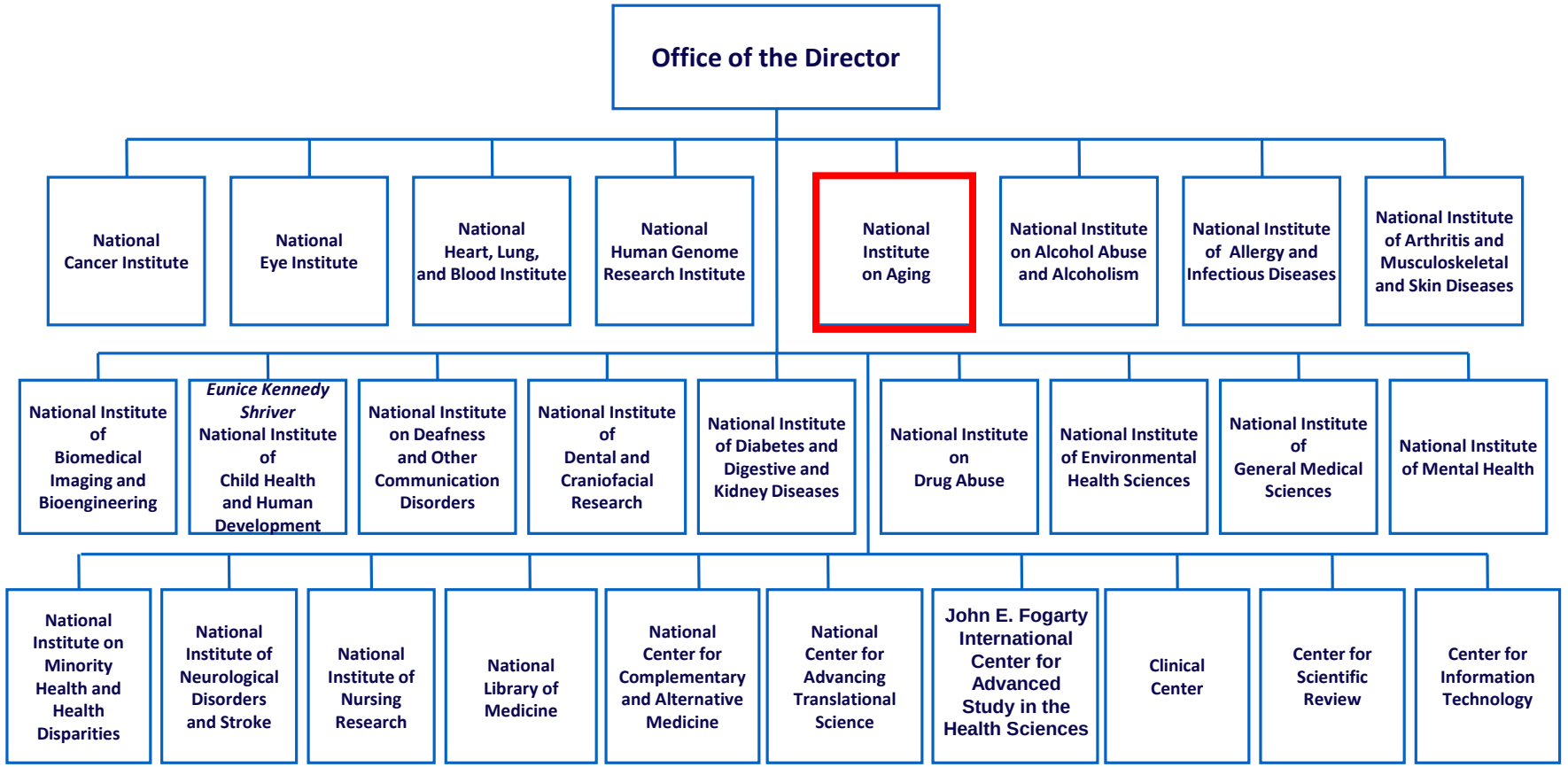
Big Data – view from NIA/NIH

Nina Silverberg
Program Director, Alzheimer's Disease Centers Program
Division of Neuroscience, NIA

May 19

The Center for Network and Storage Enabled Collaborative Computational Science Symposium

National Institutes of Health



27 Institutes and Centers (ICs)

NIH Mission

To seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life, and reduce illness and disability.

