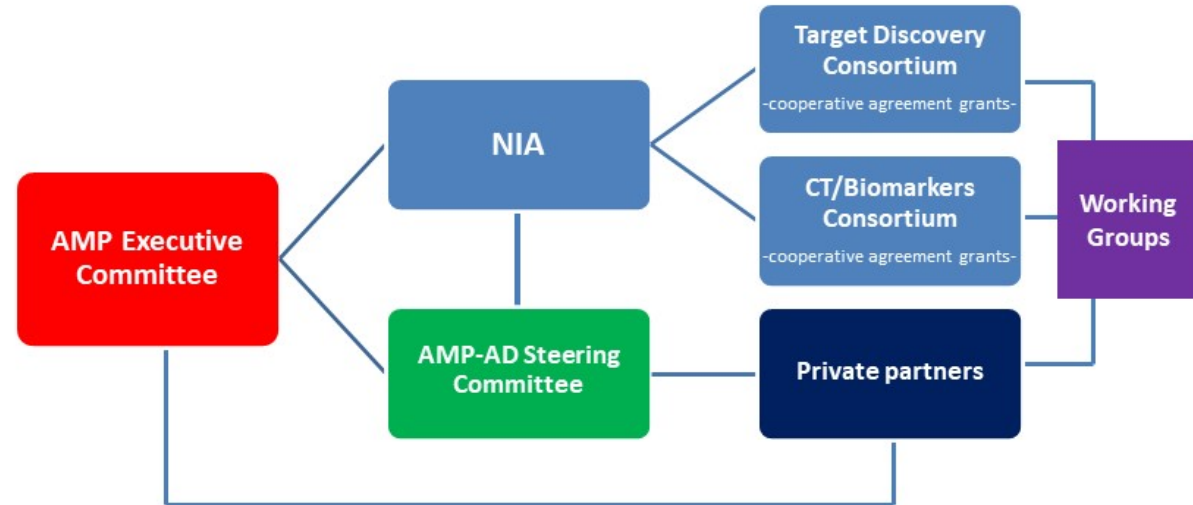


ACCELERATING MEDICINES PARTNERSHIP (AMP)

ALZHEIMER'S DISEASE

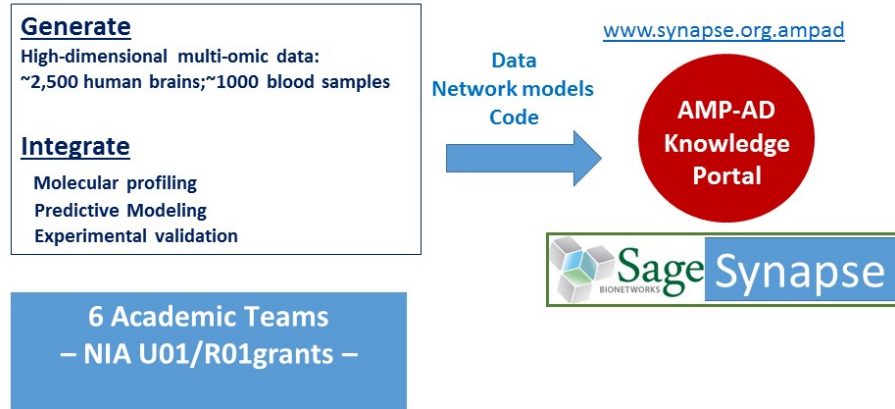
AMP-AD Partners



Managing Partner →  **FNIH**
Foundation for the National Institutes of Health

<https://www.nia.nih.gov/research/amp-ad>

Target Discovery and Preclinical Validation



Discover and carry out preclinical validation of novel disease-relevant therapeutic targets by integrating the analyses of large-scale molecular data from human brain/blood samples with network modeling approaches and experimental validation

Rapid and broad sharing of data

Biomarkers

-Tau PET imaging-



A4 **DIAN - TU**

Secondary Prevention Trials
anti-amyloid treatment



Screening/Pre-randomization data from the trials will be made broadly available through the [Alzheimer Association's GAAIN collaborative platform](#). Trial data and biological samples will also be shared after completion of the trials.

