What's happening in the ADRC Neuropathology Cores

ADRC Fall Meeting

October 16 2024

ADRC Neuropathology Steering Committee
Chair- Brittany Dugger, PhD University of California Davis ADRC
Member- Alifiya Kapasi, PhD Rush University ADRC
Member- Thomas Wisniewski, NYU Langone's ADRC

We Can Diagnose It!

IMAGE PRODUCTION CO-ORDINATING COMMITTEE

Neuropathology Core Steering Committee updates for 2024-2025

Thomas M. Wisniewski, MD
Farewell!

Alifiya Kapasi, PhD
Incoming chair!

Margaret Flanagan, MD
Welcome!!

A BIG THANK YOU TO ALL WHO APPLIED!!!!!!

New this year!!!!   Early Career representatives!!!

- Thank you, REC core, for your input!!

- **Eligible candidates included:**
- Post-docs, PhD students, early career faculty, assistant professors, associate professors, and REC scholars who are affiliated with a Neuropathology Core at an ADRC. Self-nominations are welcome.
- Not current/past R01 grantee; K, F, and other mentoring/career development grants are okay.
- Not a member of an ADRC represented by the elected committee members

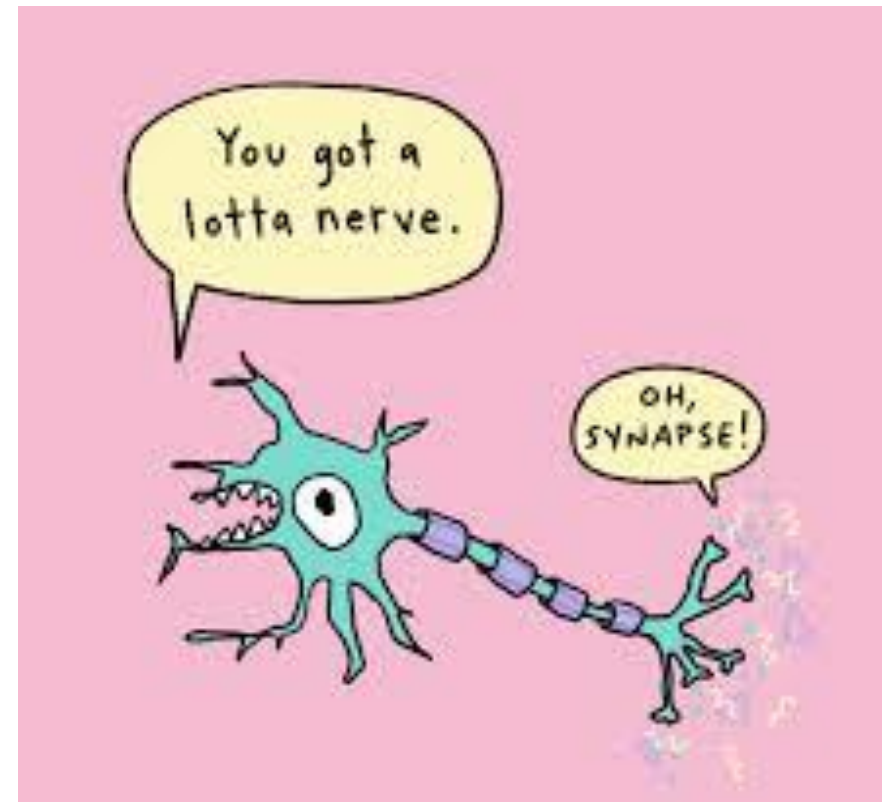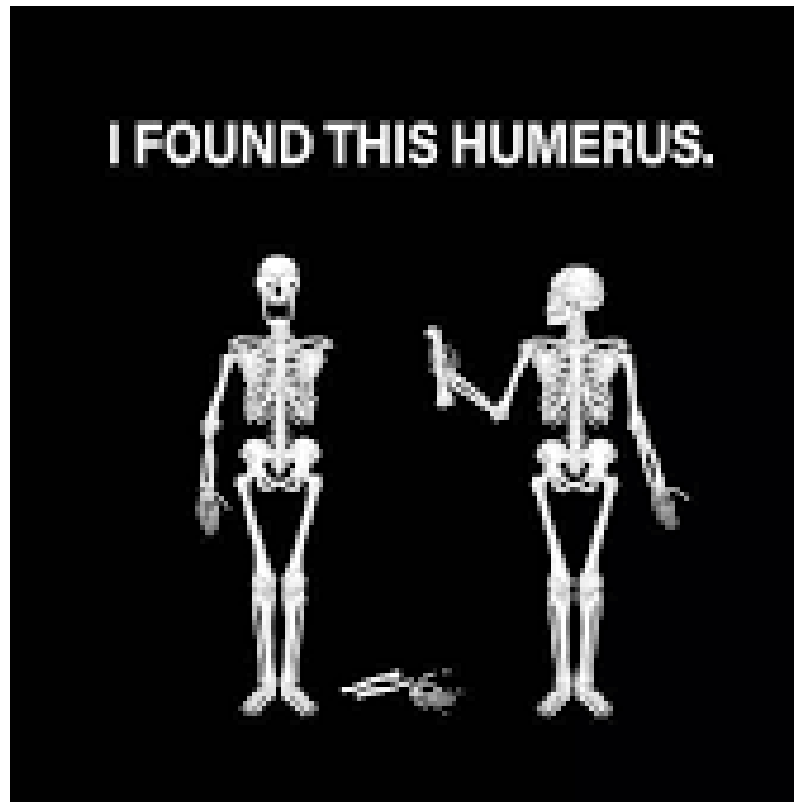# A BIG THANK YOU TO ALL WHO APPLIED!!!!!!

