



# **New Investigator Award Program Past Awardees**

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**Yuriko Katsumata, PhD & Corey McMillan, PhD**

# 2022 New Investigator Award Winner

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**Yuriko Katsumata, PhD**

Assistant Professor, University of  
Kentucky

University of Kentucky ADRC



# Application Strategies for NIAP

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**Presented by: Yuriko Katsumata (University of Kentucky)**

# Personal Introduction

2013

PhD program  
Epidemiology and Biostatistics  
University of Kentucky



Dr. David Fardo  
Statistical Geneticist

2018

Research Assistant Professor  
Biostatistics  
University of Kentucky

 Sanders-Brown  
Center on Aging

 University of  
**Kentucky**  
*College of Public Health*

2022

NACC New  
Investigator  
Award

2024

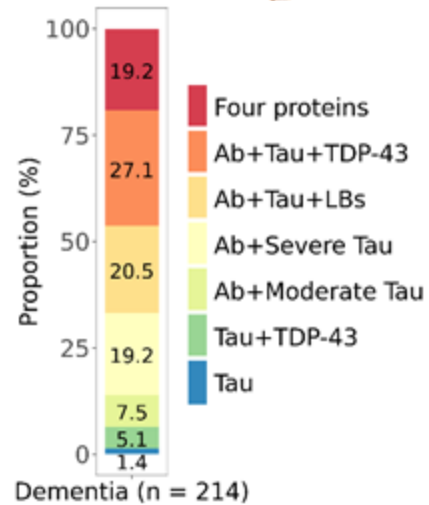
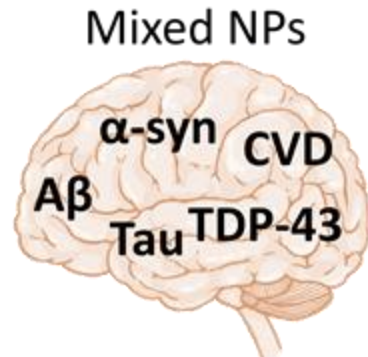
Research Associate Professor  
Biostatistics  
University of Kentucky

# New Investigator Award Project

2022

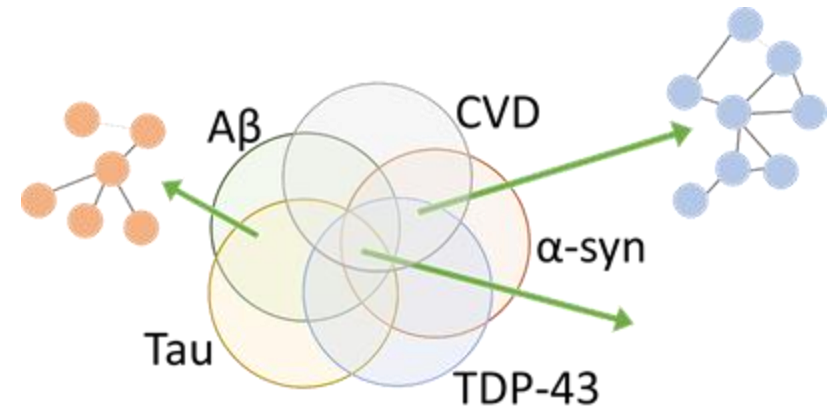
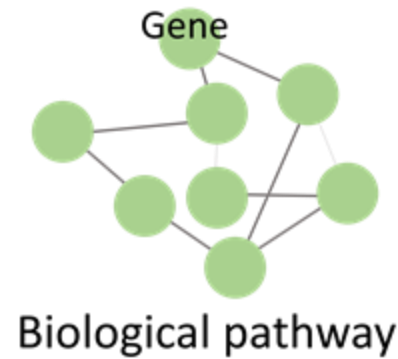
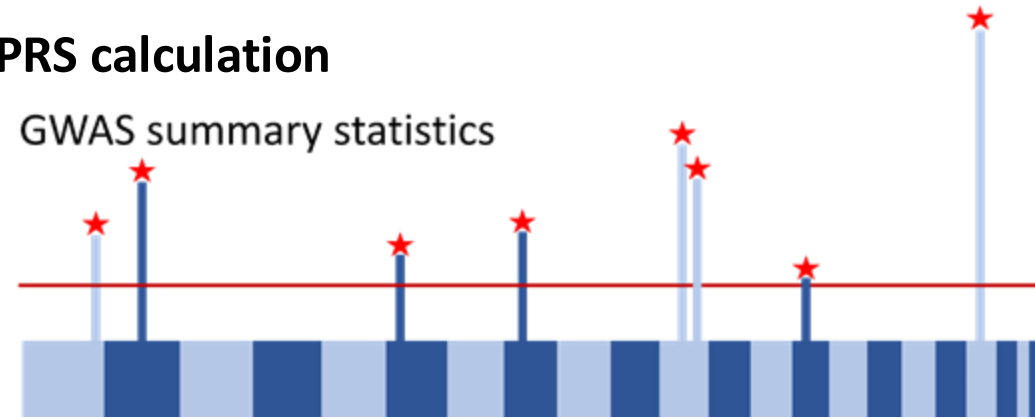
NACC New Investigator Award

