

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.



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National Cell Repository for Alzheimer's Disease

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NCRAD Update

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The Alzheimer Disease Sequencing Project



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In February of 2012, President Obama announced a new

Presidential Initiative focusing additional National Institutes of Health (NIH) resources on the important problem of Alzheimer disease (AD). He specifically directed that 25 million dollars should be allocated toward the sequencing of DNA to identify changes in DNA (variants) that increase or decrease the risk of AD. This has been extremely welcome news to the AD community and plans have been underway for the past year to ensure that these funds will be used to design the best study possible.

- The samples and data collected from
- families participating in the National
- Cell Repository for Alzheimer Disease
- (NCRAD) are essential for this
- important study. We hope that in
- the future we will be able inform our
- research subjects of the important
- findings from this study.

By including leaders not only in the field of AD genetics but also in the study of other common, complex disorders like Alzheimer disease, a study has been designed that will include both whole genome sequencing and whole exome sequencing. These two approaches allow researchers to ask different questions.

To understand these two sequencing terms, it is important to understand a bit about how the human genome is organized. Our DNA consists of about 3 billion base pairs. DNA is a long strand that along its length codes for genes (see glossary, page 4). In between genes is much of our DNA and its role is only beginning to be understood (see page four). Whole genome sequencing means that the entire sequence of an individual's DNA will be examined - all 3 billion base pairs. Whole exome sequencing will only examine the DNA sequence within genes.

Researchers will compare the DNA sequence of a large number of individuals who have developed Alzheimer disease with the DNA sequence of a large number of individuals who have not developed Alzheimer disease, although they have lived to be quite elderly. It is anticipated that changes in the DNA sequence will be found that are observed more frequently in those who develop AD and therefore increase their risk for disease. Researchers also anticipate finding DNA sequence changes that may protect some individuals from developing AD.

The samples and data collected from families participating in the National Cell Repository for Alzheimer Disease (NCRAD) are essential for this important study. We hope that in the future we will be able to inform research subjects of the important findings from this study.

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10 Things You Should Know about Lewy Body Dementias



Adapted from the Lewy Body Dementia Association, Inc.
www.lbda.org

Lewy body dementias (LBD) affect an estimated 1.3 million individuals and their families in the United States. Lewy body dementia (LBD) has been known by many names over the past 30 years such as: "Dementia with Lewy Body" (DLB), "Lewy Body Dementia" (LBD), "Diffuse Lewy Body Disease" (DLBD), "Lewy Body Disease", "Cortical Lewy Body Disease", "Lewy Body Variant of Alzheimer's Disease" or "Parkinson's Disease Dementia."

In the early 1900s, while researching Parkinson's disease, the scientist Friederich H. Lewy discovered abnormal protein deposits that disrupt the brain's normal functioning. These Lewy body proteins are found in an area of the brain stem where they deplete the neurotransmitter dopamine, causing Parkinsonian symptoms. In Lewy body dementia, these abnormal Lewy body proteins are distributed throughout other areas of the brain, including the cerebral cortex. The brain chemical acetylcholine is depleted, causing disruption of perception, thinking and behavior. Lewy body dementia exists either in pure form, or in conjunction with other brain changes, including those typically seen in Alzheimer's disease and Parkinson's disease.

Though many families are affected by this disease, few individuals and medical professionals outside of specialists like neurologists and geriatric psychiatrists are aware of the symptoms, diagnostic criteria, or even that LBD exists. There are important facts about Lewy body dementias that you should know if you, a loved one, or a patient you are treating may have LBD.

1 Lewy body dementias (LBD) are the second most common form of degenerative dementia; LBD is widely under-diagnosed: The only other form of degenerative dementia that is more common than LBD is Alzheimer's disease (AD). Many individuals who have LBD are misdiagnosed, most commonly with Alzheimer's disease if they present with a memory disorder or Parkinson's disease if they present with movement problems.