Daniel Ohm, PhD
University of Pennsylvania ADRC

Caitlin Latimer, MD, PhD
University of Washington ADRC

What else is going on in the fabulous ADRC Neuropathology Core realm?

ADRC CPC National Video Library Workgroup: Purpose and Progress

Margaret Flanagan, MD

UT San Antonio

To develop a CPC library as an educational tool (enhance our pipeline of a diverse workforce in AD/ADRD)

Meetings began January 2024 – discussion of opportunities and challenges

HIPAA/privacy/confidentiality – discussing IRB perspectives

Differences in format across ADRCs

CME?

Access to recordings – who and how

Could help messaging encouraging brain donation

Completed "scrubbing"/deidentification trial successfully using South Texas ADRC recorded CPC in Summer 2024

UKY Pete Nelson: recording & trial "scrubbing" on 9/12/2024 CPC

UCI Elizabeth Head: recording and trial "scrubbing" on 09/02/24 CPC

Met w/NACC to discuss goals of CPC library

Next we are meeting to discuss ethical/legal aspects of CPC library w/experts

Facilitated by Nina Silverberg

Jalayne Arias & Emily Largent attending

Crystal Glover (Rush) and Caitlyn Latimer (UW): institution specific feedback on questions

Slide courtesy of/adapted from Drs. Margaret Flanagan/Elizabeth Head

32 ADRCs & 63 total responses…

- **Purpose of CPCs?**
  - Training 50%
  - Case Review 43%
  - Other: consensus reviews, research ideas, community engagement

- **CPC Structure**
  - Duration: 71% 1 hour
  - Frequency: 47% monthly
  - Cases Discussed: 1-2 (71%)

- **Common Data Reviewed:** Clinical, MRI, Neuropsychology Outcomes, Biomarkers (CSF/plasma), Amyloid PET, Tau PET, Neuropathology findings

- **65% of CPCs are not recorded (HIPAA/privacy concerns)**

- **40% are willing to contribute to a video library**
  - However, some concerns were raised about confidentiality & informal discussions

- **CPC Library Development**
  - 94% Support forming working group to set guidelines ☺
  - 76% interested in attending CPCs from other ADRCs
  - 38% prefer limited access via login for select persons or ADRC groups

ADRC digital pathology working group journal club

Our mission: To facilitate the review and critical analysis of recent scientific publications and promote collaboration among researchers interested in integrating digital tools for pathology

