NCRAD Update

Newsletter of the National Cell Repository for Alzheimer's Disease Volume 9 ■ November 2006

The National Cell Repository is a repository for families with Alzheimer's Disease or severe 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.

National Cell Repository for Alzheimer's Disease
Department of Medical and Molecular Genetics
975 West Walnut St ■ IB 130
Indianapolis, IN 46202-5251
Phone: 1-800-526-2839
E-mail: alzstudy@iupui.edu
www.ncrad.org

Inside this Issue...

NCRAD Coordinator Michele Goodman at NCRAD booth during ICAD.

NCRAD GOES TO INTERNATIONAL CONFERENCE IN MADRID

By Michele Goodman
NCRAD Coordinator
Indiana University School of Medicine

In mid-July, the National Cell Repository for Alzheimer's Disease was represented at the 10th International Conference on Alzheimer's Disease and Related Disorders (ICAD) presented by the Alzheimer's Association in Madrid, Spain. Over 5,000 researchers from all over the world assembled here to share new findings on topics ranging from genetics and pathology to the treatment of Alzheimer's disease and related disorders.

NCRAD staff and colleagues from Columbia University spoke with numerous academic and commercial researchers from the United States, Europe, Australia, New Zealand, South America, and Africa among other regions. Many researchers who had been unable to locate a repository to fit their needs or unable to recruit their own families, were impressed with NCRAD and believe that it can can help them to further their research efforts.

ICAD strives to promote collaboration in the research community as we all work towards the goal of solving this complicated and devastating illness. NCRAD was also established with the spirit of collaboration. By collecting and storing information from thousands of willing families and making those resources available to researchers both nationally and internationally, we hope to further shorten the road to a better understanding of Alzheimer's disease.

A full conference summary can be viewed at http://www.alz.org/icad/overview.asp

How to Unravel the Complexity of Alzheimer's Disease

By Abraham Brown, Ph.D.
Associate Professor, Burke Medical Research Institute
and Cornell University, New York

Alzheimer's disease (AD) is a *complex* disease. The meaning of this term may differ depending on which researcher you ask. One definition of the term 'complex disease' is that it has many causes. This means the disease may have several distinct causes, each of which lead in the end to the same disease or symptoms. The early onset, familial forms of AD certainly meet this definition, since virtually identical disease symptoms are caused by mutations (DNA defects or changes) in any one of three different genes, amyloid precursor protein, presenilin 1 and presenilin 2 (see article in previous issue Volume 4, January 2004 available online at www.ncrad.org).

Another definition of 'complex disease' is that a combination of causes contributes to the resulting disease. The most common example known to the general public is heart disease, where a combination of risk factors (high blood pressure, cholesterol, obesity and genetics) increases the likelihood of developing disease. Alzheimer's disease meets this criterion as well. Recent evidence from many laboratories and clinical studies suggest that maintaining vascular health, social contacts, regular exercise and good nutrition may be helpful in delaying or staving off the onset of Alzheimer's disease. There is also good evidence that individuals who have a certain form of the Apolipoprotein E gene have an increased likelihood of developing AD.

The status of AD as a complex disease has implications for the patient, physician and researcher. For the patient and physician, multiple causes for the disease suggest multiple treatments or interventions that may help some patients but not others. It also means that the course of treatment or preventative measures may be more complex than a single pill or therapy. For the researcher, this complexity means that there may be no single, right answer to the question "what causes AD?"

The challenge of studying complex diseases is particularly daunting to researchers trying to identify new genes that contribute to the risk of developing late onset AD. It is clear that the causes of late onset AD are probably multifactorial (due to multiple factors) resulting from the combined effects of one or more genes and environmental factors. For a study to succeed in identifying genes that increase the risk for AD, it is critical to have access to large numbers of DNA samples from families with multiple members with late onset AD and an accurate diagnosis of AD, preferably obtained through an autopsy confirmation of the disease or detailed medical records.

