

# **ADRC**

# **Biofluid Biomarker Best Practices Workgroup**

## **Co-Leads:**

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# ADRC

## Biofluid Biomarker Best Practices Workgroup

- Standardization:
  - Method
  - Process
  - Analysis
- Operational best practices:
  - Comparability
  - Pooling of results
  - Clarity on performance
- = Global progress

### BBBP Workgroup Charter:

Goals for the 2024 update:

1. Develop updated best practice guidelines for collecting, preparing, and storing blood and cerebrospinal fluid (CSF) samples specific to AD biomarkers.

2. Create a standardized guideline for assay procedures (e.g. sample handling), alongside methods for quality control.

These include conducting duplicate tests and calculating coefficient of variation (CV), as well as validation and verification processes.

(Focus: Blood and CSF Protocols)

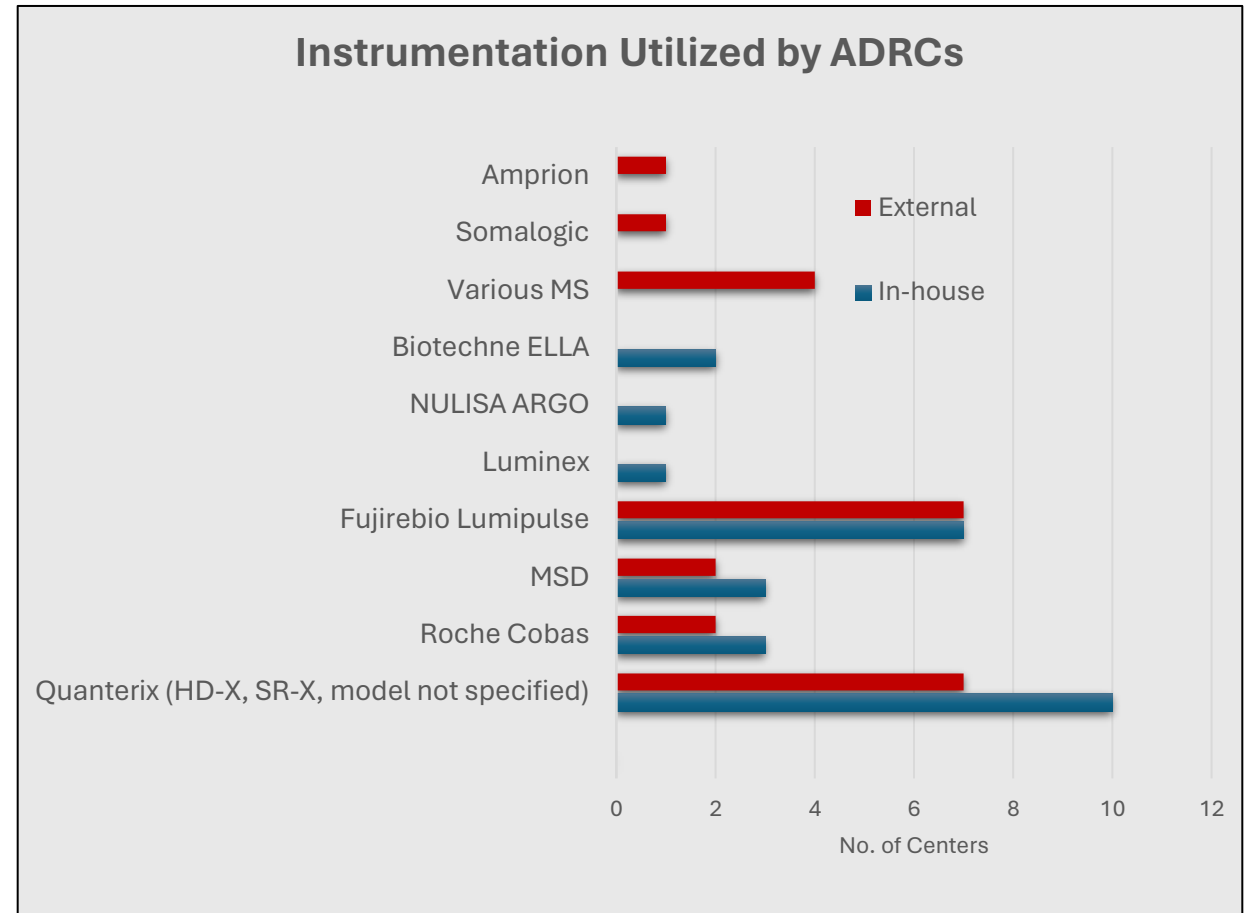
# ADRC Survey Results- Spring 2024

- Survey responses received

- 31 of 37 ADRCs responded
- 14 centers submitted SOPs overall
- 14 centers submitted blood/plasma SOPs
- +8 centers submitted CSF-specific SOPs

- Instrumentation:

- Discovery and characterization assay instrumentation:
  - e.g., Somalogic high plex and NULISA
- Validation Instruments:
  - MS/IP-MS, MSD
- Clinical instruments:
  - Roche COBAS



\*Many of the assays run on these instruments at ADRCs have manufacturer-derived standardized protocols.

