NCRAD Update

Newsletter of the National Cell Repository for Alzheimer's Disease Volume 24 • Fall 2016

Alzheimer's Biomarker Consortium-Down Syndrome (ABC-DS)

By Drs. Nicole Schupf and Ben Handen — By the time they reach 40 years of age virtually all individuals with Down Syndrome (DS) have neuropathological changes consistent with a diagnosis of Alzheimer's disease (AD), including deposition of amyloid beta (Aβ) in diffuse and neuritic plaques, and most will develop dementia by the end of their seventh decade. The increased risk for AD in adults with DS has been attributed, at least in part, to triplication and overexpression of *APP*, leading to elevated levels of Aβ peptides. However, there are large individual differences in Aβ peptide levels, and there is a wide range of age at onset of dementia. Thus, there are more complex underlying mechanisms which are not well understood and which influence risk for cognitive decline and age of onset of dementia.

NIA (National Institute on Aging) and NICHD (National Institute of Child Health & Human Development) have recently funded two large, multicenter projects that seek to identify biomarkers that can predict the risk of developing Alzheimer's disease in adults with Down syndrome. Together they will recruit over 450 adults with DS, ranging from 25 to 85 years of age. The project focuses on a longitudinal and multidisciplinary determination of key biomarkers that are likely to define the progression from normal aging to onset of dementia, including levels and rates of change in blood-based biomarkers such as β-amyloid peptides, protein, inflammatory and lipid profiles, measures of amyloid and tau, concentration in cerebrospinal fluid, neuroimaging-based changes, PET studies of brain amyloid and tau and genetic polymorphisms. These biomarkers will be combined to develop the most valid indicators of preclinical and early stages of Alzheimer's. All of the blood-based biomarkers for this study will be banked at National Cell Repository for Alzheimer's Disease.

Many researchers believe that future Alzheimer's disease treatments may be most effective in the early stages of the disease, before the onset of symptoms and before irreversible neuron loss has occurred. The goals of this study are to understand biomarker relationships and the pathways implicated in AD pathogenesis, to identify critical factors that link cerebral Aβ deposition to neurodegeneration, to develop a model for predicting risk that may allow for future therapeutic interventions before irreversible cognitive deterioration has occurred, and to set a foundation for an efficient transition from this biomarker study to a therapeutic trial to combat AD in DS, augmented by biomarker outcomes.

The grant for this prospective study is part of a National Institutes of Health initiative, Alzheimer's Biomarker Consortium-Down Syndrome (ABC-DS), that

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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 who wish to help us move toward this goal.

INDIANA UNIVERSITY
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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
Website: www.ncrad.org

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supports two collaborative teams seeking Alzheimer's disease biomarkers in people with Down Syndrome. Drs. Nicole Schupf, Ira Lott, and Wayne Silverman lead a team of investigators from Columbia University Medical Center, the University of California, Irvine, Kennedy Krieger Institute/Johns Hopkins University, Massachusetts General Hospital/Harvard, the New York State Institute for Basic Research in Developmental Disabilities, and the University of North Texas Health Sciences Center. Drs. Benjamin Handen, William Klunk, and Brad Christian lead a team of investigators from the University of Pittsburgh, the University of Wisconsin, Madison, the University of Cambridge, and Barrow Neurological Institute. ■

The IDEAS and ANGI Studies

Adapted from Alzheimer's Association brochure —
A new four-year research study, conducted by the Alzheimer's Association and the American College of Radiology (ACR) began recruitment in 2016. This new study is called IDEAS: The Imaging Dementia Evidence for Amyloid Scanning Study. In this study, scientists want to learn how images of the brain may be able to help doctors treat their dementia patients, and if that treatment may lead to better results.

The IDEAS Study will focus on brain images called amyloid PET scans. PET stands for Positron Emission Tomography. These scans can show if amyloid plaques are building up in the brain. Amyloid plaques are sticky clumps of protein in the brain. Plaques are associated with Alzheimer's disease, but can also be seen with aging and other brain disorders. The presence or absence of amyloid plaques will help doctors determine the likelihood that dementia related symptoms are caused by Alzheimer's disease.

If the plaques are present, PET imaging will highlight them. A radiopharmaceutical, which is also called a radioactive tracer, will stick to the plaques for a short time, allowing the plaques to be seen. The tracer has been approved by the U.S. Food and Drug Administration (FDA), and will be injected into the subject's blood through an I.V. for the amyloid PET scan. Medicare has agreed to cover the cost of these scans for this research study.

Subjects are eligible to participate in the IDEAS study if they:

- Are a Medicare beneficiary, 65 years of age or older
- Have ongoing memory problems or confusion and the subject's doctor has not found a cause of the symptoms
- Have a medical history and cognitive testing that supports the diagnosis of either dementia or mild cognitive impairment, but the cause is unclear.
- Have possible Alzheimer's disease, but the signs and symptoms are unusual.

