

NCRAD Updates



Support by: U24AG021886

NCRAD and ADRC Partnership

- NCRAD had partnered with the ADRCs for many years to support discovery and new initiatives
 - Centralized DNA from ADRC participants to support APOE genotyping, GWAS, whole exome sequencing and whole genome sequencing
 - NCRAD and the ADRCs work together to support NIA initiatives

Alzheimer Disease Center Fluid Biomarker Initiative (ADCFB)

- **Alzheimer Disease Center Fluid Biomarker Initiative**
 - Blood-only initiative from the well characterized ADRC participants
 - DNA, RNA, plasma, serum, PBMCs
 - These samples support new research discoveries
 - All data generated from ADRC samples at NCRAD must be shared with the research community

Counts of ADCFB Subjects with Each Sample Type

| Condensed Diagnoses | DNA | PBMC | Plasma | RNA | Serum | CSF |
|--|--------------|------------|--------------|------------|------------|-----------|
| Alzheimer's disease (AD) | 349 | 102 | 349 | 86 | 89 | 0 |
| FTLD, other | 16 | 6 | 16 | 8 | 8 | 0 |
| Lewy body disease (LBD) | 15 | 3 | 15 | 3 | 3 | 0 |
| Not applicable, not cognitively impaired | 718 | 193 | 718 | 122 | 123 | 0 |
| Other* | 178 | 55 | 178 | 41 | 45 | 0 |
| N/A (don't match to NACC yet) | 902 | 253 | 902 | 227 | 231 | 22 |
| Grand Total | 2,178 | 612 | 2,178 | 487 | 499 | 22 |

***Other:** Includes anxiety disorder, bipolar disorder, Cognitive impairment due to alcohol abuse, Cognitive impairment due to medications, Cognitive impairment due to systemic disease or medical illness, Cognitive impairment for other specified reasons, Depression, Human immunodeficiency virus (HIV), Other neurologic, genetic, or infectious condition, Other psychiatric disease, Prion disease (CJD, other), Progressive supranuclear palsy (PSP), Traumatic brain injury (Tbi), Vascular brain injury or vascular dementia including stroke.

- **Full UDS dataset available at NACC, subset of data in NCRAD catalog**
- **Genetic data at NIAGADS, links available through NCRAD catalog**

New NCRAD Initiatives

- Following recent NCRAD renewal, it was clear plasma biomarkers were a key area of research
- NCRAD works with studies to ensure uniform sample collection and processing
- Next logical step was to establish the NCRAD Biomarker Assay Laboratory (NCRAD BAL)

Why establish a lab with NCRAD with a focus on core biomarkers

- NCRAD banks samples from many studies so we can have efficient/integrated process for core biomarker analysis and return of results to studies
- Studies without a biomarker focus can partner with NCRAD to include core biomarkers with minimal effort and possibly add scientific interest
- Limited focus on core biomarker assays allows for longitudinal quality monitoring and consistent delivery of results over time
 - Initial Assays: P-tau, NfL, $A\beta_{1-40}$ and $A\beta_{1-42}$
 - Next to be validated: GFAP/NfL 2-Plex assay

NCRAD Biomarker Assay Laboratory Works with Other Laboratories

- Ensure that data from different labs can be analyzed together
 - Performance characteristics of biomarker assays
 - Comparison of research results across labs and platforms
 - Standardization of research results through reference standards
 - Standardization and testing of pre-analytical conditions
 - Quality control and performance testing

NCRAD Administrative Supplements

- Establish the NCRAD biomarker assay laboratory including equipment and initial assay validation
- Provide validated assays on NCRAD banked samples including:
 - Up to 4,000 ADRC samples
 - ~2,000 ADCFB in house
 - ~2,000 to be transferred from ADRCs
 - ~2,000 Indianapolis Ibadan plasma samples

NCRAD Competitive Revision

- NCRAD will be submitting a competitive revision in the Fall of 2022
 - Include funds to support plasma assays on all samples sent by the ADRCs going forward
 - Results will be returned to the ADRCs
 - Include funds to support centralized banking and plasma assays for additional studies, particularly those enrolling diverse participants

Biomarker Assay Laboratory Website

- Website provides updates about assays available
- Includes link to request a quote or letter of support for non ADRC/UDS subjects

<https://www.ncrad.org/biospecimens-data/bal.html>

Biomarker Assay Laboratory (BAL)

For more than 30 years, NCRAD has been a key research infrastructure for NIA to support ADRD research. NCRAD's mission has grown from a DNA storage repository for genetic studies to a specialized research repository that supports a broad range of biospecimens and focuses on the aspects of sample collection, storage, distribution, and processing. NCRAD's success is driven by the use of standard operating procedures to ensure uniformity and to minimizing the impact of preanalytical variables on downstream sample analyses.

With the establishment of the Biomarker Assay Laboratory (BAL), NCRAD has expanded our services to include processing of well-established fluid-based biomarkers and provide more support to research studies. The goal is to ensure standardized processing and reliable research biomarker results. This approach allows for longitudinal quality monitoring and consistent delivery of results over time, as well as the opportunity for cross-laboratory comparability studies.

Plasma assays currently* available in the BAL:

- P-tau 181 NFL
- NFL
- AB40
- AB42

*GFAP/NFL 2-Flex assay validation to start early 2022

All assays processed at the NCRAD Biomarker Assay Laboratory are research-based results only. For investigators interested in CLIA results, requests can be facilitated by NCRAD, in collaboration with C2N.

To request a quote and/or letter of support for the above assays through NCRAD, please complete the following form.

BAL Investigators



Jeff Dage,
Ph.D.

Jeff Dage, Ph.D., joined Indiana University School of Medicine from Eli Lilly & Co in August of 2021 as a Senior Research Professor of Neurology and Primary Member, Stark Neurosciences Research Institute. He is a NCRAD co-investigator and is the Scientific Director of the Biomarker Assay Laboratory.



Kristen
Russ, Ph.D.

Kristen Russ, Ph.D., has been with Indiana University School of Medicine since August 2018. In 2021, she joined NCRAD as an Assistant Research Professor of Medical and Molecular Genetics. She is a NCRAD co-investigator and the Biomarker Assay Laboratory Director.

Uniform Sample Collection

To ensure the highest quality and most consistent assay results, NCRAD recommends standard uniform collection of biospecimens as outlined by the Standardization of Alzheimer's Blood Biomarkers (SABB) working group.

Verberk, I. M., Misdorp, E. O., Koelwijh, J., Ball, A. J., Blennow, K., Dage, J. L., ... & Teunissen, C. E. Characterization of pre-analytical sample handling effects on a panel of Alzheimer's disease related blood based biomarkers. Results from the Standardization of Alzheimer's Blood Biomarkers (SABB) working group. *Alzheimer's & dementia: the journal of the Alzheimer's Association*.

NCRAD recommends the use of polypropylene for all collection and processing materials.

BAL Schematics - CSF
BAL Schematics - Serum
BAL Schematics - Plasma, Buffy Coat

Additional Resources

Collection of Biospecimens
BAL Schematics - CSF
BAL Schematics - Serum
BAL Schematics - Plasma, Buffy Coat
Overview of Blood-based Biomarkers Available

Questions/Comments

Email: alzstudy@iu.edu
Phone: 800-526-2839

Local ADRC Plasma

- ADRCs that have locally banked plasma on UDS subjects not at NCRAD and are interested in having biomarkers run at the NCRAD BAL.....
 - Contact: Kaci Lacy (lacy@iu.edu) to start the process