2 LBD can have three common presentations: Some individuals will start out with a movement disorder leading to the diagnosis of Parkinson's disease and later develop dementia. This is typically diagnosed as Parkinson's disease dementia. Another group of individuals will start out with a memory disorder that may look like AD, but over time two or more distinctive features become apparent leading to the diagnosis of 'dementia with Lewy bodies' (DLB). Lastly,

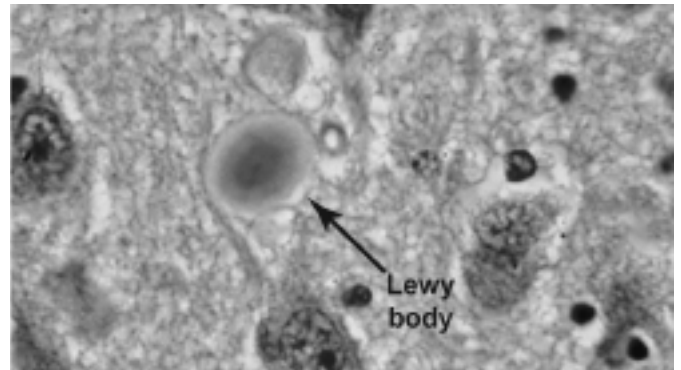


Photo: www.genome.gov

a small group will first present with neuropsychiatric symptoms, which can include hallucinations, behavioral problems, and difficulty with complex mental activities, leading to an initial diagnosis of LBD. Regardless of the initial symptom, over time all three presentations of LBD will develop very similar cognitive, physical, sleep and behavioral features, all caused by the presence of Lewy bodies throughout the brain.

3 The most common symptoms of LBD include:

- Dementia: problems with memory and thinking
- Hallucinations: seeing or hearing things that are not really present
- Cognitive fluctuations: unpredictable changes in concentration and attention
- Parkinson-like symptoms: rigidity or stiffness, shuffling gait, tremor, slowness of movement (bradykinesia)
- Severe sensitivity to neuroleptics (medications used to treat hallucinations)
- REM Sleep Behavior Disorder: a sleep disorder where people seemingly act out their dreams

4 The symptoms of LBD are treatable: Currently there is only one medication approved specifically for the treatment of one form of LBD. Most medications prescribed for LBD are approved for a course of treatment for symptoms related to other diseases such as Alzheimer's disease and Parkinson's disease with dementia and offer symptomatic benefits for cognitive, movement and behavioral problems.

5 Early and accurate diagnosis of LBD is essential: Early and accurate diagnosis is important because LBD patients may react to certain medications differently than AD or PD patients. A variety of drugs, including anticholinergics and some antiparkinsonian medications, can worsen LBD symptoms.

6 Traditional antipsychotic medications may be contraindicated for individuals living with LBD: Many traditional antipsychotic medications (for example, Haldol, Mellaril) are commonly prescribed for individuals with Alzheimer's disease and other forms of dementia to control behavioral symptoms. However, LBD affects an individual's brain differently than other dementias. As a result, these medications can cause a severe worsening of movement and a potentially fatal condition known as neuroleptic malignant syndrome (NMS). NMS causes severe fever, muscle rigidity and breakdown that can lead to kidney failure.

7 Early recognition, diagnosis and treatment of LBD can improve the patients' quality of life: LBD may affect an individual's cognitive abilities, motor functions, and/or ability to complete activities of daily living. Treatment should always be monitored by your physician(s) and may include: prescriptive and other therapies, exercise, diet, sleep habits, changes in behavior and daily routines.

8 Individuals and families living with LBD should not have to face this disease alone: LBD affects every aspect of a person - their mood, the way they think, and the way they move. LBD patients and families will need considerable resources and assistance from healthcare professionals and agencies. The combination of cognitive, motor and behavioral symptoms creates a highly challenging set of demands for continuing care. LBDA was formed to help families address many of these challenges.



9 Physician education is urgently needed: An increasing number of general practitioners, neurologists, and other medical professionals are beginning to learn to recognize and differentiate the symptoms of LBD from other diseases. However, more education on the diagnosis and treatment of LBD is essential.

10 More research is urgently needed! Research needs include tools for early diagnosis, such as screening questionnaires, biomarkers, neuroimaging techniques, and more effective therapies. With further research, LBD may ultimately be treated and prevented through early detection and neuroprotective interventions. Currently, there is no specific test to diagnose LBD.

The NCRAD Autopsy Program



At NCRAD, we encourage pre-planning of autopsies for individuals affected with AD and for healthy non-affected individuals who wish to donate their brain tissue. Planning in advance helps ensure all of the necessary steps at the time of death are completed smoothly to avoid any undue burden to the family at a difficult time, and to facilitate the removal and processing of the brain tissue as quickly as possible.

Any questions or concerns regarding autopsy in general, autopsy planning, or an existing plan, may be directed to the NCRAD staff by phone at (800) 526-2839 or by e-mail at alzstudy@iu.edu. Please do not hesitate to contact us at any time.