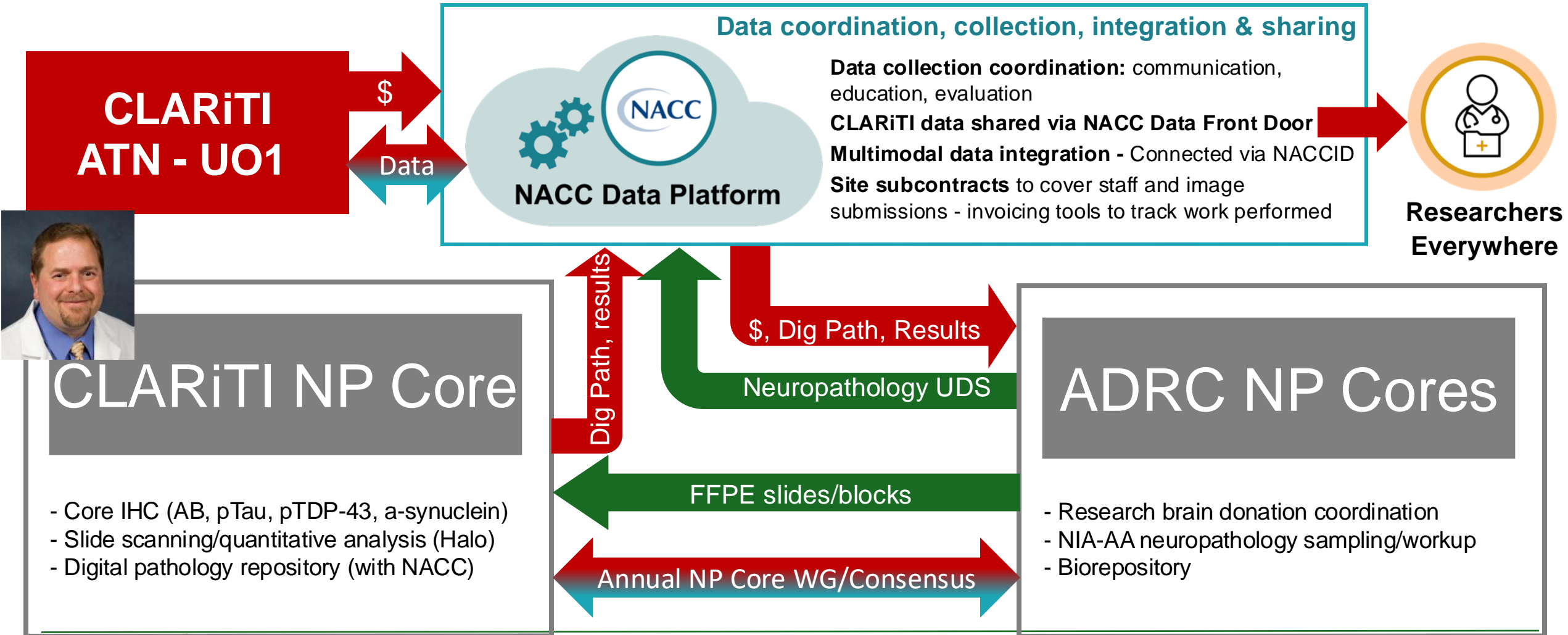Returning this fall as a bimonthly seminar series

We are actively seeking speakers, please email Kurt.Farrell@mssm.edu if you are interested, times are flexible!

Check us out on YouTube, scan the QR code!

Slide courtesy of/adapted from Dr. Kurt Farrell

Neuropathology Core Overview: CLARiTI
(CLarity in ADRD Research Through Imaging)

CLARiTI ATN - UO1

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Data

NACC Data Platform

Data coordination, collection, integration & sharing

Data collection coordination: communication, education, evaluation

CLARiTI data shared via NACC Data Front Door

Multimodal data integration - Connected via NACCID

Site subcontracts to cover staff and image submissions - invoicing tools to track work performed

