Cell Repository for AD.



Step 9b



Step 10a



Step 10b



Step 11

Research Opportunities

Delaying the Progression of Driving Impairment in Individuals with Mild Alzheimer's Disease

- Purpose: To determine whether the medication memantine delays the progression of driving impairment in patients with mild Alzheimer's Disease.
- Eligibility: Subjects with clinical diagnosis of mild Alzheimer's Disease over the age of 60.
- Locations: FL
- Contact: Lori Fisher, M.A.
PH: 1-561-297-0502
E-mail: lfisher8@fau.edu

The Genetics of Late Alzheimer's Disease (LOAD)

- Purpose: To identify families with multiple members diagnosed with late-onset Alzheimer's Disease. Families will be characterized clinically and blood samples will be collected to establish cell lines. If a blood sample is not available, autopsy samples will be collected for DNA extraction and storage. Our goal is to recruit 1,000 families over the course of the study. Clinical and demographic data from these families will be collected at the local site and coded data, without identifiers, will be sent and included in a national database of families with Alzheimer's Disease. This database, along with the biological samples, will be housed at the National Cell Repository for Alzheimer's Disease (NCRAD) at Indiana University.
- Eligibility: Two siblings (brothers or sisters) who developed AD after the age of 60 and another family member over 50 who may have memory loss or a family member over 60 who does not have any memory loss. Participants can live anywhere in the U.S. and can be of any racial or ethnic background.
- Locations: (sites in following states, but participation is open to subjects all over the United States)
FL, IL, IN, MN, MO, NY, PA, TX, WA
- Contact: 1-800-526-2839
E-mail: alzstudy@iupui.edu

GIFT: Genetic Investigation in Frontotemporal Dementia and Alzheimer's Disease

- Purpose: To perform DNA studies to evaluate the genetic contribution to Alzheimer's Disease (AD) and Frontotemporal Dementia (FTD). Using a microarray-based approach, 80 genes related to neurodegeneration will be resequenced in order to identify rare mutations or risk-associated genetic variants.
- Eligibility: Subjects with clinical diagnosis of AD or FTD. Healthy volunteers.
- Locations: CA, GA
- Contact: GIFT webpage
<http://geschwindlab.neurology.ucla.edu/gift>

A randomized, clinical trial of Vitamin E and Memantine in Alzheimer's Disease (TEAM-AD)

- Purpose: The primary study hypothesis is that compared with placebo, alpha-tocopherol, memantine (Namenda), or the combination will significantly delay clinical progression in mild to moderately demented patients with AD
- Eligibility: Men and women over 40 years and older with clinical diagnosis of AD
- Locations: FL, IA, MD, MA, MI, MN, OH, SC, TX, WI and Puerto Rico
- Contact: Susan Love, 612-467-3342, email: lovex008@tc.umn.edu or Julie Tomaska, 612-467-1563, email: Julie.tomaska@va.gov

Effect of LY2062430 on the Progression of Alzheimer's Disease (EXPEDITION)

- Purpose: To determine if LY2062430 (solanezumab *USAN adopted name, INN pending, a humanized anti-A Beta peptide immunoglobulin G-1, IgG1, monoclonal antibody being developed for treatment of AD) will slow cognitive and functional decline in AD as compared with placebo. Sponsored by Eli Lilly and Company
- Eligibility: Men and women 55 years and older, diagnosed with Alzheimer's disease
- Locations: AZ, AR, CA, CO, CT, FL, GA, IN, KY, MD, MA, MI, MO, NM, NY, NC, OH, OK, OR, PA, RI, SC, SD, UT, VT, VA, CANADA (4 locations)
- Contact: 1-877-CTLILLY (1-877-285-4559) or in IN: 317-615-4559

Raloxifene for Women with Alzheimer's Disease

- Purpose: To determine whether Raloxifene, a selective estrogen receptor modulator (SERM), improves cognitive function in women with Alzheimer's disease.
- Eligibility: Women 60 years and older with clinical diagnosis of AD.
- Locations: CA, IL, IN
- Contact: Narinder Bolara
PH: 1-650-721-3308
E-mail: nbolaria@stanford.edu

We Need Your Help Untangle the Mystery Of Alzheimer's

Autopsy is still the only way to definitively diagnose the specific kind of dementia affecting an individual. Please contact us if you are interested in pursuing an autopsy for a family member with dementia.

