The National Cell Repository for Alzheimer's Disease (NCRAD) is a data and specimen collection source for families with Alzheimer's 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 for AD. Many family members have provided blood samples, which researchers use to study 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
Hereditary Genomics Division
Health Information and Translational Sciences Building
410 West 10th Street, HS 4000
Indianapolis, IN 46202-3002

Phone: 1-800-526-2839
e-mail: alzstudy@iu.edu
New Website: www.ncrad.org

Inside this issue

NCRAD Update

Newsletter of the National Cell Repository for Alzheimer's Disease Volume 23 • Fall 2015

The National Cell Repository for Alzheimer's Disease (NCRAD) Celebrates Our Silver Anniversary — 25 Years

The National Cell Repository for Alzheimer's Disease (NCRAD) is celebrating its 25th anniversary this year. With the participation of the more than 900 families in NCRAD, and the 21 other studies providing samples, we have significantly advanced Alzheimer's disease (AD) research. In the past 25 years, NCRAD has sent nearly 200,000 biological samples to over 125 different researchers all over the world. Data and samples from our repository have resulted in more than 400 scientific publications and this number continues to grow every day. NCRAD families have been, and continue to be, critical in many aspects of important AD research.

NCRAD has updated its look!

As part of our 25 year celebration, NCRAD has updated its look! We have a new logo and a new website.

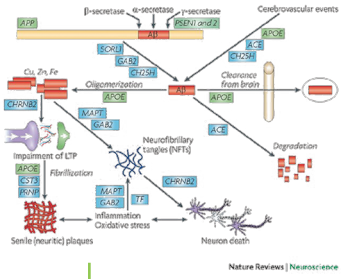
NCRAD

Please be sure to check out our completely re-designed website at:

www.ncrad.org

We hope you find it informative!

We have developed a timeline to highlight advances in the field of AD and dementia research and the role NCRAD has played over the past 25 years. The participation of families with dementia is vitally important for scientific research seeking to understand why individuals develop AD and related dementias. We are hopeful that any new knowledge gained from such research will help lead to preventions, treatments, and cures for this disease. The NCRAD staff and all researchers using data and samples from NCRAD families are extremely grateful for your participation. Thank you! ■

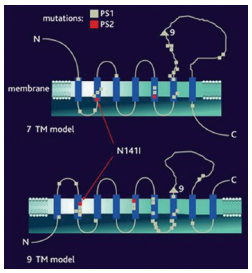


1987 — APP IS THE FIRST GENE WITH MUTATIONS FOUND TO CAUSE AN INHERITED FORM OF ALZHEIMER'S DISEASE

1990 — ESTABLISHED NCRAD FAMILY STUDY WITH DR. P. MICHAEL CONNEALLY

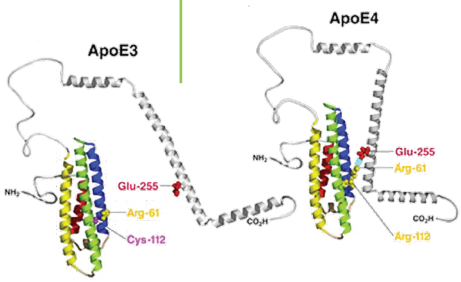
1991 — NCRAD SENT OUT FIRST 200 SAMPLES TO QUALIFIED INVESTIGATORS

1992 — MUTATIONS IN PS1 GENE FOUND TO CAUSE INHERITED EARLY ONSET ALZHEIMER'S DISEASE



1993 — MUTATIONS IN PS2 GENE FOUND TO CAUSE INHERITED EARLY ONSET ALZHEIMER'S DISEASE

1993 — APOE4 IS THE FIRST GENETIC RISK FACTOR FOUND TO INCREASE RISK OF ALZHEIMER'S DISEASE



1993 — MORE THAN 500 FAMILES ENROLLED IN THE NCRAD FAMILY STUDY

1994 — PRESI… DIAGN…

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Research Opportunities:

4 Repeat Tauopathy Neuroimaging Initiative (4RTNI)

- Purpose: To identify the best methods of analysis for tracking PSP and CBD over time. The results from this study may be used in the future to calculate power for clinical drug trials, as this study aims to identify the most reliable outcome measures.
- Eligibility: Men and women ages 45 to 90 years, diagnosis of Progressive Supranuclear Palsy or Corticobasal Degeneration (CBD)
- Locations: CA
- Contact: PH: 415-476-9578 or 4RTNI webpage: www.memory.ucsf.edu/research/studies/4rtni

Advancing Research and Treatment for Frontotemporal Labor Degeneration (ARTFL)

- Purpose: "New therapies targeting some of the molecular causes of FTLD are rapidly becoming available for testing in human clinical trials. The ARTFL's goal is to prepare for clinical trials of these new therapies by evaluating people who might eventually be candidates for participation in clinical trials and by developing new diagnostic technologies to evaluate the effectiveness of new treatments for FTLD."
  (Citation: https://www.rarediseasesnetwork.org/ARTFL/index.htm)
- Locations: CA, FL, IL, MA, MD, MN, MO, NC, NY; Canada
- See this website for more information: https://www.rarediseasesnetwork.org/ARTFL/index.htm

Dominantly Inherited Alzheimer Network (DIAN)

- Purpose: To study brain changes in people who carry an Alzheimer's disease mutation in order to determine how the disease process develops before the onset of symptoms.
- Eligibility: Men and women ages 55 to 80 years, diagnosis of mild to moderate Alzheimer's disease, good general health and medically able to undergo neurosurgery.
- Locations: USA - CA, IN, MA, MO, NY, RI; United Kingdom; Australia
- Contact: PH: 314-286-2683 or DIAN webpage: http://www.dian-info.org

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1995

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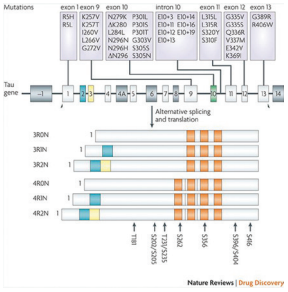
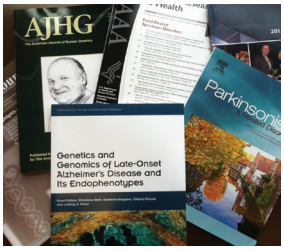
1998

MAPT WAS THE FIRST GENE FOUND TO BE ASSOCIATED WITH HEREDITARY FRONTOTEMPORAL DEMENTIA



2001

60 PUBLICATIONS HAVE BEEN GENERATED USING NCRAD RESOURCES



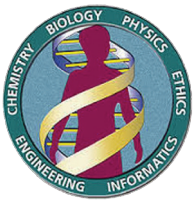
2002

DR. TATIANA FOROUD BECAME PRINCIPAL INVESTIGATOR OF NCRAD

2002

NCRAD EXPANDED TO BANK SAMPLES FROM OTHER STUDIES

2003



COMPLETION OF THE HUMAN GENOME PROJECT ANNOUNCED

2005

NCRAD BANKS SAMPLES FOR FOUR DIFFERENT STUDIES

2006

REACHED 3,000 SAMPLED SUBJECTS IN NCRAD FAMILY STUDY

2007

NCRAD MOVED TO NEW OFFICE BUILDING

20

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Longitudinal Evaluation of Familial Frontotemporal Dementia Subjects (LEFFTDS)

- Purpose: To model the rates of decline in clinical function of those suffering from Frontotemporal Labor Degeneration (FTLD) and identify genetic and biofluid factors that modify these rates.
- Eligibility: Must be a member of a family with a known mutation, have a reliable informant who personally speaks with or sees that subject weekly, the subject and informant must be fluent in English, the subject must be willing to undergo yearly evaluations for a period of three years, and the subject must be willing to undergo neuropsychological testing and MRI imaging.
- Locations: CA, FL, MA, MO, NY, PA; Canada
- Contact:

  Mayo Clinic Rochester
  Alzheimer's Disease Research Center
  507-284-1324

  Mayo Clinic Florida
  Memory Disorder Clinic
  904-953-6523

Meet the newest member of our NCRAD staff, Jan Hamer

Jan Hamer, BS is a newcomer to the Department of Medical and Molecular Genetics. She recently graduated from Indiana University with degrees in Biology and Neuroscience.
Jan serves as a research coordinator and her duties include sample accessioning, family follow-up mailings, medical history questionnaire mailings and data validation. To reach Jan directly, please email jehamer@iu.edu or call 317-278-1150.

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 email or by phone.

- **Phone:** 1-800-526-2839
- **Email:** alzstudy@iu.edu
- **Website:** www.ncrad.org

NCRAD WAS DESIGNATED THE SAMPLE REPOSITORY FOR THE ALZHEIMER'S DISEASE GENETICS CONSORTIUM AND BEGAN RECEIVING SAMPLES FROM THE ALZHEIMER'S DISEASE CENTERS

PRESIDENT OBAMA ANNOUNCED A NEW PRESIDENTIAL INITIATIVE FOCUSING ADDITIONAL NIH RESOURCES ON ALZHEIMER'S DISEASE. ALZHEIMER'S DISEASE SEQUENCING PROJECT WAS INITIATED

NCRAD LABORATORY MOVES INTO NEW SPACE

08 2008 2009 2010 2011 2012 2015

SENT OVER
MPLES FROM
AND NCRAD
STUDIES TO
CENTER FOR
TED DISEASE
H (CIDR) FOR
SSOCIATION
UDY (GWAS)

NCRAD BEGAN RECEIVING RNA, PLASMA, AND SERUM SAMPLES

PRESIDENT OBAMA SIGNS NATIONAL ALZHEIMER'S PROJECT ACT (NAPA) INTO LAW

NCRAD NOW BANKS SAMPLES FOR 20+ STUDIES, AIDED IN OVER 400 PUBLICATIONS, AND PROVIDED MORE THAN 120 RESEARCHERS WITH NCRAD SAMPLES

Center for Inherited Disease Research
Johns Hopkins University

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.nia.nih.gov/Alzheimers
Tel: 301-495-3311 or 800-438-4380
** ADEAR lists all 29 Alzheimer 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.theaftd.org
Tel: 267-514-7221 or 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://cjdfoundation.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/

***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

National Society of Genetic Counselors
http://www.nsgc.org/
Tel: 312-321-6834

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

NCRAD Partners with NIH-funded ARTFL and LEFFTDS Studies

Brad Boeve, MD,
Mayo Clinic Rochester

Adam Boxer, MD, PhD,
University of California
San Francisco

Howie Rosen, MD,
University of California
San Francisco

NCRAD will be acting as a cell repository for two new studies: ARTFL, The Advancing Research and Treatment for Frontotemporal Lobar Degeneration consortium, and LEFFTDS, Longitudinal Evaluation of Familial Frontotemporal Dementia Subjects.

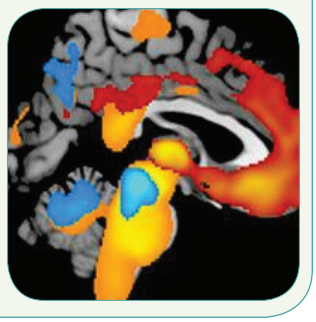
ARTFL (U54NS092089) is a consortium of academic medical centers partnered with patient support organizations dedicated to conducting clinical research in sporadic and familial frontotemporal lobar degeneration (FTLD) syndromes. Funded by the National Institutes of Health (NIH), ARTFL is part of the Rare Diseases Clinical Research Network (RDCRN). The study is based at the University of California, San Francisco, under the direction of PI Adam Boxer, MD, PhD, and co-PI Howard Rosen, MD. Including UCSF, there are 14 clinical study sites in the US and Canada. ARTFL is a partnership between academic investigators, patient advocacy groups, including the Association for Frontotemporal Degeneration, the Bluefield Project, Corticobasal Degeneration Solutions, Cure PSP and the Alzheimer's Drug Discovery Foundation, and the NIH.

