AMP-AD: Target Discovery and Preclinical Validation

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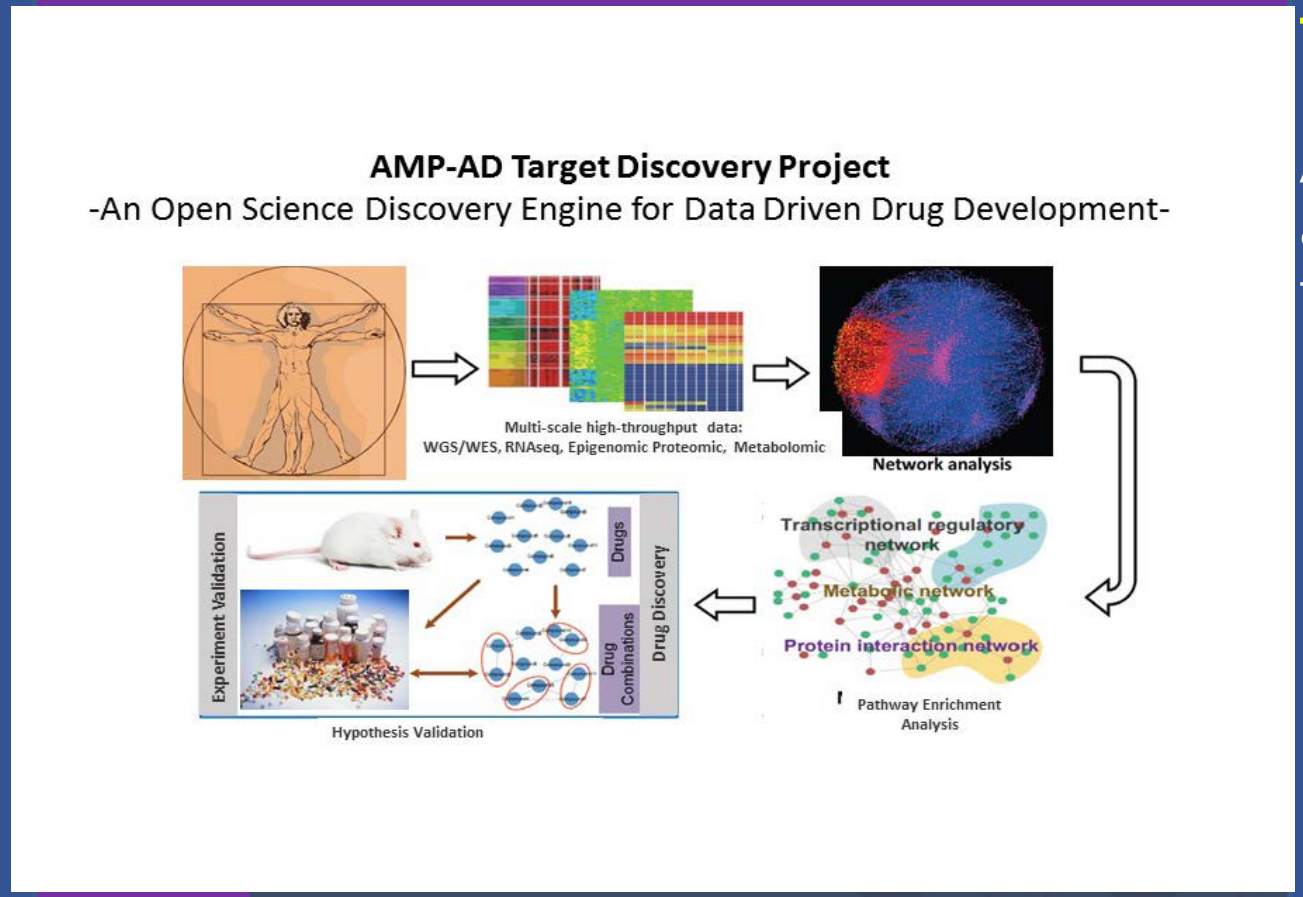
AMP: Alzheimer's Disease (AD)



TARGET DISCOVERY PROJECT:

Apply a systems biology approach to discover and validate the next generation therapeutic targets in an open science forum:

- ❑ Integrate multi-omics human data from well phenotyped cohorts to build network models of disease, followed by early target validation in multiple cell-based and preclinical models.
- ❑ Develop a data portal to enable rapid and broad sharing of data and analytical results.