To be part of the study, subjects will need to be evaluated by a doctor who is an IDEAS Study dementia specialist. Subjects will also visit an IDEAS Study PET facility for a brain amyloid PET scan upon physician referral. This could be at a hospital or an outpatient center. After the amyloid PET scan, subjects complete a follow-up visit with the dementia specialist to discuss results.

Subjects participating in the IDEAS Study are also offered the opportunity to participate in additional related add-on projects. One of those projects is based out of the National Cell Repository for Alzheimer's Disease (NCRAD) and is called ANGI (Amyloid Neuroimaging and Genetics Initiative). The purpose of the ANGI study is to pair the clinical information and brain imaging (amyloid PET scan) used in IDEAS, or other related studies, with DNA obtained from a saliva sample. DNA is the genetic material in our body which is made up of a series of genes. Genes are the unit of our DNA that determine things such as eye color, hair color, and other more complex physical characteristics or traits. The information and DNA samples that are collected as part of this study will be used to help scientists identify genetic factors contributing to cognitive impairment, dementia, and other disorders. In addition, the information and DNA samples may also be used to better understand brain imaging findings. The information collected in ANGI may help scientists understand why patients respond differently to medications and treatments used to treat cognitive impairment and/or dementia. It is hoped that the research made possible by ANGI will ultimately lead to the development of new therapies that will slow or prevent cognitive impairment and dementia.

To learn more, go to: www.IDEAS-Study.org/patients ■

IDEAS
Imaging Dementia—Evidence For Amyloid Scanning

ANGI
Amyloid Neuroimaging & Genetics Initiative

Meet the newest members of our NCRAD staff

Madeline Potter

Madeline Potter, BA has been with the Department of Medical and Molecular Genetics since January of 2015 and is a newcomer to NCRAD. Madeline serves as a research coordinator and her duties include data validation, regulatory documentation, publication tracking and sample requests. She also helps complete annual chart reviews.

To reach Madeline directly, please email **mkpotter@iu.edu** or call (317)278-9546.

Kristi Wilmes

Kristi Wilmes, MS is a newcomer to NCRAD and has been with the Department of Medical and Molecular Genetics since 2015. Kristi has a Master of Science in Clinical Research Administration. Her duties include coordinating studies within NCRAD, data validation and working with study sites to ensure efficiency.

To reach Kristi directly, please email **wilmesk@iu.edu** or call (317)274-7546.

Kaci Lacy

Kaci Lacy, BS is a newcomer to the Department of Medical and Molecular Genetics. She graduated from Indiana University in 2013 with a BS in Biology. Kaci is a research coordinator and her duties include sample accessioning, preparing sample kits, and data validation.

To reach Kaci directly, please email **lacy@indiana.edu** or call (317)278-1170.

From left to right: Kelly Horner, Dr. Tatiana Foroud, Kristi Wilmes, Kelley Faber, Madeline Potter, Jan Hamer, Kaci Lacy

Research Opportunities:

4 Repeat Tauopathy Neuroimaging Initiative – Cycle 2 (4RTNI-2)

- Purpose: To identify the most reliable methods of analysis for tracking CBD, PSP and o/vPSP over time. The results from this study may be used in the future to calculate statistical power for clinical drug trials. This study will also provide information about the relative value of novel imaging techniques for diagnosis, as well as the value of imaging techniques versus testing of blood, urine and cerebrospinal fluid (CSF) biomarkers.
- Eligibility: Men and women ages 40 to 80, diagnosis of Progressive Supranuclear Palsy or Corticobasal Degeneration (CBD)
- Locations: CA
- Contact: PH: 415-476-9578 or 4RTNI2 webpage: http://memory.ucsf.edu/research/studies/4rtni2

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

Advancing Research and Treatment for Frontotemporal Lobar 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: Columbia University, University of California in Los Angeles, University of California in San Diego, University of California in San Francisco, Harvard/Massachusetts General Hospital, Johns Hopkins University, University of North Carolina, Mayo Clinic in Rochester, Mayo Clinic in Jacksonville, University of Pennsylvania, Northwestern University, University of Toronto, University of British Columbia, and Washington University
- See this website for more information: https://www.rarediseasesnetwork.org/ARTFL/index.htm

Longitudinal Evaluation of Familial Frontotemporal Dementia Subjects (LEFFTDS)

- Purpose: To model the rates of decline in clinical function of those suffering from Frontotemporal Lobar 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: Mayo Clinic, Rochester, MN, University of California, San Francisco, CA, University of Pennsylvania, Mayo Clinic, Jacksonville, FL, University of British Columbia, Washington University, Columbia University, Harvard University
- Contact:

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

  Mayo Clinic Florida
  Memory Disorder Clinic
  904-953-6523

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's disease. Please send us your ideas by email or by phone.

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

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.
https://www.nia.nih.gov/alzheimers/alzheimers-disease-research-centers

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.

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

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