The AD Sequencing Project > continued from page 1

GLOSSARY OF GENETIC TERMS

*Glossary of terms adapted from:
www.genome.gov/glossary*

DNA

DNA is the chemical name for the molecule that carries genetic instructions in all living things. The DNA molecule consists of two strands that wind around one another to form a shape known as a double helix. Each strand has a backbone made of alternating sugar (deoxyribose) and phosphate groups. Attached to each sugar is one of four bases-adenine (A), cytosine (C), guanine (G), and thymine (T). The two strands are held together by bonds between the bases; adenine bonds with thymine and cytosine bonds with guanine.

SEQUENCE

The DNA sequence is the arrangement (or order) of the 4 bases along the DNA strand.

CHROMOSOMES

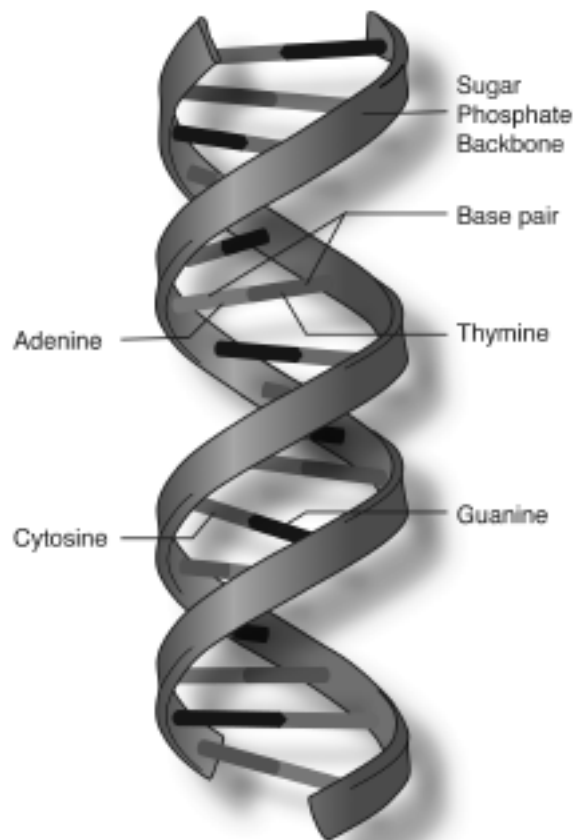
DNA is organized into 23 pairs of chromosomes. One member of each chromosome pair is inherited from an individual's mother and the other member of the pair is inherited from an individual's father.

GENES

The basic physical unit of inheritance. Genes are passed from parents to offspring and contain the information needed to specify traits. Genes are arranged, one after another, on chromosomes. A chromosome contains a single, long DNA molecule, only a portion of which corresponds to a single gene. Humans have approximately 20,000 genes arranged on their chromosomes.

MUTATION

Along the DNA strand where the bases are located, an error can be introduced. This is similar to creating a typographical mistake in a word that is part of a sentence. This error might exchange one base (A,C,T,G) for another. It might remove a single base or several bases. It could also be an insertion of a base or bases that should not be in the sequence at that place. When a mutation occurs within a gene, it can alter the product that the gene is supposed to make. It may result in an abnormal product. It may cause the product not to be made at all or it might cause too much or too little of the product to be made. Any of these changes could cause an individual to develop a particular disease or they might cause an individual to respond poorly to a particular medication.



Double Helix

DNA SEQUENCING

DNA sequencing is a laboratory technique used to determine the exact sequence of bases (A, C, G, and T) in a DNA molecule. The DNA base sequence carries the information a cell needs to assemble protein and RNA molecules. DNA sequence information is important to scientists investigating the functions of genes. The technology of DNA sequencing was made faster and less expensive as part of the Human Genome Project.

ENCODE PROJECT

The National Human Genome Research Institute (NHGRI) launched a public research consortium named ENCODE, the Encyclopedia Of DNA Elements, in September 2003, to carry out a project to identify all functional elements in the human genome sequence. The project started with two components - a pilot phase and a technology development phase.