This is where NCRAD is a special and unique resource. NCRAD has focused its efforts on enlisting and following families that have more than one member affected by AD. They have created a very important resource for researchers in three ways. First, families are encouraged to provide NCRAD with detailed medical records, allowing a more confident diagnosis of Alzheimer's disease. Second, blood samples from these important families are a key resource for genetic studies. Third, autopsy confirmation of AD in over 400 individuals from these families has verified the diagnosis of AD and made that person's data as well as their family's data even more valuable to researchers. All these factors make it more likely that through the use of samples from NCRAD families, we can identify new genes that contribute to the risk of developing late onset AD.

In order to emphasize the importance of careful diagnosis and autopsy confirmation in genetic studies of late onset AD, I will briefly describe a study that I published in collaboration with two genetic statisticians, Derek Gordon PhD, at Rutgers University, and Stephen Finch at Stony Brook University. We re-analyzed genetic data from late onset AD patients that was collected about 10 years ago by the National Institutes of Mental Health. About 25% of the siblings with AD were autopsy confirmed; the rest were clinically diagnosed. When we performed analysis using only the group of siblings with autopsy confirmed AD, we found evidence for late onset AD risk genes in parts of the human genome that had not previously been identified. Our interpretation of this surprising finding is that using autopsy confirmation provided a more accurate diagnosis of the disease. Inclusion of families without autopsy confirmation of AD may have allowed individuals into the study who may have had a type of dementia that was not AD. Using only those families with autopsy confirmation has allowed us to find evidence for a new AD gene that was previously hidden.

We have now begun follow-up experiments using the samples from the NCRAD collection to confirm our observations. Samples that we have obtained from the NCRAD collection have allowed us to more than double the number of "Gold Standard" autopsy-proven sibling pairs available for our genetic studies. This was only possible by the cooperation of caretakers and clinicians and the dedicated staff at NCRAD.

A Tale of Two Nurses

By Joanne Norton and Denise Levitch
Washington University in St. Louis

From left to right - LOAD Study Coordinators Joanne Norton and Denise Levitch

Well, here we are at the airport again. This time, though, we are experiencing a 3-hour delay on our trip to Salt Lake City. Wow! We have been to more than half of the states in the contiguous USA to see participants and to Toronto, Canada for one of the coordinator meetings. Through the Genetics of Late Onset Alzheimer Disease Study (LOAD) we have met so many wonderful families and their friends along the way. And we have had some memorable experiences over the past four years.

There was the time when, in Virginia at a family reunion, a terrible thunderstorm came through while we were drawing blood. We were on the second floor of a church on a hot and humid day when suddenly all of the lights and air conditioning went out. So we guided willing participants up from the reunion and continued to consent folks and draw blood by candlelight…….. and we did not miss one.

We have had a wide variety of accommodations and we have some favorites. In Northwestern Missouri we were treated to an amazing bed and breakfast in an old large Victorian home filed with history. In Louisiana, which was still reeling from Hurricane Katrina and displaced persons, we first stayed in the former kitchen of a working plantation. Then we stayed in a bed and breakfast on a bayou: it was peaceful, brand new and very comfortable.

One trip was to Mason City, Iowa- the airport with a rock and roll history. When we arrived at the airport for our return flight, we found that it had been canceled and they were not sure, when the next flight would be. We decided to drive to Minneapolis to try to catch our connecting flight. We missed it by minutes- but had a great time exploring the airport- it was like being at a mall.

> “Thanks to all of you for giving us the opportunity to help and be part of the cure!”

Everyone has been so hospitable- from offering cookies, cheese plates, etouffee with a salad on the side and entire meals, to a ride in their motor boat on a lake. We have fed llamas in western Missouri, posed on an antique tractor in southern Iowa and rounded up cows in central Alabama in a Lincoln Town Car. We have had some amazing times.

But, the most amazing part of our travels is meeting all of you. You take the time to answer all of our questions. You have so much on your plates and yet you welcome us into your homes. We often feel like cherished extended family members. With all of us working together and supporting this research study, we are sure to find answers. Thanks to all of you for giving us the opportunity to help and be part of the cure!