We appreciate your support in helping us unravel the mystery of devastating diseases, like Alzheimer's.



For more information
call **1-800-526-2839**
or email alzstudy@iupui.edu

Sources for Information and Support

AARP

Driver safety classes

1-888-AARP-NOW

* **Alzheimer's Association**

<http://www.alz.org>

Tel: 312-335-8700 or 800-272-3900

Alzheimer's Disease Education and Referral Center (ADEAR)

<http://www.nia.nih.gov/Alzheimers>

Tel: 301-495-3311 or 800-438-4380

* ADEAR lists all 29 Alzheimer's Disease Centers (ADCs) and their contact information.

Family Caregiver Alliance

<http://www.caregiver.org>

Tel: 415-434-3388 or 800-445-8106

National Parkinson Foundation

<http://www.parkinson.org/>

Tel: 305-547-6666 or 800-327-4545

Parkinson's Disease Foundation (PDF)

www.pdf.org

Tel: 212-923-4700 or 800-457-6676

Society for Progressive Supranuclear Palsy

<http://www.psp.org>

Tel: 410-486-3330 or 800-457-4777

National Organization for Rare Disorders (NORD)

<http://www.rarediseases.org>

Tel: 203-746-6518 or 800-999-NORD (6673)

Center for Disease Control and Prevention (CDCP)

<http://www.cdc.gov>

Tel: 800-311-3435

Creutzfeldt- Jakob Foundation Inc.

<http://cjd.foundation.org>

Tel: 954-704-0519 or 305-891-7579

* **ClinicalTrials.gov** is a registry of federally and privately supported clinical trials conducted in the United States and around the world. ClinicalTrials.gov gives you information about a trial's purpose, who may participate, locations, and phone numbers for more details. This information should be used in conjunction with advice from health care professionals.

<http://www.clinicaltrials.gov/>

No phone number available

National Society of Genetic Counselors

<http://www.nsgc.org/>

Tel: 312-321-6834

* These are good sources for research opportunities in your area.

The Alzheimer's Project > continued from page 1

14. The Nanney-Felts Family: Late-Onset Alzheimer's Genetics
15. The Quest for Biomarkers

The ALZHEIMER'S PROJECT highlights a number of prominent AD researchers who have been using the National Cell Repository for Alzheimer Disease samples and data to study AD. In particular, in the videos highlighting the genetics of AD (THE ALZHEIMER'S PROJECT: MOMENTUM IN SCIENCE), you will see researchers such as Drs. Schellenberg and Hardy, who have studied samples from NCRAD families for many years. You can learn more about why we collect specific types of data and see Dr. Mayeux, who not only leads the Late Onset Alzheimer Disease Study, but has also requested many NCRAD samples throughout the video about late onset AD (the Nanney-Felts Family: Late-Onset Alzheimer's Genetics). Dr. DeKosky, who is one of the researchers highlighted in the early onset AD segment (The DeMoe Family: Early-Onset Alzheimer's Genetics) and his colleagues at the University of Pittsburgh has requested samples from NCRAD for several studies.

Your valuable contributions including information about your family history of AD, the clinical symptoms of disease, blood samples for DNA and in many cases the brain tissue from your loved ones, have allowed researchers to learn about AD and are likely the key to our future success in unlocking better treatments for AD.

Education and Outreach Campaign

Along with the films and other materials, HBO, NIA, the Alzheimer's Association and other collaborators are leading an education and outreach campaign to bring wider understanding about research in Alzheimer's disease and greater knowledge of resources for caregivers.

The Project is offering DVDs of the films to thousands of communities nationwide, providing viewer discussion guides, information resources, and practical details about hosting a community event to promote education and discussion about Alzheimer's on a local level.

Resources

- THE ALZHEIMER'S PROJECT website: (www.hbo.com/alzheimers) featuring the films, information resources, and interactive channels.
- Alzheimer's Tribute Wall on Facebook: (www.alzheimerstributewall.com)
- A companion book, *The Alzheimer's Project: Momentum in Science*, published by Public Affairs Books.

Collaborators

- NIA provided scientific and technical guidance to the films and other aspects of the Project.
- The Alzheimer's Association
- The Fidelity Charitable Gift Fund
- The Geoffrey Beene Gives Back Alzheimer's Foundation