Dr. Randall J. Bateman – Disclosure

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NIH R01AG053267 (DIAN-TU NexGen)
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The Tracy Family Stable Isotope Labeling Quantitation (SILQ) Center donors Richard Frimel, David & Amy Payne, John & Linda Tracy, Pat and Jane Tracy, Tom & Catherine Tracy, Robert Willman.

DIAN-TU Pharma Consortium: Active: Biogen, Eisai, Eli Lilly & Co., Janssen, Roche/Genentech. *Previous: AbbVie, Amgen, AstraZeneca, Forum, Mithridion, Novartis, Pfizer, Sanofi, United Neuroscience*

DIAN-TU Trial Companies: Eli Lilly and Co., Roche, Janssen, Eisai, Avid Radiopharmaceuticals, Cerveau Technologies

Editorial Board: Alzheimer's and Dementia, Alzheimer's Research and Therapy, The Journal of Prevention of Alzheimer's Disease

Consulting Relationships (12 months): Roche Gantenerumab Global Advisory Board (unpaid), Biogen AD Franchise Scientific Committee (unpaid)

Companies:

- Dr. Randall J. Bateman co-founded C2N Diagnostics and receives income from C2N Diagnostics for serving on the scientific advisory board. Washington University has equity ownership interest in C2N Diagnostics.
  - Dr. Bateman is an inventor of the stable isotope labeling kinetics, blood plasma assay, methods of diagnosing AD with phosphorylation changes, neurofilament light chain assays and materials, and newer tau assays technologies licensed by Washington University to C2N Diagnostics. Through these relationships, Washington University, Dr. Bateman is entitled to receive royalties and/or equity from the license agreement with C2N.
  - C2N Diagnostics will be analyzing samples from the Knight Family DIAN-TU-001 trial of E2814 for primary, secondary, and exploratory endpoints. Should the DIAN-TU trials impact the value of C2N Diagnostics, Washington University (WU) and Dr. Randall Bateman could directly benefit.

KNIGHT FAMILY DIAN TU Dominantly Inherited Alzheimer Network Trials Unit

SILQ CENTER

hopecenter for neurological disorders

C-BRAIN AI-Powered Discovery & Potential Applications

Randall Bateman M.D.
Charles F. and Joanne Knight Distinguished Professor of Neurology
DIAN and DIAN-TU PI and Director
Washington University School of Medicine

Washington University in St. Louis School of Medicine

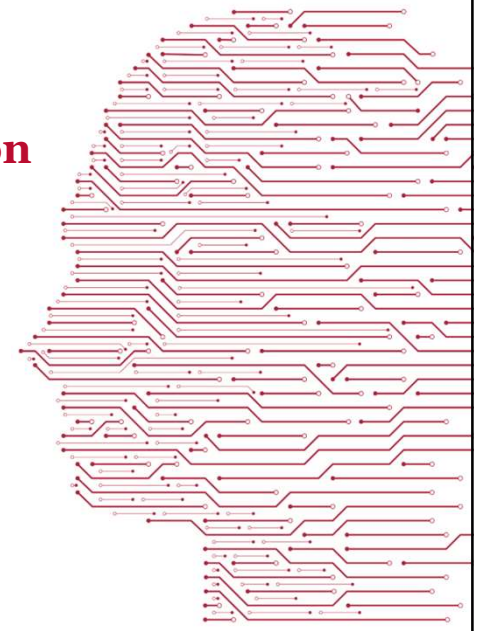
DIAN Dominantly Inherited Alzheimer Network

Knight ADRC Alzheimer's Disease Research Center WASHINGTON UNIVERSITY ST. LOUIS

Consortium for Biomedical Research and Artificial Intelligence in Neurodegeneration (C-brAIn)

www.c-brain.org

A Pioneering Initiative in AI-Driven Discovery



Randall J. Bateman, MD

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C-BRAIN Major & Key Contributing Members