ARTFL will establish a large cohort of patients with FTLD syndromes including Corticobasal Degeneration Syndrome (CBD or CBS), primary progressive aphasias (PPA) including semantic variant (svPPA) and non-fluent variant (nvPPA), behavioral variant Frontotemporal Dementia (bvFTD), Frontotemporal Dementia with Amyotrophic Lateral Sclerosis (FTD-ALS), and Progressive Supranuclear Palsy (PSP). Healthy family members of patients with genetic causes of FTLD will also be enrolled.

Approximately 1,560 patients and family members will participate in clinical evaluations that will include history and examination, cognitive testing, and questionnaires and surveys, and collection of blood. Patients and family members with familial FTLD syndromes may be followed longitudinally and undergo brain MRI. The goal is to discover new biomarkers for disease activity, standardize diagnostic criteria, and identify a large group of potential participants for clinical trials of new therapeutic agents. Patients will not need to participate in all procedures to enroll in ARTFL.

ARTFL is closely connected with LEFFTDS. This study (U01AG045390) is being jointly led by PI Brad Boeve, MD, at the Mayo Clinic Rochester, and co-PI Howard Rosen, MD, at UCSF, and is jointly funded by the NIA and NINDS. Encompassing eight clinical sites in the US and Canada,

This image shows where MRI scans taken one year apart in two types of FTLD measured the greatest loss of brain tissue. Red-yellow areas indicate the relative severity of atrophy in people with behavioral variant frontotemporal dementia (bvFTD), whereas yellow-orange-blue areas show annual tissue loss in progressive supranuclear palsy (PSP). Color images superimposed on MRI of a healthy adult brain. *[Image courtesy of Shubir Dutt, Howard Rosen, Adam Boxer, UCSF, first published on Alzforum.]*



LEFFTDS is enrolling 300 participants from families with known mutations in one of the three genes most commonly associated with FTLD: microtubule associated protein tau (***MAPT***, sometimes also referred to as ***"Tau"***), ***GRN***, and ***C9ORF72***. The 300 LEFFTDS participants are a subset of the ARTFL enrollees. The clinical and imaging procedures for LEFFTDS and ARTFL are identical. The studies share the same clinical, imaging (Laboratory of Neuro Imaging [LONI] at USC), and biological specimens repositories (NCRAD). The biomarker protocols are identical as well, but LEFFTDS collects more types of biological specimens than ARTFL. Compared with ARTFL, LEFFTDS is more focused and intense. While ARTFL is enrolling participants with a strong family history of FTLD regardless of whether a mutation has been found in that family, LEFFTDS is only enrolling families where a known mutation has been found in one of the three targeted genes. Both studies are enrolling symptomatic and asymptomatic family members. Participants need not know their own genetic status, but would know that a gene has been identified in their family. While LEFFTDS is seeing each patient for three annual visits and acquiring brain imaging at each visit, ARTFL is seeing family members twice over one year and is only acquiring imaging in asymptomatic patients. All participants in LEFFTDS will be asked to contribute CSF (have a lumbar puncture) while this is currently only occurring in ARTFL patients with symptomatic Progressive Supranuclear Palsy. LEFFTDS collects Peripheral Blood Mononuclear Cells (PBMCs) suitable for generation of induced pluripotent stem cells and RNA suitable for gene