ACCELERATING MEDICINES PARTNERSHIP (AMP)

ALZHEIMER'S DISEASE - Target Discovery and Preclinical Validation Project

Generate
High-dimensional multi-omic data:
~2,500 human brains;~1000 blood samples

Integrate
Molecular profiling
Predictive Modeling
Experimental validation

6 Academic Teams
– NIA U01/R01grants –

Data
Network models
Code

www.synapse.org.ampad

AMP-AD Knowledge Portal

Sage BIONETWORKS Synapse

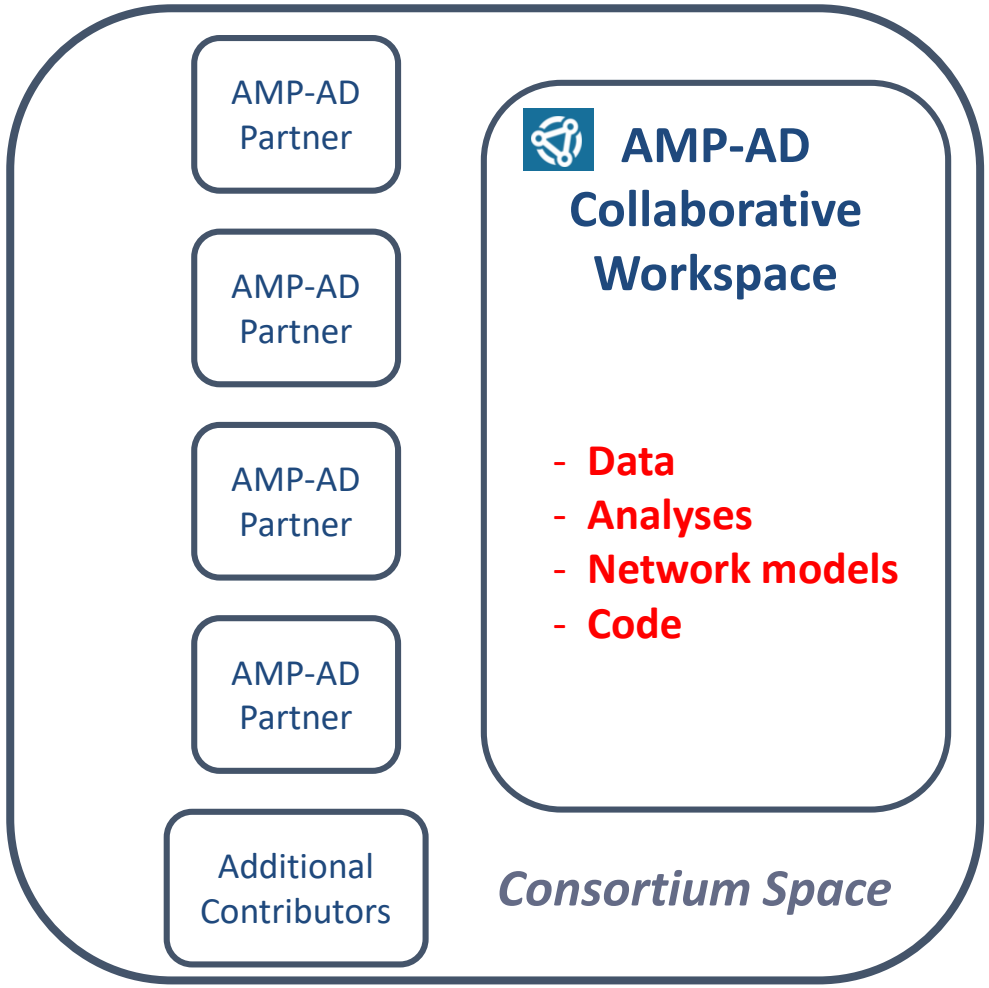
ACCELERATING MEDICINES PARTNERSHIP (AMP)

ALZHEIMER'S DISEASE - Target Discovery and Preclinical Validation Project

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	DNA-M, H3K9Ac, miRNA, 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*
Validation	SRM Proteomics, iPSCs lines	iPSC, drosophila, mouse	mouse	Mouse, cell culture, drosophila	NA	mouse

Data Enablement and Coordination of Collaborative Analyses:
Sage Bionetworks, Principal Investigator – Lara Mangravite

CENTRALIZED DATA RESOURCES



Quarterly Data Depositions

AMP-AD* Knowledge Portal

Public space

Launched - March 4, 2015

-Data released as soon as QC is completed
-Open but Controlled Access (DUA)

-No publication embargo imposed on the use of data after they have been made available through the public portal

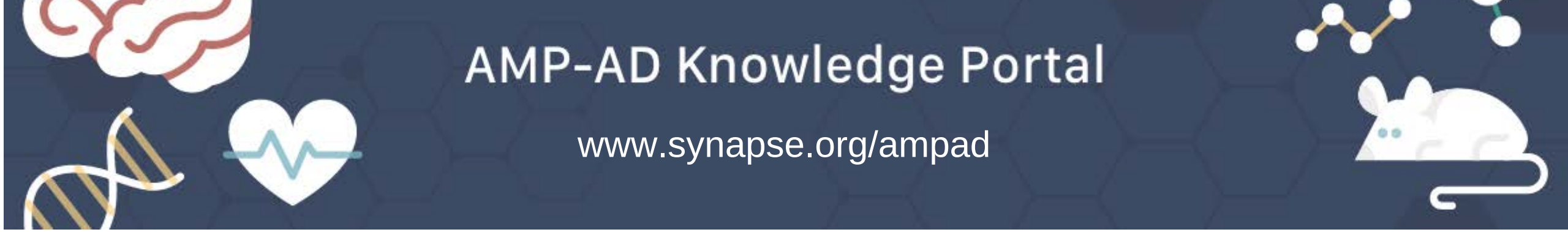
***AMP-AD Knowledge Portal – www.synapse.org/ampad**

Quarterly Public Data Releases

60,000 files shared by **42 investigators** across **22 institutions** representing samples from **36 research studies**

1309 total users* with **55 new users** per month

www.synapse.org/ampad



What's in the portal?