ALZFORUM NETWORKING FOR A CURE

Alzheimer's Disease Data Initiative

ALZHEIMER'S ASSOCIATION

Bristol Myers Squibb

DOLBY FAMILY VENTURES

Alzheimer's Drug Discovery Foundation

Gates Ventures

Johnson&Johnson

RAINWATER Charitable Foundation

ROBERTSON FOUNDATION

Sage Bionetworks

sanofi

THE 10,000 BRAINS PROJECT

Washington University in St. Louis

Anonymous

Key Member

Eisai

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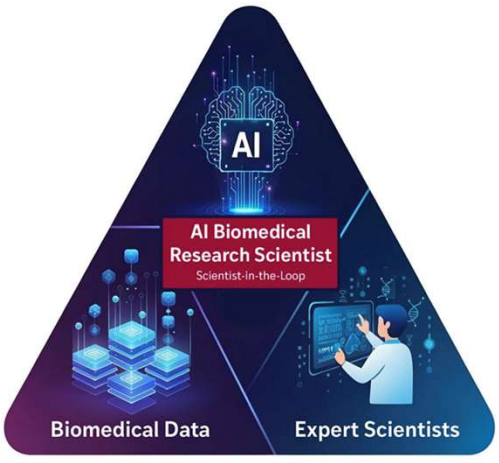
Consortium Mission, Scope, and Deliverables

- **Mission**: Make important health discoveries faster, with a focus on Alzheimer's disease, related dementias, and neurodegeneration.
- **Scope**: Bring AI into every stage of research, from forming ideas to running experiments, and develop a comprehensive and useful AI assistant for scientists.
- **What we will deliver**:
  - **Year 1:** an easy-to-use AI platform for neurodegenerative researchers, with three initial working tools
  - **Year 2:** a more capable AI assistant that can draft and generate research work
  - **Year 3:** an AI assistant that can carry out much of the research on its own, with human oversight

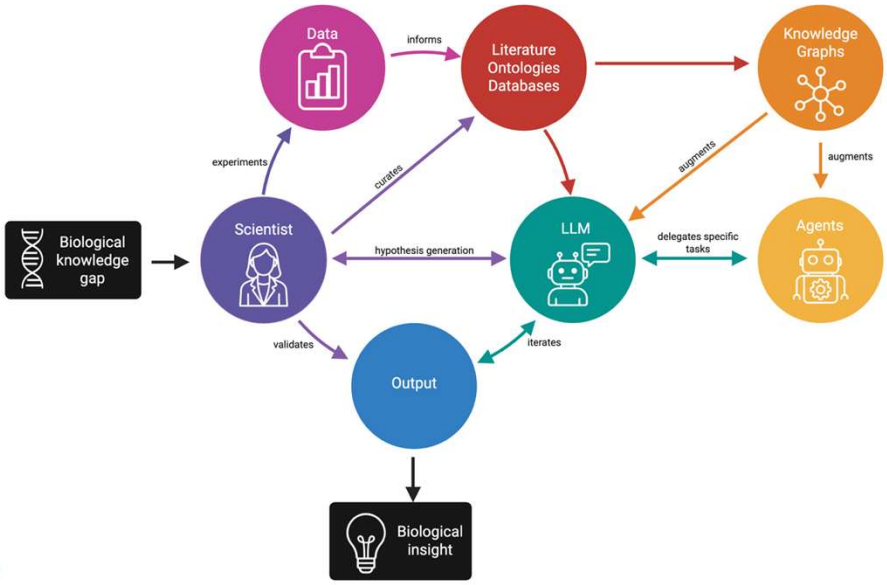
C-BRAIN impact in accelerating discovery of causal mechanisms in brain aging and neurodegeneration



Major Distinguishing Features:

- Unique and non-public **datasets** for AI discovery of causal mechanisms
- Deep expertise from **AI and biomedical research groups** (>200 research teams involved)
- Proven experience in successful translation and impact (blood tests, prevention trials, and ground-breaking discoveries)