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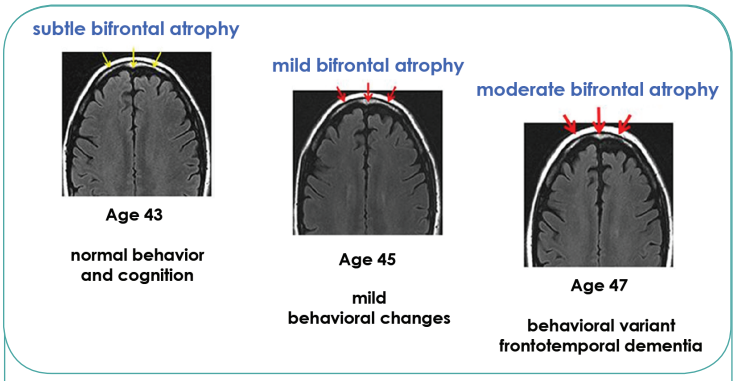

Longitudinal MRI scans of a person carrying a pathogenic mutation in the gene encoding MAPT, who becomes symptomatic during this time. *[Image courtesy of Brad Boeve, Kejal Kantarci and Clifford Jack, Jr., Mayo Clinic, first published on Alzforum.]*

expression analysis. While ARTFL does not currently do this, plans are being made to collect all the same biospecimens in ARTFL that are collected in LEFFTDS. The database containing the ARTFL data will also include an indication of whether this participant is a LEFFTDS co-enrollee.

Investigators at ARTFL and LEFFTDS sites are excited to be involved in this large collaborative effort to create this ongoing clinical research infrastructure with the generous support of the NIH, NIA, and NINDS. ■

National Cell Repository for Alzheimer's Disease
Hereditary Genomics Division

Health Information and Translational Sciences Building
410 West 10th Street • HS 4000
Indianapolis, IN 46202-3002

INDIANA UNIVERSITY
SCHOOL OF MEDICINE

Phone: 1-800-526-2839
E-mail: alzstudy@iu.edu
Website: www.ncrad.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 personality
9. Changes in mood or behavior
10. Loss of initiative

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

Photo Credits for NCRAD Timeline: *(By order of year)*

- **1987:** APP gene mutation published by Bertram, L and Tanzi, R.E, Thirty years of Alzheimer's disease genetics: the implications of systematic meta-analyses. Nat Rev Neurosci, 2008. 9(10): p.768-778.
- **1990:** Dr. P. Michael Conneally portrait courtesy of Office of Visual Media, Indiana University
- **1992:** PS1 gene mutation published by Hum Mol Genet, 1997. 6: p.1639–1646. (https://www.cnsforum.com/educationalresources/imagebank/dementia_alzheimers/presen_mut_alz)
- **1993:** APOE gene mutation published by Huang Lab, Neurological Disease (http://labs.gladstone.ucsf.edu/huang/pages/apoe-research)
- **1994:** Official portrait of President Reagan (1981) courtesy of Ronald Reagan Library
- **1998:** MAPT gene mutation published by Brunden, K.R., Trojanowski, J.Q., and Lee, V.M.Y., Advances in tau-focused drug discovery for Alzheimer's disease and related tauopathies. Nature Reviews Drug Discovery, 2009. 8: p.783-793.
- **2001:** Journal articles photo courtesy of the Department of Medical and Molecular Genetics, Indiana University
- **2002:** Dr. Tatiana Foroud portrait courtesy of Office of Visual Media, Indiana University
- **2003:** Human Genome Project logo courtesy of the U.S. Department of Energy, Human Genome Project (http://www.ornl.gov/hgmis)
- **2005:** Indiana University Health Information and Translational Sciences Building (HITS) photo courtesy of Department of Medical and Molecular Genetics, Indiana University
- **2008a:** ADGC (Alzheimer's Disease Genetics Consortium) logo by University of Pennsylvania
- **2008b:** CIDR (Center for Inherited Disease Research) logo by Johns Hopkins University
- **2011:** President Obama photo courtesy of the Department of Defense Public Domain
- **2012:** We Can't Wait Campaign photo courtesy of https://www.whitehouse.gov