Biological samples and clinical data from the LOAD study are being maintained at NCRAD. For more information please see http://ncrad.iu.edu/Participate/index.asp

New Protocol Being Launched by NCRAD

By Kate Kreiner
NCRAD Coordinator
Indiana University School of Medicine

The goal of NCRAD is to help researchers identify the genes that contribute to Alzheimer's disease and other related dementias. To help researchers achieve this goal, we are implementing a new aspect of our study. In this article, we will share with you some of the details of this new protocol and how you and your family members might be able to participate.

Changes in memory can occur at any time, and in some instances may be an early finding of possible Alzheimer's disease. There has been extensive research by a number of different scientists who have sought to study these early memory changes. NCRAD is eager to help scientists who want to better understand the relationship between normal memory changes and those changes that might precede Alzheimer's disease or related dementias.

To help scientists perform these studies, NCRAD has selected a short series of memory tests that can be administered over the telephone. NCRAD coordinators will be contacting family members who are over the age of 65 and have donated blood samples to NCRAD. There are over 1300 individuals who meet these criteria. Because this is a large number of individuals and due to the the time required to complete the memory questions by telephone, we will be sending out notices to families over the course of the coming year. So, families should not worry if they are not contacted immediately.

We are asking family members who **may** or **may not** have some memory difficulty to consider completing these brief memory tests. These questions will typically take about 20-30 minutes to complete, and are best completed when the individual is in a quiet location and will not be disturbed while the questions are being answered. Because this is part of a research study, we will not be able to provide individuals with any results concerning their test performance or the performance of other family members.

It is only through the active participation of families with Alzheimer's disease or related dementias that we will be able to unravel the genetics of dementia. NCRAD is very hopeful that the data we are able to collect through these memory tests will help increase the usefulness of the NCRAD study samples.

If you have any questions about this new initiative, please feel free to contact NCRAD staff at 1-800-526-2839 or by email at alzstudy@iupui.edu.

NCRAD READER RESPONSE SURVEY

we want to hear from you!

- What topics/questions would you like covered in future *NCRAD Update* Issues?

_____

_____

- What resource information would you like provided in future Issues?

_____

_____

- Moving? Please let us know your new address:

_____
Name Phone

_____
Street Address

_____
City State Zip

- Please share your stories with us. Tell us how Alzheimer's, NCRAD, or research has affected your life.

Send this to National Cell Repository for Alzheimer's Disease ■ Department of Medical and Molecular Genetics ■ Attention Kate Kreiner ■ 975 West Walnut Street – IB 130 Indianapolis, Indiana 46202-5251

Research Opportunities

MIRAGE: Multi-Institutional Research in Alzheimer's Genetic Epidemiology

- Purpose: In the third phase of this study, researchers continue to evaluate genetic and non-genetic risk factors for Alzheimer's disease. There is a particular emphasis on exploring whether risk factors for vascular disease are also contributing risk factors for AD. It is hoped that by obtaining data from 1000 families, these associations can be better understood.
- Eligibility: Siblings (brothers and sisters) both of whom are at least 60 years of age, one of which has been diagnosed with Alzheimer's disease, willing to undergo a blood draw and a MRI scan along with answering questions regarding their family history.
- Contact: Kelly Horner
  Ph: 1-800-526-2839
  or email: kjhorner@iupui.edu

Alzheimer's Disease Neuroimaging Initiative

- Purpose: To examine how brain imaging technology can be used with other tests to measure the progression of mild cognitive impairment (MCI) and early Alzheimer's disease. This information will aid future clinical trials by providing a standard assessment tool to measure the effects of treatments being studied.
- Eligibility: Minimum Age 50 Maximum Age 90, Both Genders, Disease stages: Pre-Clinical, Early, and Middle. Participants will be classified as either MCI patients, AD patients, or healthy controls
- Locations: AL, AZ, CA, CT, DC, FL, GA, IL, IN, KS, KY, MD, MO, NV, NH, NY, NC, OH, OR, PA, SC, TX, VT, WI
- Contact: ADEAR Center at 800-438-4380 or web address: http://www.nia.nih.gov/Alzheimers/ResearchInformation/ClinicalTrials/ADNI.htm