How the AI Biomedical Scientist works



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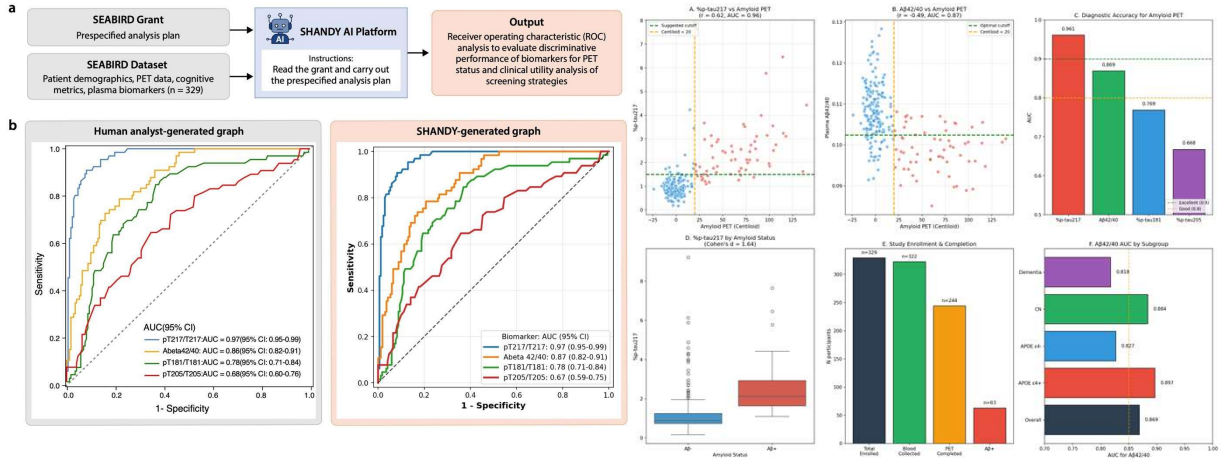
C-BRAIN's progress toward an AI "biomedical scientist"

- Three agentic AI tools in late-stage development (open-source release on 07/26)
  - **Literature Review and Data Synthesis Agent**: reads the vast body of dementia research in minutes, spotting connections across studies and promising new ideas to test that no person could find by hand.
  - **Data Analysis Agent**: gathers experiments that didn't work (often never published) from universities and drug companies, so researchers don't waste time and money repeating dead ends.
  - **Critical Reasoning Agent**: an AI "virtual reviewer" that checks study designs, conclusions, and draft papers against established knowledge and statistical standards, making the science more rigorous and reliable.
- OpenScientist (research paper under review; free to use today)
  - An AI assistant that takes a research question and scientific data (genetics, proteins, brain imaging, and more), then repeatedly forms and tests ideas against published research, and finishes with a report of what it found.

WashU

Example: the AI runs the analysis itself, completing months of work in about an hour



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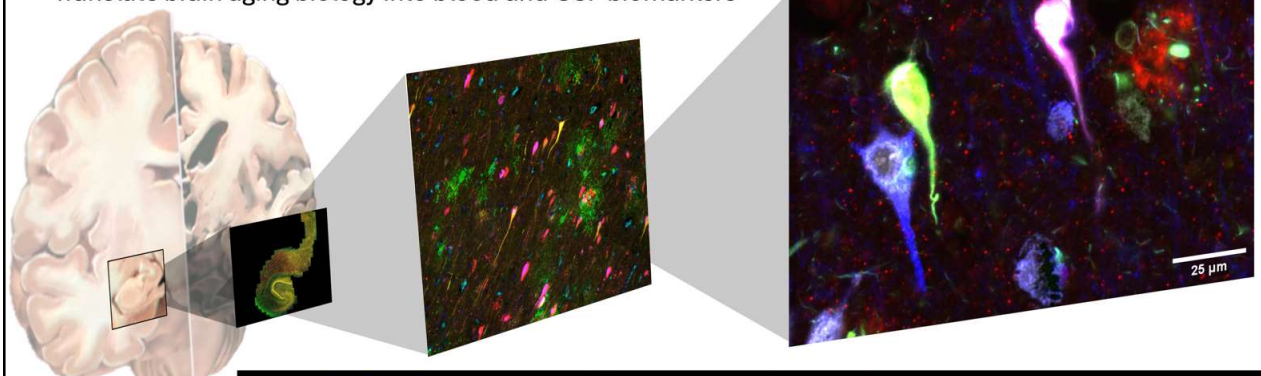
Brain Aging is the Root Biology of Neurodegeneration.