FY2017 Priorities:

- **Foundation for Discoveries: Basic Research**
- **The Promise of Precision Medicine**
- **Applying Big Data and Technology to Improve Health**
- **Stewardship to Inspire Public Trust**

NIH

Initiatives that Support Computational and Mathematical Sciences

- **Biomedical Information Science and Technology Initiative (BISTI)**

  Promote the optimal use of computer science and technology to address problems in biology and medicine by fostering collaborations and interdisciplinary initiatives **(bisti.nih.gov)**

- **Big Data to Knowledge Initiative (BD2K)**

  Develop new approaches, standards, methods, tools, software and competencies that will enhance the use of biomedical Big Data by supporting research, implementation and training in the data sciences **(datascience.nih.gov/bd2k)**

- **Interagency Modeling and Analysis Group (IMAG)**

  Provide an open forum for communication among government representatives for trans-agency activities that have a broad impact in science **(imagwiki.nibib.nih.gov)**

- **NSF/NIH Joint program in Mathematical Biology**

  Bring mathematics and statistics into the core of biological and biomedical research and to broaden the use of innovative mathematics in understanding life processes.

BD2K

FY17 Priorities for NIH

Big Data to Knowledge (BD2K)

- Coordinate access to and analysis of the many types of biological and behavioral ‘big data’ being generated by biomedical scientists

- Develop innovative and transformative computational approaches, tools, and infrastructures to make ‘big data’ and data science a prominent component of biomedical research

- Enable data sharing and utilization through the development of a new shared, interoperable cloud computing environment: *the ‘Commons’*

Big Data to Knowledge (BD2K)

- launched in 2014 to:
  - facilitate broad use of biomedical big data
  - develop and disseminate analysis methods and software
  - enhance training relevant for large-scale data analysis
  - and establish centers of excellence for biomedical big data.
  - supported initial efforts toward making data sets “FAIR”
    - Findable, Accessible, Interoperable, and Reusable.
- Second phase: will test the feasibility of, and develop best practices for, making NIH funded datasets and computational tools available in a shared space that multiple scientists can access remotely.

BD2K

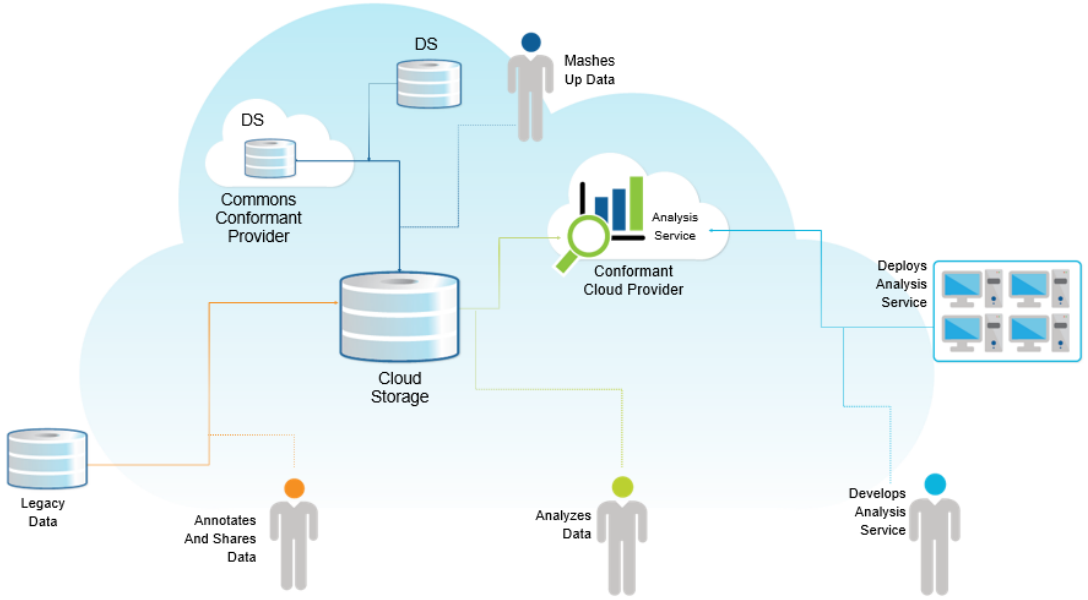
Role of Data Sciences at NIH

FAIR	Enable broad data sharing and reuse of data Findable, Accessible, Interoperable, and Re-usable (FAIR)
Commons	Support biomedical discovery by enabling the sharing of digital objects
Training	Enable an effective and diverse biomedical, data science workforce
Sustainability	Develop An NIH Vision For Economic, Technical, And Social Stewardship Of Biomedical Data Repositories.