Researchers Everywhere

Dig Path, results

$, Dig Path, Results

Neuropathology UDS

CLARiTI NP Core

- Core IHC (AB, pTau, pTDP-43, a-synuclein)
- Slide scanning/quantitative analysis (Halo)
- Digital pathology repository (with NACC)

FFPE slides/blocks

Annual NP Core WG/Consensus

ADRC NP Cores

- Research brain donation coordination
- NIA-AA neuropathology sampling/workup
- Biorepository

Slide courtesy of/adapted from Dr. Sterling Johnson

Connecting Machine Readable Digital Human AD/ADRD
Neuropathological Library Platforms for Advanced Analytics (U24
Clinical Trial Not Allowed)

RFA-NS-22-062

Brain Digital Slide Archive: An Open Source Platform for Data Sharing and Analysis of Digital Pathology (U24NS133949)

- **Dr. David Gutman, Emory**
- **Dr. Thomas Pearce, Pittsburgh**
- **Dr. Brittany Dugger, UC-Davis**
- **Dr. Lee Cooper, Northwestern**

Focus on Computer Resources

The Digital Slide Archive: A Software Platform for Management, Integration, and Analysis of Histology for Cancer Research

David A. Gutman[1,2,3], Mohammed Khalilia[1], Sanghoon Lee[1], Michael Nalisnik[2], Zach Mullen[4], Jonathan Beezley[4], Deepak R. Chittajallu[4], David Manthey[4], and Lee A.D. Cooper[2,3,5]

Cancer Research

Federated Digital Pathology Platform for AD/ADRD Research and Diagnostics (U24NS133945)

- **Dr. Pete Nelson, Kentucky**
- **Dr. Cody Bumgardner, Kentucky**
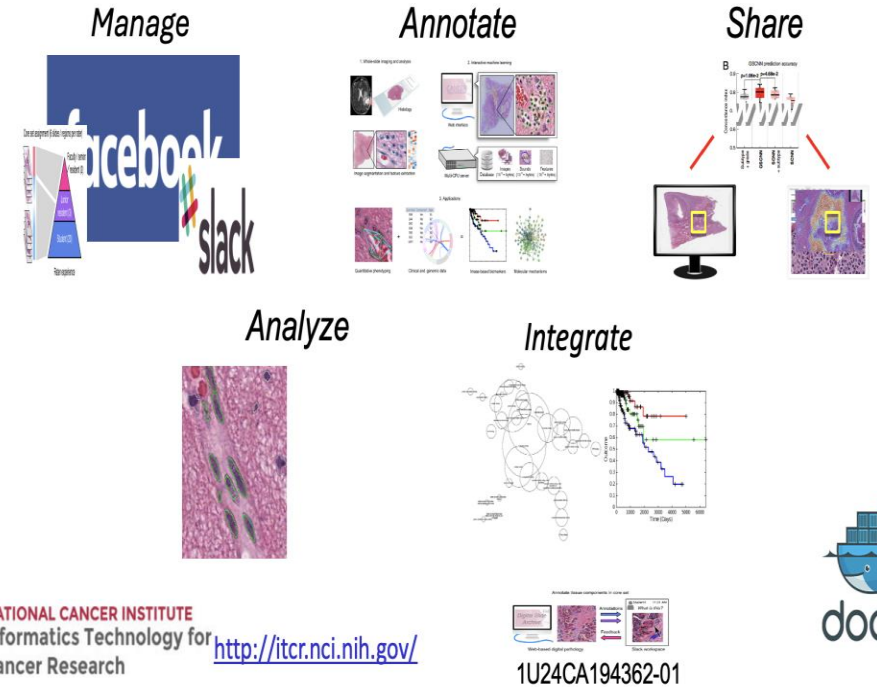- **Dr. Maggie Flanagan, UTHSA**

Brain Digital Slide Archive (Adapt existing mechanisms for federated model of WSI storage & interaction tailored for AD/ADRD research and diagnostics)

Slide courtesy of/adapted from Dr. Maggie Flanagan

Enhance & leverage DSA infrastructure for 'BDSA'