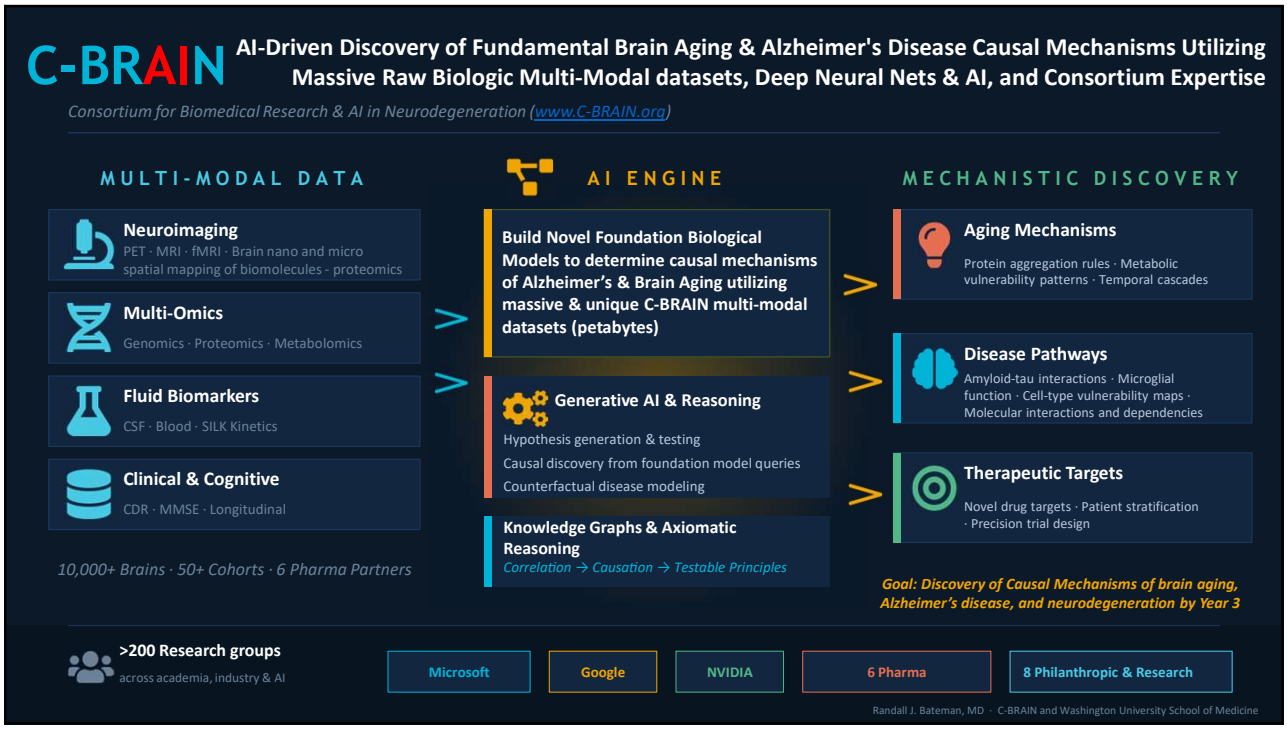
Measuring brain changes across the lifespan at multiple levels: organ, tissue, cellular and molecular scales.

- Build reference datasets from healthy aging to preclinical and clinical AD
- Map aging-associated cellular states and microenvironments in human brain tissue
- Predict disease risk, progression and therapeutic response
- Accelerate development of interventions that slow or prevent Alzheimer's disease
- Enable earlier detection and precise patient selection for clinical trials
- Translate brain aging biology into blood and CSF biomarkers



Miranda Orr Lab

Neuronal vulnerability | Microglial activation | Plaque niche | pTau | Age-associated astrocytes



The Future: a day without Alzheimer's

- Currently can slow the progression of mild symptoms and have highly accurate diagnoses with blood tests
- Prevention – delaying the onset by years – is likely coming in the next few years
- At-risk patients will be screened (much like cholesterol is checked for heart attack prevention)
- We will need breakthroughs on how to prevent the neurodegeneration process from taking hold – the key is ***brain aging***
- AI will accelerate our ability to discover these breakthroughs leading to preventable disease

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ACKNOWLEDGMENTS

The research participants

C-BRAIN executive team: Ade Ojewole (Chief Technology Officer), **Eric Landsness** (Associate Director), **Anna Santacruz** (Operations Director), **Sarah Naylor** (SILQ Center Executive Director)
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SEABIRD and SUNBIRD: David Carr, Tammie Benzinger, Mackenzie Hofford, **Nupur Ghoshal**, Yan Li, Melody Li, Brian Gordon, Suzanne Schindler, Eric Lenze, Sarah Hartz, Jessica Mozersky, Siobhan Sutcliffe, Ruijin Lu, Carlos Cruchaga, Chengie Xiong, Ganesh Babulal
ADRC: John Morris, Suzanne Schindler, Chengjie Xiong, Tammie Benzinger, Anne Fagan, Brian Gordon, David Holtzman
SILQ Center: Nupur Ghoshal, Donald Elbert, Tim Miller, Ross Paterson, Bruce Patterson

THE FOUNDATION FOR BARNES-JEWISH HOSPITAL

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