AMP-AD Project A (Biomarkers) Progress:

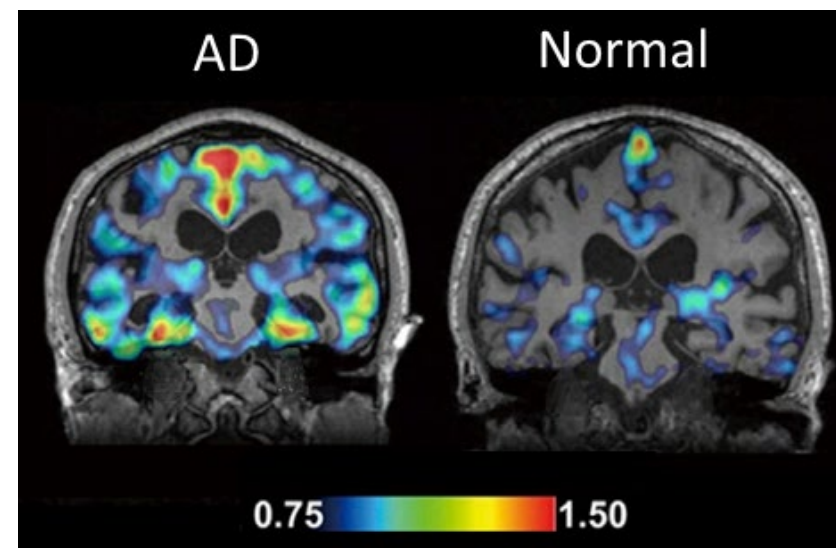
Project A: Supplement NIA-supported Phase II/III secondary prevention trials testing several anti-amyloid therapies with tau PET imaging (AV1451).

▪ **Anti-Amyloid Treatment in Asymptomatic Alzheimer's Disease Trial (A4 Trial):** Target ~1600 scans, 4 timepoints. *Trial enrollment complete.*

- *Quantitative pre-randomization data now available (LONI).*
- *Process to de-identify and share raw imaging and GWAS data and distribute biosamples in progress.*

▪ **Dominantly Inherited Alzheimer Network (DIAN) Trial:** Target 365 scans, 4 timepoints. *Trial enrollment complete.*

- *Preparations for sharing of pre-randomization data in progress.*



Distribution of tau across brain with AD

A4 Quantitative pre-randomization data available now ([LONI](#))

ACCELERATING MEDICINES PARTNERSHIP (AMP)

ALZHEIMER'S DISEASE - Target Discovery and Preclinical Validation Project

RFA AG13-013

Academic Teams	Broad-Rush	Mt Sinai	UFL/ISB /Mayo	Emory	Duke	Harvard/ MIT
Principal Investigators	De Jager, Bennett	Schadt, Zhang	Golde, Price, Taner	Levey	Kaddurah-Daouk	Yankner, Tsai
Human Data source	ROSMAP	Mt Sinai Brain Bank	Mayo Brain Bank	All	ADNI	ROSMAP
Molecular Data Types	RNAseq	RNAseq Whole exome seq	RNAseq	All Proteomics	Metabolomic	Txpn Factors
Target Identification	Bayesian networks	Bayesian networks	Innate Immunity Networks	Bayesian Networks	Systems analysis	REST
Preclinical Validation	iPSCs Cell lines	iPSC, drosophila, mouse	mouse	Mouse, cell culture, drosophila	NA	mouse

Apply a systems biology approach to discover and validate the next generation therapeutic targets using an open science research model:

- Generate multi-omics human data from postmortem brain tissue and plasma samples (well phenotyped cohorts and brain banks)
- Build network models of targets/pathways
- Carry out early target validation in multiple cell-based and animal models.
- Develop a data portal to enable rapid and broad sharing of data and analytical results.

Data Coordination and Integrated Analysis
Sage Bionetworks (Mangravite)

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ALZHEIMER'S DISEASE - Target Discovery and Preclinical Validation Project

COMPLETED:

1. Centralized data resource established – AMP-AD Knowledge Portal
2. Rich genomic, proteomic, metabolomic human data (raw and processed) made available and being widely used
3. Network models of targets developed and made available
4. Animal models molecular phenotypes evaluated relative to human networks
5. Web-based interface for sharing target nominations and analytical outputs developed - AGORA platform
6. ~100 annotated target predictions and additional 480 key driver genes made publicly available.