- Supports multiple slide-scanning vendors & file types

- Provides application programming interfaces (APIs) in vendor agnostic manner for:
  - accessing image data
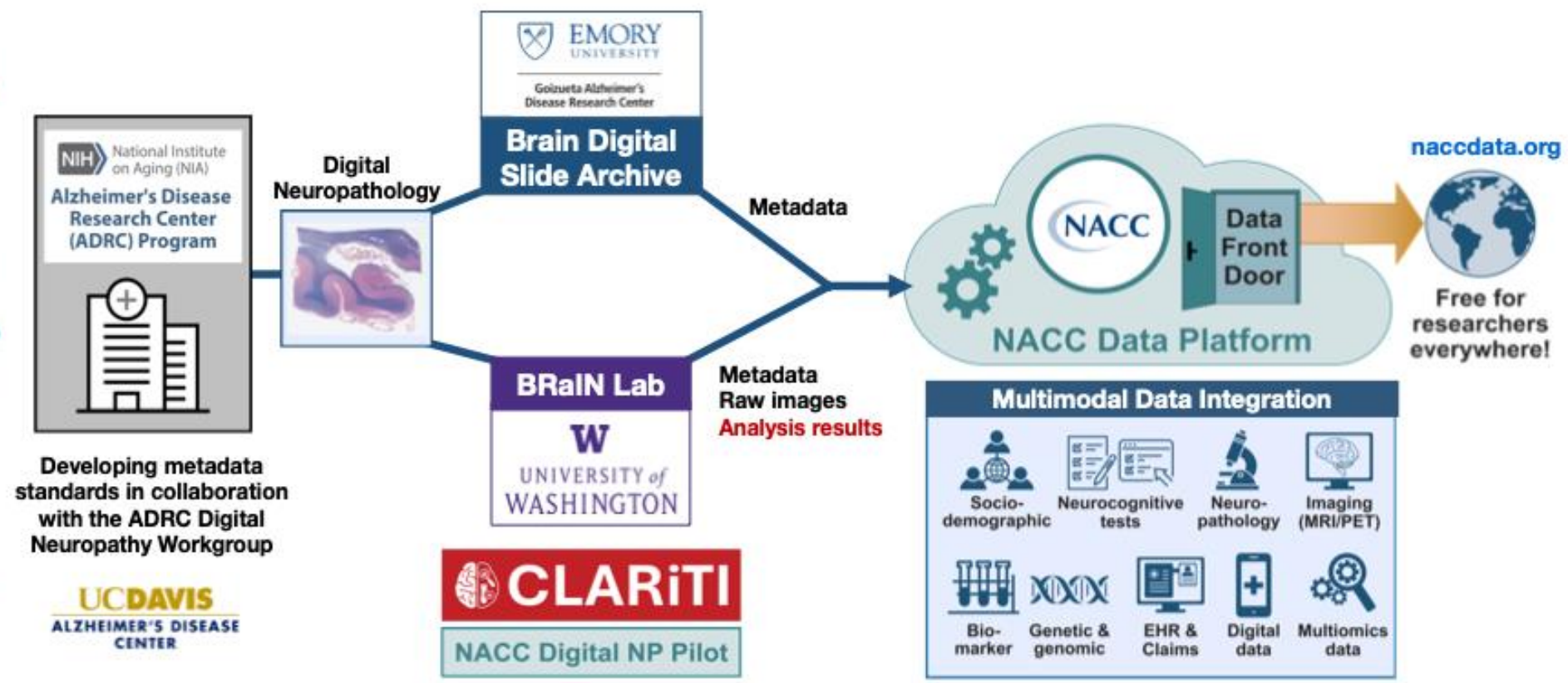 - creating/querying annotations
  - deploying image analysis

Adapt existing DSA mechanisms for our federated model of WSI storage & interaction

- *tailor **for AD/ADRD research & diagnostics***

NACC Supplement from NIA so support development of standards and pipelines to support and promote digital pathology resources, sharing, and research

Slide courtesy of/adapted from Dr. Sarah Biber

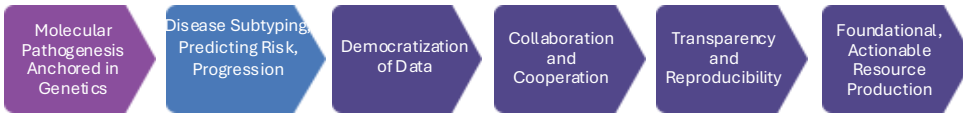# Digital Neuropathology Metadata Standardization

NACC, Brain Digital Slide Archive, CLARiTI, and the ADRC Neuropathology Core Steering Committee are collaborating on creating a standardized list of metadata associated with digital neuropathology images.