BD2K

The Commons as Innovation Accelerator

NIH proposes a **community-owned** cloud-based electronic ecosystem ("**Commons**") where researchers can **store, share, and utilize** their own, and others', sharable Digital Objects.

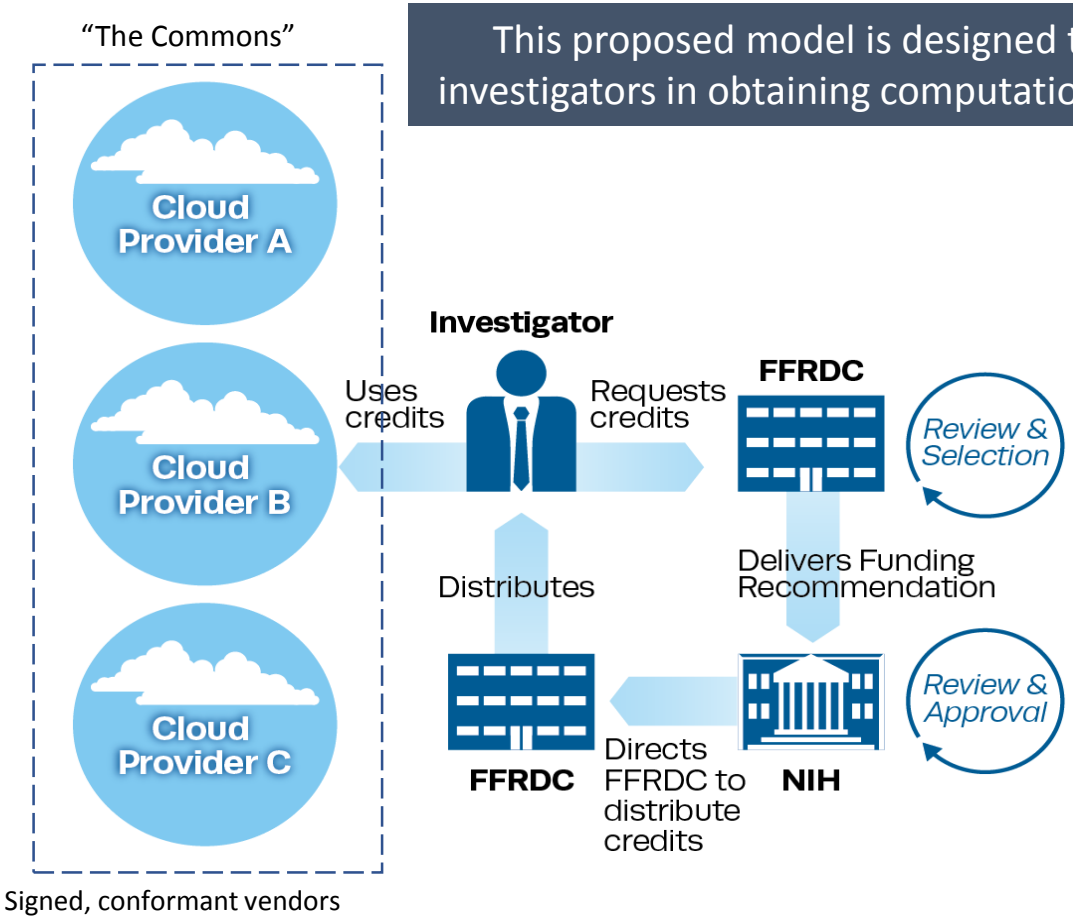


How can this best be **supported** so as to reduce long-term costs, increase re-use of Digital Objects, and promote the overall scientific output of the nation?

BD2K

Commons Credits Pilot

This proposed model is designed to help NIH better support biomedical investigators in obtaining computational resources to perform novel research.



BD2K

It's Easy to Participate in the Commons Credits Pilot

Each step is designed to be as simple and low effort as possible to help reduce the barriers to entry and participation.