15 human studies

3 rat models

22 model system studies

7043 human samples

10 drosophila models

17 mouse models

14 diagnoses

15 genomic data modalities

13 human cell models

AMP-AD Knowledge Portal
Rich Multi-Omics and Clinical Data from Antemortem Cohorts – ROS/MAP

Genomics

SNP genotypes
WGS

Transcriptomics

RNAseq
mRNAarray
miRNAarray

ROS/MAP Cognitive Aging Cohorts
NCI/MCI/AD

Biosamples
dorsolateral prefrontal cortex, plasma

Data Generated by AMP-AD Teams
Columbia-Broad-Rush/Emory/Duke

Epigenomics

ChIPseq/H3K9ac
Methylation array

Clinical

age ad dx, age death, sex, edu, apoe, ethnicity, braak, ad reagan score, mmse, cerad. cogdx

Full complement of phenotypic data
www.radc.rush.edu

Proteomics

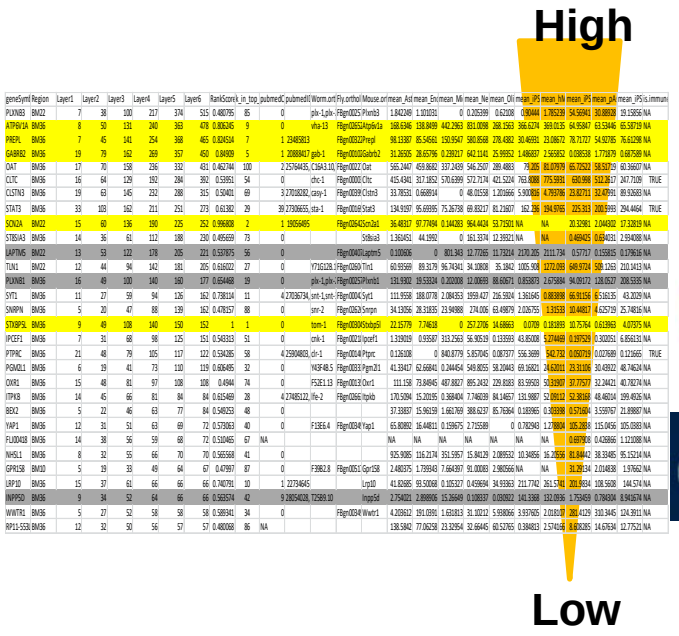
Metabolomics

Imaging

RADC Research Resource Sharing Hub

Wall of Targets

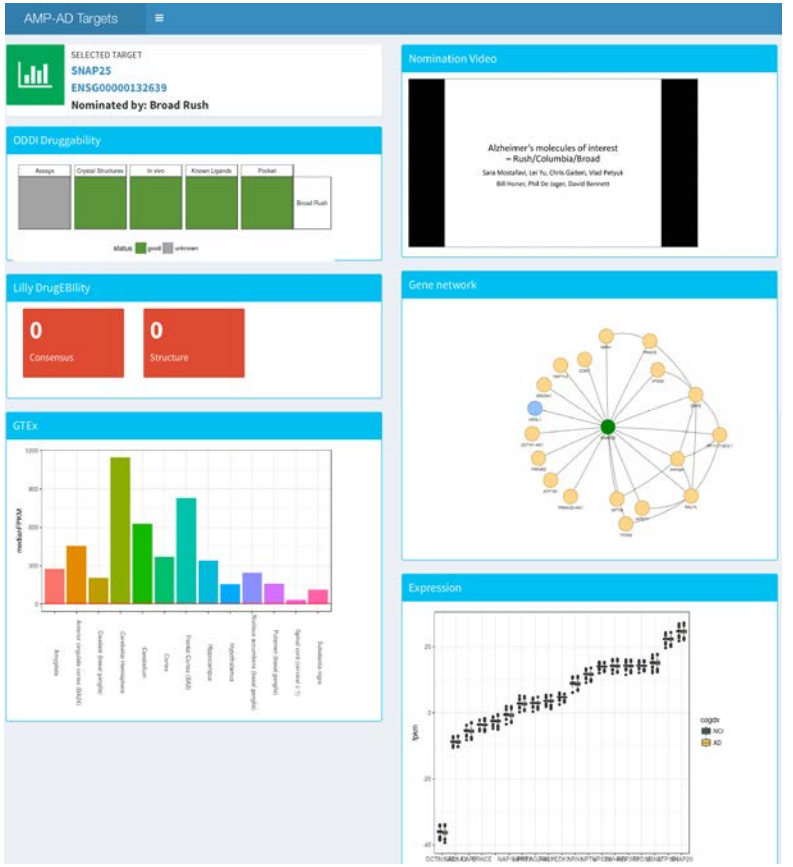
Standardized, aggregated evaluation of evidence



High

Drugability Index

Low



Daily and Logsdon
Sage Bionetworks

Release of AMP-AD preliminary target nominations
AAIC 2018