Goals:

- Interoperability between various digital neuropathology efforts across the ADRC program (e.g., CLARiTI, Brain Digital Slide Archive, Digital Neuropathology Pilot)

- Produce a minimum viable metadata set to be tied to digital neuropathology image data that will be shared with researchers worldwide via the NACC Data Platform

Stay tuned! We will be sharing this metadata list with NP Core Leaders for feedback.

Slide courtesy of/adapted from Brittany Hale, NACC

National Institutes of Health
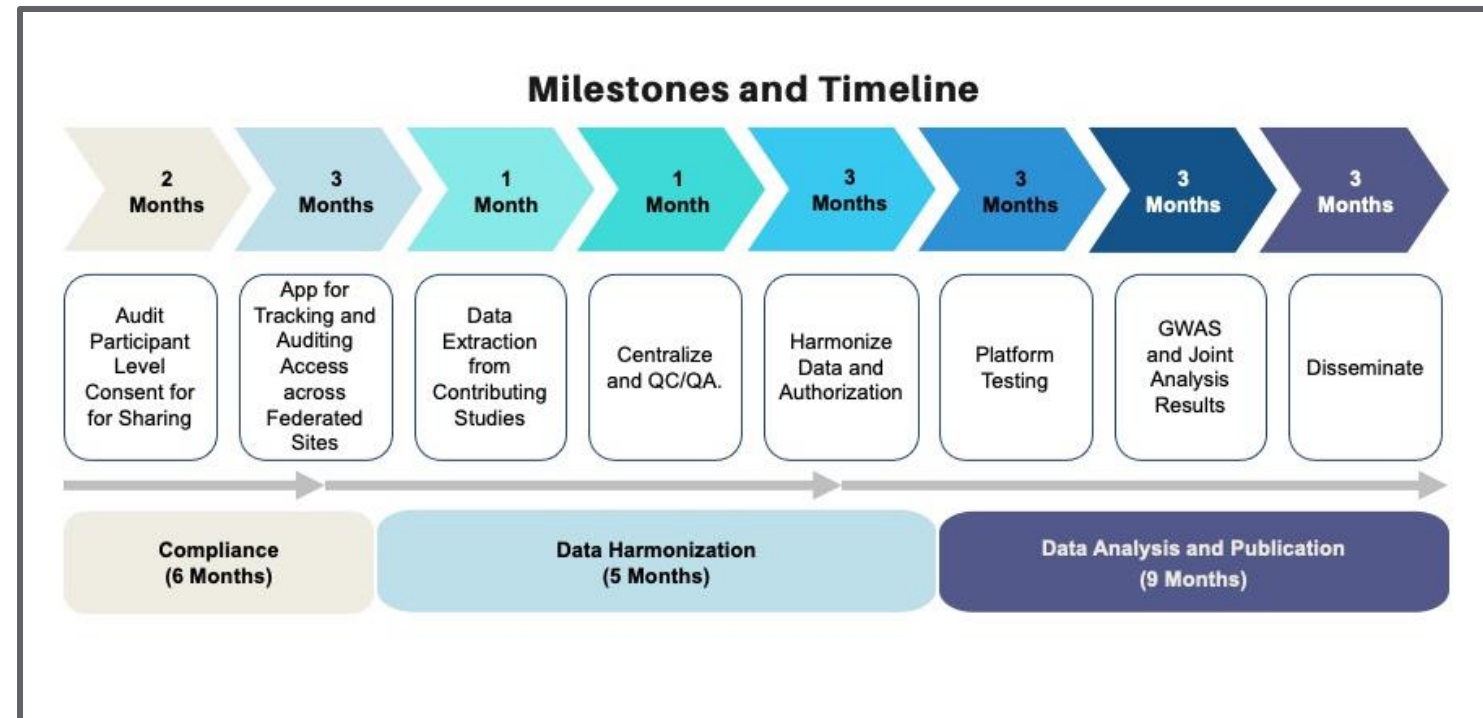Center for Alzheimer's and Related Dementias