- Applications are < 2 pages, and should be easy to complete in less than 1 day.
- Credits will be disseminated within 8 weeks post-cycle close, and are available for 12 months.
- Investigators focus on the science, MITRE handles invoicing.
- Participants' forum on Portal for sharing and discussion.

commons_credits@mitre.org

Ongoing research which utilizes big data storage: Examples

High Interest in Digital Technologies

IoT

CART --
Collaborative Aging (in P

- Interagency initiative w
  - NIA, NIBIB, NCI, N

$1M HOMESHARE GRANT AWARDED BY NSF

BY KAY CONNELLY | OCTOBER 18, 2016 | UNCATEGORIZED

August 2016 – The HomeSHARE initiative is a geographically distributed testbed to design, develop, and evaluate pervasive home-based technologies for aging-in-place. IU is the lead institution, with partners at University of Colorado, University of Virginia, Clemson University and University of Washington.

BOOKMARK THE PERMALINK.

NIH National Institute on Aging
Turning Discovery Into Health

Home | Health and Aging | Resear

Home

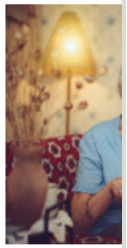
NEWSROOM

NIH initiative tests in-home technology to he age in place

January 25, 2017

Many older adults want to live at home independently as they age. Sometime from their family and friends—and the right technology. A new initiative led b Health (NIH) aims to help seniors age in place by developing a research platf related in-home sensors and other technologies.

CART—Collaborative Aging (in Place) Research Using Technology—unites NIH, academic, and industry experts to develop and test unobtrusive tools that record and track real-time changes in older adults' health status and activities. Launched in October 2016, the $7 million, 4-year project will take place in more than 200 homes in rural and urban communities across the United States.



"This project will provide a systematic way of investigating technology that may enable older people to remain independent and avoid hospitalizations and transitions into care facilities," said Nina Silverberg, Ph.D., of the National Institute on Aging project.

- Concepts-of-Interest:
- Review and address key regulatory

NIH National Institutes of Health
Turning Discovery Into Health

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ACD Precision Medicine Initiative Working Group Public Workshop

Mobile and Personal Technologies in Precision Medicine Workshop

On July 27–28, 2015, the Precision Medicine Initiative (PMI) Working Group of the Advisory Committee to the NIH Director (ACD) hosted a public workshop on the scientific, methodological and practical considerations to inform the incorporation of mobile and personal technologies in the national research cohort of one million or more volunteers. The workshop will be was held at the Intel Corporation campus in Santa Clara, California, and was videocast.

This workshop built on the unique scientific questions developed during the April 28–29 workshop, digital health data perspectives shared during the May 28–29 workshop, and

Email Updates

Sign up to receive email updates about the Precision Medicine Initiative.

Sign up for updates

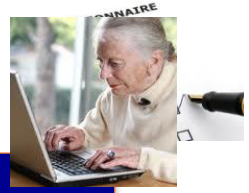
Related Links

- PMI Working Group Final Report (pdf)
- NEJM Perspective: A New Initiative on Precision Medicine
- Precision Medicine Initiative and Cancer Research
- Precision Medicine Initiative