ONGOING:

1. Open source research tools for de-risking dark targets
2. Single cell RNAseq profiling (human and mouse)
3. **Novel biomarker discovery efforts – linked pilot projects**

ACCELERATING MEDICINES PARTNERSHIP (AMP)

ALZHEIMER'S DISEASE - Target Discovery and Preclinical Validation Project

[RFA AG18-013](#) / [RFA AG18-014](#)

NIA investment: ~\$60M over the next 5 years

AMP-AD Data Coordinating Center (U24):

Sage Bionetworks

U01 Grants:

Duke U-Helmholtz U-U of Rotterdam

Icahn Institute at Mount Sinai

Arizona State University

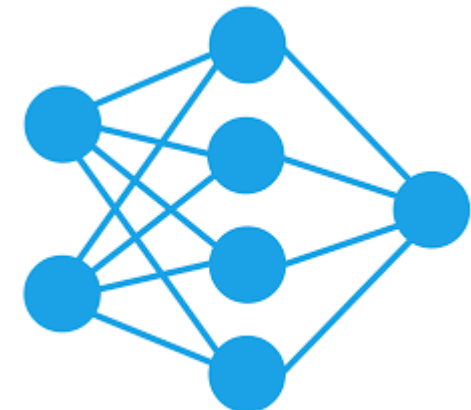
Columbia-Rush

Emory-Baylor

UFL-Mayo-ISB



Highly Networked Collaborative Projects

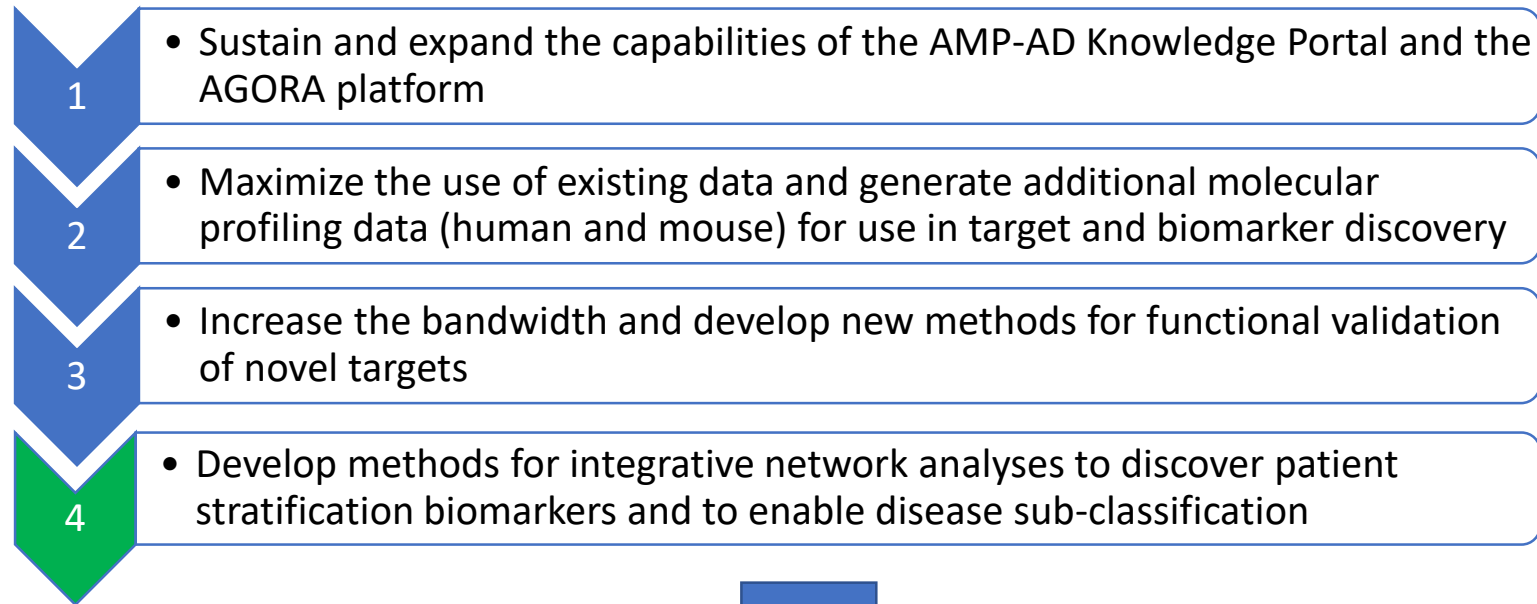


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ALZHEIMER'S DISEASE - Target Discovery and Preclinical Validation Project

Foundation of the AMP-AD Target Discovery and Preclinical Validation Project 2.0

[RFA-AG18-013](#)
[RFA-AG18-014](#)



opportunity to continue and expand the partnership

ACCELERATING MEDICINES PARTNERSHIP (AMP)

ALZHEIMER'S DISEASE - Target Discovery and Preclinical Validation Project