Depression in Alzheimer's Disease

- Purpose: To demonstrate whether the medication sertraline (Zoloft®) helps people with Alzheimer's disease. Through this study we hope to find out if treating depression can slow the progression of Alzheimer's disease.
- Eligibility: People who suffer from memory loss, Alzheimer's disease, and symptoms of depression. Participants must also be accompanied by their caregiver.
- Locations: CA, MD, NY, PA, SC
- Contact: Ann Morrison, PhD, RN
  PH: 410-614-4605
  E-mail: amorris7@jhmi.edu

Huperzine A in Alzheimer's Disease

- Purpose: To evaluate the safety and efficacy of the Chinese herb huperzine A in the treatment of Alzheimer's disease in a randomized controlled trial of its effect on cognitive function.
- Eligibility: Age 55 + with probable AD, stable condition 3 months prior to screening. If interested, speak with contact about other eligibility requirements.
- Locations: AL, CA, DC, FL, GA, IL, NV, NJ, NY, NC, OR, PA, SC, TX
- Contact: Carolyn Ward, MSPH
  PH: 202-784-6671
  E-mail: cw2@georgetown.edu

Prevention of Alzheimer's Disease by Vitamin E and Selenium (PREADVISE)

- Purpose: As a prevention trial, PREADVISE is trying to find out if taking selenium and/or Vitamin E supplements can help to prevent memory loss and dementia such as Alzheimer's disease.
- Eligibility: Ages: 60 - 90, Male. Accepts Healthy Volunteers
- Locations: AL, AK, CA, CO, DC, FL, GA, IA, KS, KY, MD, MA, MI, MN, MS, MO, MT, NE, NV, NJ, NY, OH, OK, PA, SD, TN, TX, WA, WI, CANADA, PUERTO RICO
- Contact: Cecil R. Runyons
  PH: 1-859-257-1412 Ext. 235
  E-mail: preadvise@lsv.uky.edu

Anti-Oxidant Treatment of Alzheimer's Disease

- Purpose: To examine the safety and effectiveness of two anti-oxidant treatment regimens in patients with mild to moderate Alzheimer's disease. The anti-oxidant treatments include vitamin E+ C+ alpha –lipoic acid, and Coenzyme Q (CoQ).
- Eligibility: Ages 60-85, Both Genders, Diagnosis of probable Alzheimer's Disease.
- Locations: AL, AZ, CA, FL, NY, OH, OR, PA, SC, WA
- Contact: ADCS Anti-Oxidant Study webpage http://adcs.ucsd.edu/Anti-Oxidant_protocol.htm or Linda Mandelco E-mail: linda.mandelco@med.va.gov

Valproate in Dementia (VALID)

- Purpose: To demonstrate whether valproate therapy delays the emergence of agitation and/or psychosis in outpatients with probable Alzheimer's disease (AD) who have not experienced agitation and psychosis in their illness. A secondary aim is to determine whether valproate therapy delays the progression of cognitive and functional measures of illness. This trial will also assess the tolerability and safety of low-dose, long-term valproate therapy.
- Eligibility: Ages 55 - 90 with probable AD
- Locations: CA, CT, DC, FL, GA, IL, MI, MO, NV, NY, OH, PA, RI, SC, TN, TX,VT, VA
- Contact: Laura Jakimovich, RN, MS
  PH: 585-760-6578
  E-mail: laura_jakimovich@urmc.rochester.edu

Sources for Information and Support

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.alzheimers.org
Tel: 301-495-3311 or 800-438-4380
** ADEAR lists all 29 Alzheimer's Disease Centers (ADCs) and their contact information.

Depression and Related Affective Disorders Association (DRADA)
www.drada.org
Tel:703-610-9026

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://cjdfoundation.org

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.

INDIANA UNIVERSITY
SCHOOL OF MEDICINE

National Cell Repository for Alzheimer's Disease
Department of Medical and Molecular Genetics
975 West Walnut Street ▪ IB 130
Indianapolis, Indiana 46202-5251