ORCATECH
SENSING LIFE KINETICS

OREGON HEALTH & SCIENCE UNIVERSITY
OHSU

Which has brought us to BMDs in Trials…

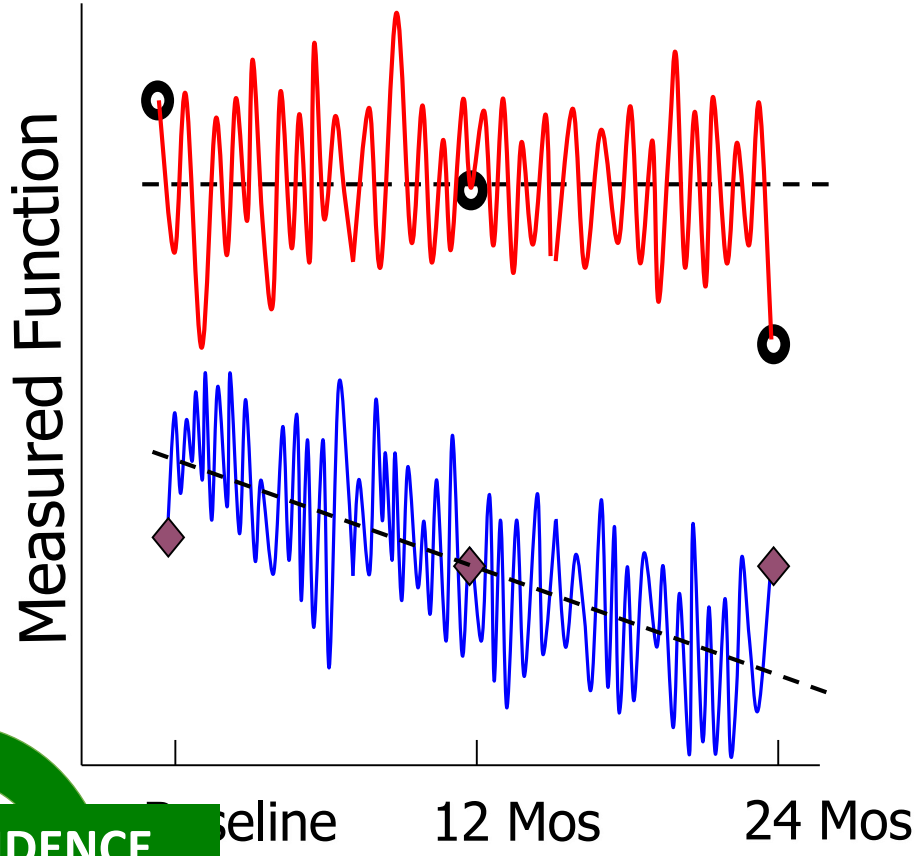


- Real-time
- Continuous
- Home-based
- Objective
- Unobtrusive
- Ambient

- Pervasive Computing
- Wireless Technologies
- "Big Data" Analytics

EVIDENCE

?



ORCATECH
SENSING LIFE KINETICS

OREGON HEALTH & SCIENCE UNIVERSITY
OHSU

Technology ‘agnostic’ pervasive computing platform for continuous home-based assessment and Tx

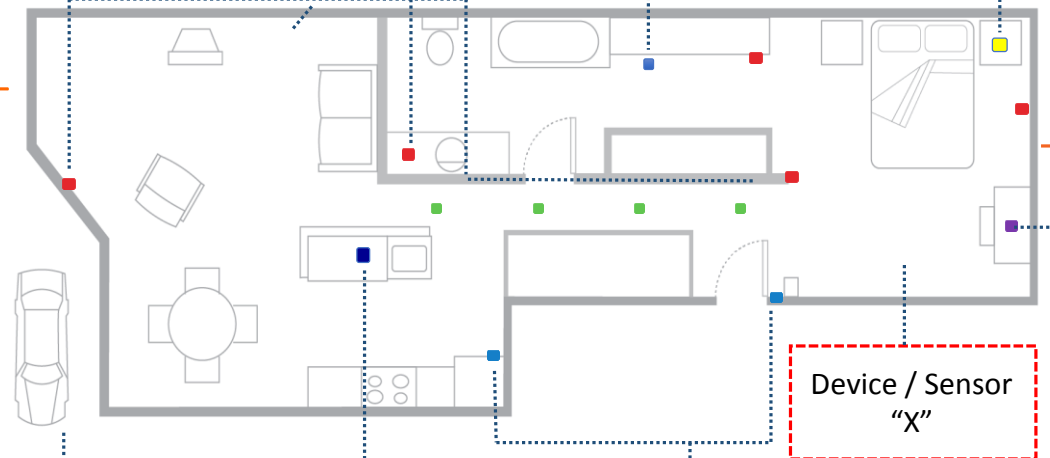
Studies Cohorts

- Life Laboratory Cohort
- Life Laboratory - BC
- AIMS Transitions
- EVALUATE - AD
- iCONECT - MI/OR
- CART - 202 Portland
- CART - VA VISN 20
- CART - MARS Chicago
- CART - PRISM Miami
- ACTC Studies XYZ

Activity, Sleep, Mobility
Time & Location

Body Composition, Pulse, Temperature, $C0_2$

MedTracker



ORCATECH Secure Data Backend - Digital Data Repository

Secure Internet

Data Scientists
University Collaborations
PHARMA
Health Industry

Device / Sensor “X”