## Pathway-specific polygenic risk scores on mixed neuropathologies



### PRS calculation

GWAS summary statistics



# New Investigator Award project

Received: 7 July 2023 | Revised: 28 November 2023 | Accepted: 30 November 2023

DOI: 10.1002/alz.13741

RESEARCH ARTICLE

Alzheimer's & Dementia®  
THE JOURNAL OF THE ALZHEIMER'S ASSOCIATION



## Genetic associations with dementia-related proteinopathy: Application of item response theory

Yuriko Katsumata<sup>1,2</sup> | David W. Fardo<sup>1,2</sup> | Lincoln M. P. Shade<sup>1</sup> | Xian Wu<sup>1,2</sup> |  
Shama D. Karanth<sup>3,4</sup> | Timothy J. Hohman<sup>5</sup> | Julie A. Schneider<sup>6,7,8</sup> |  
David A. Bennett<sup>6,7,8</sup> | Jose M. Farfel<sup>7,8</sup> | Kathryn Gauthreaux<sup>9</sup> | Charles Mock<sup>9</sup> |  
Walter A. Kukull<sup>9</sup> | Erin L. Abner<sup>2,10</sup> | Peter T. Nelson<sup>2,11</sup> | The Alzheimer's Disease  
Neuroimaging Initiative<sup>12</sup> | The National Alzheimer's Coordinating Center

ALZHEIMER'S ASSOCIATION

AAIC >24

## Proteinopathies and Biological Pathway-based Alzheimer's Disease Polygenic Risk Score

Yuriko Katsumata<sup>1,4</sup>, Xian Wu<sup>1,4</sup>, Khine Zin Aung<sup>1,4</sup>, Inori Tsuchiya<sup>1,4</sup>, Lincoln M. Shade<sup>1,4</sup>, Shama Karanth<sup>5,6</sup>, Kathryn Gauthreaux<sup>7</sup>, Charles Mock<sup>7</sup>,  
Walter A. Kukull<sup>7</sup>, Erin L. Abner<sup>2,4</sup>, Peter T. Nelson<sup>3,4</sup>, David W. Fardo<sup>1,4</sup>

*1* Department of Biostatistics, *2* Department of Epidemiology and Environmental Health, *3* Department of Pathology, *4* Sanders-Brown Center on Aging, University of Kentucky, Lexington, KY  
*5* Department of Surgery, *6* UF Health Cancer Center, University of Florida, FL, *7* National Alzheimer's Coordinating Center, Department of Epidemiology, University of Washington, WA

# Application Experience and Strategy

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- Specific Aims
  - What is my interest?
  - What are knowledge gaps?
- Approach
  - To fill the knowledge gaps, what should I do and what can I do?

# Application Experience and Strategy

- Specific Aims

- What is my interest?

- **Mixed neuropathologies** and **genetics**

- What are **knowledge gaps**?

- What we know and what we don't know?

- Pure Alzheimer's disease is not common

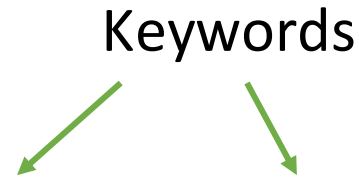
- There is no optimal classification criteria for mixed neuropathologies

- Genetic risks of mixed neuropathologies are unknown

- Diverse biological pathways may be differentially responsible for mixed neuropathologies

Spec  
Aim1

Spec Aim2 and  
3





# Application Experience and Strategy

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- Approach
  - To fill the knowledge gaps, what should I do and what can I do?
    - How to define mixed neuropathologies

# Application Experience and Strategy

- Approach

- To fill the knowledge gaps, what should I do and what can I do?
  - How to define mixed neuropathologies

Neuropathology	NACC variable	0	1	2	3
A score	NPTHAL	Phase 0	Phase 1/2	Phase 3	Phase 4/5
B score	NAC				Stage 5/6
C score	NAC				Frequent
TDP-43 in amygdala	NPT				
TDP-43 in limbic	NPT				
TDP-43 in Neocortex	NPTDPE	No	Yes		
Lewy bodies	NACCLEWY	No	Others	Neocortex	
HS	NPHIPSCL	No	Yes		

**# of combinations of NPs**

**3,072 ways**

# Application Experience and Strategy

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- Approach

- To fill the knowledge gaps, what should I do and what can I do?
  - How to define mixed neuropathologies

Describe



- Dimensionality reduction
- # of dimensions

# Application Experience and Strategy

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- Approach

- To fill the knowledge gaps, what should I do and what can I do?
  - How to define mixed neuropathologies

Describe {

- Dimensionality reduction
- # of dimensions

1. We will apply a dimensionality reduction method...

# Application Experience and Strategy

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- Approach

- To fill the knowledge gaps, what should I do and what can I do?
  - How to define mixed neuropathologies

Describe {

- Dimensionality reduction
- # of dimensions

1. We will apply a dimensionality reduction method...
2. We will apply the **item response theory** which is a dimensionality reduction method...