Preparation for new data types like digital pathology as well as CARD's upcoming connection to the Clinical Center will be streamlined

Digital Pathology Infrastructure

- Verily ViewPoint WorkBench
- 15 partners across academia and non-profit for 300 + CDEs & data
- Staged for success
  - Tabular data
  - Genetics + Spatial
  - Algorithm "bake off"
  - Harmonized reprocessing

Foundational CDEs being used at NACC and ADRC for interoperability

Milestones and Timeline

2 Months	3 Months	1 Month	1 Month	3 Months	3 Months	3 Months	3 Months
Audit Participant Level Consent for for Sharing	App for Tracking and Auditing Access across Federated Sites	Data Extraction from Contributing Studies	Centralize and QC/QA.	Harmonize Data and Authorization	Platform Testing	GWAS and Joint Analysis Results	Disseminate

Compliance (6 Months)	Data Harmonization (5 Months)	Data Analysis and Publication (9 Months)

Email Mike Nalls mike@datatecnica.com if interested!

Special Session on Brain Donation
(hosted by ORE Core & Neuropathology Core)

Wednesday, October 16

9:00 AM - 9:05 AM		*5min*
Introduction	Dorothy Farrar-Edwards, PhD Wisconsin ADRC	Crystal M. Glover, PhD Rush University ADRC
9:05 AM - 10:00 AM		*55min*
Panel Discussion	Moderator: Crystal M. Glover, PhD Rush University ADRC	Katherine Brandt, MM Massachusetts ADRC
	Darby Morhardt, PhD Northwestern ADRC	Tish Hevel Brain Donor Project
	Arline Faustin, MD NYU ADRC	Nancy Cherico, PhD Boston University ADRC Participant Perspective

Collaboration between the Neuropathology and ORE Core steering committees

Thank you panelists and moderators!!!

	N	frequency (out of 8,188)
Asian	74	1%
Hispanic/Latino	290	4%
Black	311	4%

Top centers

Center name	Hispanic/Latino decedents
UCSD	58
USC	42
UC-Davis	30
Columbia University	25
UCSF	23

Center name	Black decedents
Rush University	51
UC-Davis	33
Washington University, St. Louis	30
Emory University	23
Johns Hopkins University	18
Northwestern University	18

Center name	Asian decedents
UCSF	12
USC	8
UC-Davis	7
Massachusetts ADRC	6
UC-Irvine	6

of participants who have autopsy data available by center in NACC as of September 2024 data freeze

Center name	American Indian/Alaskan Native decedents
UC-Irvine	2
UCSF	2
University of Kansas	1
Oregon Health & Science University	1
UCSD	1
University of Texas, Southwestern	1
Total	**8**

Center Name	Pacific Islander decedents
UCSF	3
USC	2
Northwestern University	1
Total	**6**

Neuropathology Core Session

10:20 AM - 10:35 AM _15min_

What's Happening in the ADRC Neuropathology Core

Brittany Dugger, PhD
UC Davis ADRC

10:35 AM - 10:50 AM _15min_

Brain Donation Survey Results

Alifiya Kapasi, PhD
Rush University Medical Center

10:50 AM - 11:00 AM _10min_

Culture-Centric Narrative as a Tool for Messaging about Brain Donation

Jennifer Lingler, PhD, RN
University of Pittsburgh ADRC

11:00 AM - 11:10 AM _10min_

Enrollment into Brain Donation in a Diverse Cohort of Oldest Old - Lessons Learned from the Life After 90 Study

Rachel Whitmer, PhD
UC Davis ADRC

11:10 AM - 11:20 AM _10min_

Q&A