Link to the Encode Project is:

<http://www.genome.gov/10005107#a-1>

Research Opportunities

Dominantly Inherited Alzheimer Network (DIAN)

- Purpose: To study brain changes in people who carry an AD mutation in order to determine how the disease process develops before the onset of symptoms.
- Eligibility: Men and women ages 18 and older with a biological parent or sibling with AD caused by a known mutation. All participants must be able to speak and read English, and must provide contact information for someone who knows them well and would be willing to answer questions about their memory and thinking.
- Locations: USA - CA, IN, MA, MO, NY, RI; United Kingdom; Australia
- Contact: PH: 314-286-2683 or the DIAN website, <http://www.dian-info.org>

Randomized, Controlled Study Evaluating CERE-110 in Subjects with Mild to Moderate Alzheimer's Disease

- Purpose: To evaluate the potential benefits of CERE-110 in the treatment of Alzheimer's disease. CERE-110 is an experimental drug that is designed to help the nerve cells in the brain function better. CERE-110 uses a virus to transfer a gene that makes Nerve Growth Factor (NGF, a protein that may make nerve cells in the brain healthier and protect them from dying. The virus used in CERE-110 does not cause disease in people; it has been carefully studied in laboratory animals and is in the early stages of being tested in people.
- Eligibility: Men and women ages 55 to 80 years of age, a diagnosis of mild to moderate Alzheimer's disease, a study partner who can attend all study visits, good general health and medically able to undergo neurosurgery.
- Locations: AL, AZ, CA, DC, GA, NY, NC OH, SC, UT
- Contact: PH: 858-622-5863 or 858-458-8853
OH, SC, TX, WI, and Puerto Rico
- Contact: Susan Love, PH: 612-467-3342, e-mail: lovex008@tc.umn.edu, or Julie Tomaska, PH: 612-467-1563, e-mail: julie.tomaska@va.gov

Alzheimer's Disease Neuroimaging Initiative 2 (ADNI2)

- Purpose: The purpose of this study is to build upon the information obtained in the original Alzheimer's Disease Neuroimaging Initiative (ADNI1) and ADNI-GO (Grand Opportunity: a study funded through an NIH grant under the American Recovery and Reinvestment Act), 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 (AD). This information will aid in the early detection of AD, and in measuring the effectiveness of treatments in future clinical trials.
- Eligibility: Men and women 55 - 90 years of age; with a diagnosis of mild to moderate Alzheimer's disease. All other cohorts are closed at this time.
- Locations: AL, AZ, CA, CT, DC, FL, GA, IA IL, IN, KS, KY, MA, MD, MI, MN, MO, NC, NH, NV, NY, OH, OR, PA, RI, SC, TX, WI, Canada
- Contact: Ph: 1-800-438-4380 or the ADNI website: www.adni-info.org

Neuroimaging in Frontotemporal Dementia (NIFD)

- Purpose: To identify the best methods for imaging and analysis for tracking frontotemporal lobar degeneration (FTLD) over time.
- Eligibility: Individuals between the ages of 45 and 90 who meet the criteria for behavioral variant frontotemporal dementia (bvFTD), semantic dementia (SD), progressive nonfluent aphasia (PNFA), or healthy aging. A study partner who has frequent contact with the volunteer and can provide information about them and accompany them to study visits is also required. All volunteers must be willing and able to undergo testing procedures and agree to follow-up.
- Locations: CA, MN, MA
- Contact: Marissa Urbano, PH: 415-476-0670, e-mail: murbano@memory.ucsf.edu

NCRAD Welcomes Your Ideas and Suggestions

- We hope that you and your family find the NCRAD Newsletter informative. We would welcome suggestions on future topics for articles, questions you would like to ask the NCRAD doctors or anything you would like shared with our readers about your family's experience with Alzheimer disease. Please send us your ideas by e-mail or by phone.
- **Phone** 1-800-526-2839 • **E-mail** alzstudy@iupui.edu

And Check Out the NCRAD Website!

- The NCRAD staff encourages you to visit our website at www.ncrad.org for study information. On the site we provide valuable information regarding participation in NCRAD, Alzheimer's disease and genetics, and our autopsy program. There are also a number of helpful website links and information about other studies in which our participants may be interested. Previous copies of NCRAD newsletters are also available on the site for viewing and downloading.

Resources 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.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.

Assisted Living Directory, Assisted Living Facilities Information & Senior Care

<http://www.assisted-living-directory.com/>

The Association for Frontotemporal Dementias (AFTD)

<http://www.ftd-picks.org/>

Tel: 866-507-7222

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. (CJD)

<http://cjd.foundation.org>

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

National Society of Genetic Counselors

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

Tel: 312-321-6834

* **Research Match** is a free service that pairs volunteers interested in participating in research opportunities from surveys to clinical trials with researchers. Open to all, including healthy volunteers.

<http://www.researchmatch.org>

* **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/>

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

10 Signs of Alzheimer's Disease

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.

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.



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