# ADRC Survey Results- April 2024

## Internal Assays (Performed “In house”)

Biomarker	Frequency	% Centers
Ab40	15	48.40%
Ab42	15	48.40%
GFAP	13	41.90%
NfL	13	41.90%
NRGN	13	41.90%
pT181-Tau	13	41.90%
pS217-Tau	14	45.20%
pT205-Tau	1	3.20%
pT231-Tau	10	32.30%
TotalTau	6	19.40%
BD-Tau	1	3.20%
MTBR-Tau	1	3.20%
sTREM2	1	3.20%
Secernin	1	3.20%
UCHL1	1	3.20%
Vilip1	1	3.20%

## External Assays

Biomarker	Frequency	% Centers
Ab40	10	32.30%
Ab42	10	32.30%
GFAP	6	19.20%
NfL	7	22.40%
NRGN	1	3.20%
pT181-Tau	4	12.80%
pS217-Tau	6	19.20%
pT205-Tau	1	3.20%
pT231-Tau	6	19.20%
TotalTau	6	19.20%
BD-Tau	1	3.20%
MTBR-Tau	1	3.20%
sTREM2	3	9.60%
Secernin	1	3.20%
UCHL1	1	3.20%
Vilip1	2	6.40%
SNAP25	2	6.40%
SNCA	1	3.20%
pSer129-SNCA	1	3.20%
SNCB	1	3.20%
YKL40	2	6.40%
pS202-Tau	1	3.20%
pS212-Tau	1	3.20%
pNfH	1	3.20%
NfH	1	3.20%
APOE	1	3.20%
Cytokines	1	3.20%
SAA	1	3.20%
NPTX2	1	3.20%

ATN Most Common

Expansion of novel Tau targets

Synaptic biomarkers

Inflammation biomarkers

**Vascular  
biomarkers???**

# Novel Biomarkers vs. Standardization

What should be standardized at this time?

- Novel Tau targets (Brain-derived Tau, MTBR- Tau and N-terminal fragments)
- Intensely studied but not yet commonplace...unlike pS217-Tau (2-3 years)  
Other P-Tau (e.g., pThr205) and Tau binding proteins

Increased interest in Synaptic biomarkers for loss and change (NRGN, SNCB, other)

Neuroinflammation biomarkers (sTREM2, cytokines, so many others!!)

Technology buildouts and performance validation takes 2-5 years

Antibody discovery, assay derivation and stabilization takes time

More cross-assay, cross-platform round-robin studies needed when appropriate

## Criteria discussed by the Workgroup:

1. **Weight of evidence: At least 5-10 large cohort studies assessing the target, multiple platforms**
2. **Assay QC well qualified and transparent**
3. **Clinical ranges are understood (what should the results look like?)**
4. **Used by multiple ADRCs and in different cohorts**

# Collection and Preanalytical Processing

## Specimen processing

- Standardized centrifugation
- Consistent and QC tested materials for biofluids
- Overnight fasting - assay dependent SOPs only (Should reflect real world sampling/context of use)
- No major suggested changes in collection SOPs at this time.

## Storage/Integrity/Security

Standardized ATN assays including pS217-Tau are stable at 4 C for short periods

Minimize freeze thaws (<3x)

Redundancy is recommended (split samples into multiple locations to avoid loss)

Freezer alarms/temp records: Routinely monitored by remote notification and data download

## Thaw and Run

Monitor/Control Temp and establish performance limits

Standardize operational bench time to avoid temporal variance between runs

Ex: Temperature dependent changes in Tau signal (et al., 2023)

\*Collected information from published studies, centers, and KOLs  
->>being analyzed to formulate recommendations.

# Next steps:

- Collect feedback on the initial plan presented today
- Further formulate the recommendations for presentation at the AAIC in July 2024.
- Update 2014 guidelines:
  - “Formulate a detailed guide to standardize assay procedures for AD biomarkers, focusing on elevating the consistency and accuracy of test results.”
- Draft a report summarizing the findings and make available for broad review. (September 2024)
- Finalize documents and resources and upload for public use.

# Workgroups are soliciting feedback!!

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