# Application Experience and Strategy

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- Approach

- To fill the knowledge gaps, what should I do and what can I do?
  - How to define mixed neuropathologies

Describe {

- Dimensionality reduction
- # of dimensions

1. We will apply a dimensionality reduction method...
2. We will apply the **item response theory** which is a dimensionality reduction method...
3. We will apply a **generalized partial credit model (GPCM)** within the **item response theory** framework which is a dimensionality reduction method...

# Application Experience and Strategy

- Approach

- To fill the knowledge gaps, what should I do and what can I do?
  - How to define mixed neuropathologies

Describe {

- Dimensionality reduction
- # of dimensions

1. We will apply a dimensionality reduction method...
2. We will apply the **item response theory** which is a dimensionality reduction method...
3. We will apply a **generalized partial credit model (GPCM)** within the **item response theory** framework which is a dimensionality reduction method...
4. We will apply a **generalized partial credit model (GPCM)** within the **item response theory** framework which is a dimensionality reduction method...  
The GPCM will be run with the **“mirt” R package**...

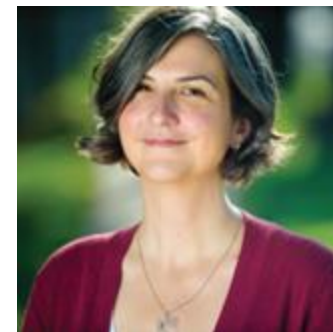
# Mentorship and Support



Dr. David Fardo  
Statistical Geneticist



Dr. Peter Nelson  
Neuropathologist



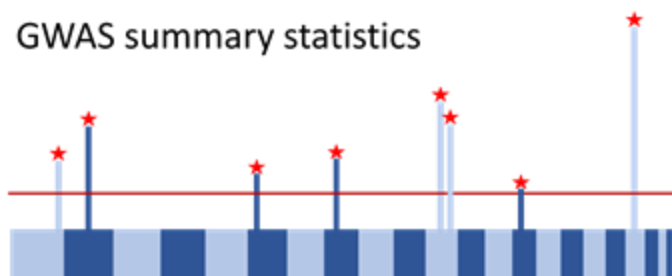
Dr. Erin Abner  
Epidemiologist

Polygenic risk score

Mixed neuropathology

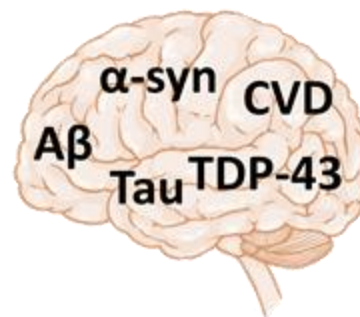
Statistical Modeling

GWAS summary statistics

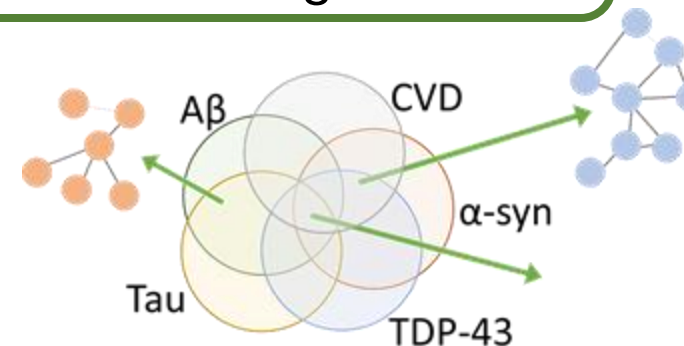


+

Mixed NPs



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# Career Impact

2024

Research Associate Professor  
Biostatistics  
University of Kentucky

Mentee



Mentor



Xian Wu, PhD #

University of Kentucky ADRC



Rather than looking at how just one factor influences Alzheimer's disease onset, Wu wants to look at how both genetic and environmental factors, like a particular mutation in a gene or exposure to smoking, interact in the context of Alzheimer's. In particular, she will look at this genetic-environmental overlap in late-onset Alzheimer's disease, during midlife and later life, and across ethnracial groups.

<https://naccdata.org/nacc-productivity/2024-new-investigator-award-winners>

# Advice for Prospective Applicants

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- Have multiple mentors with different expertise
  - Sign up for the NIAP Mentorship Program
  - Reach out to other mentors
- Generate an attractive specific aim page
- Write detailed approach
- Do not procrastinate
  - Polish your proposal again and again
  - Get suggestions and comments from as many people as possible

# Acknowledgment



THE NIA ALZHEIMER'S DISEASE RESEARCH CENTERS PROGRAM  
**National Alzheimer's Coordinating Center**

 Sanders-Brown  
Center on Aging

PI & Director



Dr. Linda Van Eldik

Mentors



Dr. David Fardo



Dr. Peter Nelson



Dr. Erin Abner

**Thank you!**





# Connect with me!

**Yuriko Katsumata, PhD**

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[katsumata.yuriko@uky.edu](mailto:katsumata.yuriko@uky.edu)