Driving

Phone Activity/EMA

Doors Open/Close

Computer Activity

ORCATECH
SENSING LIFE KINETICS

Kaye et al. Journals of Gerontology, 2011; Lyons et al. Frontiers in Aging Neuroscience, 2015

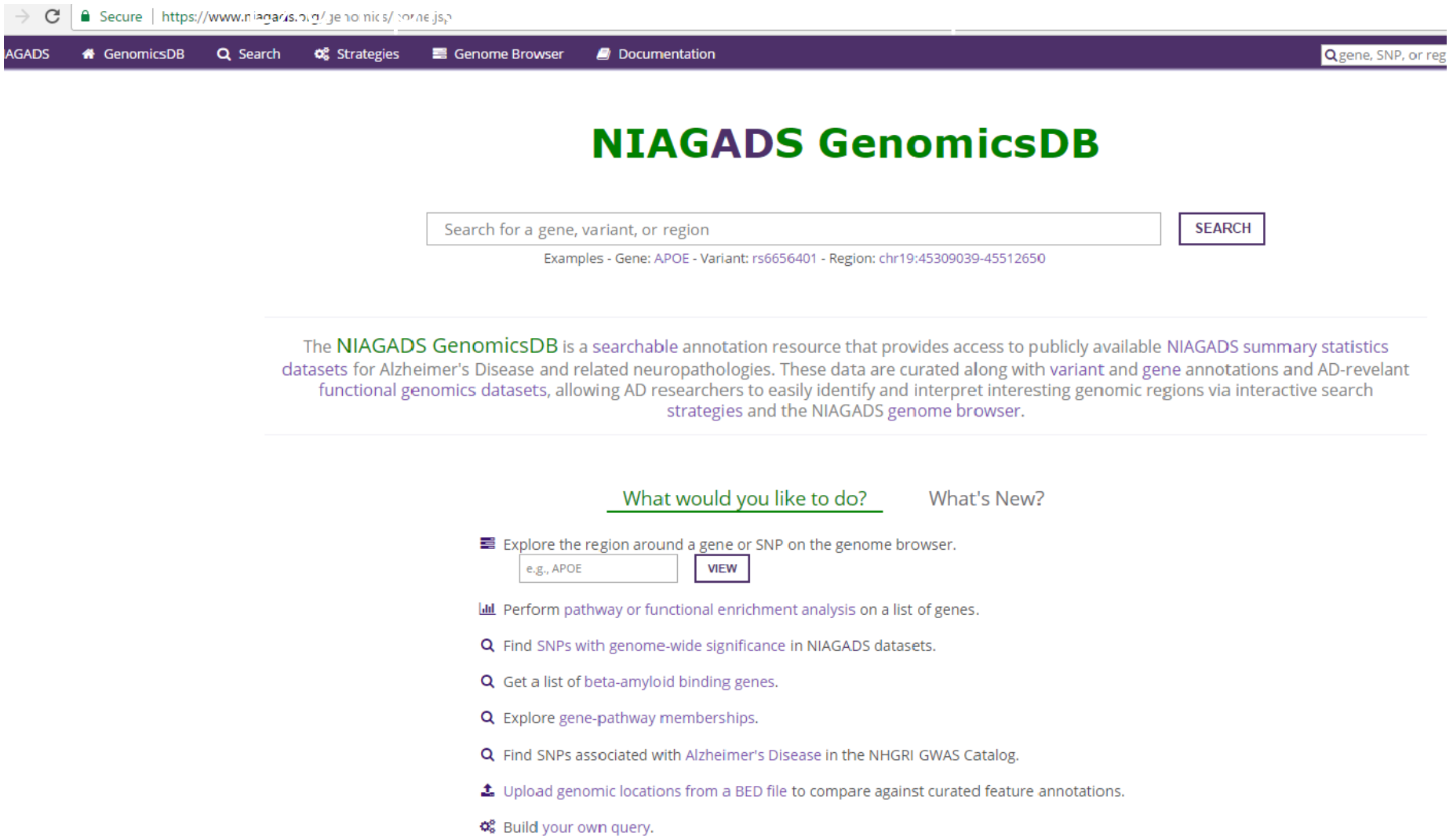
Sample project (two sites, one in MI)

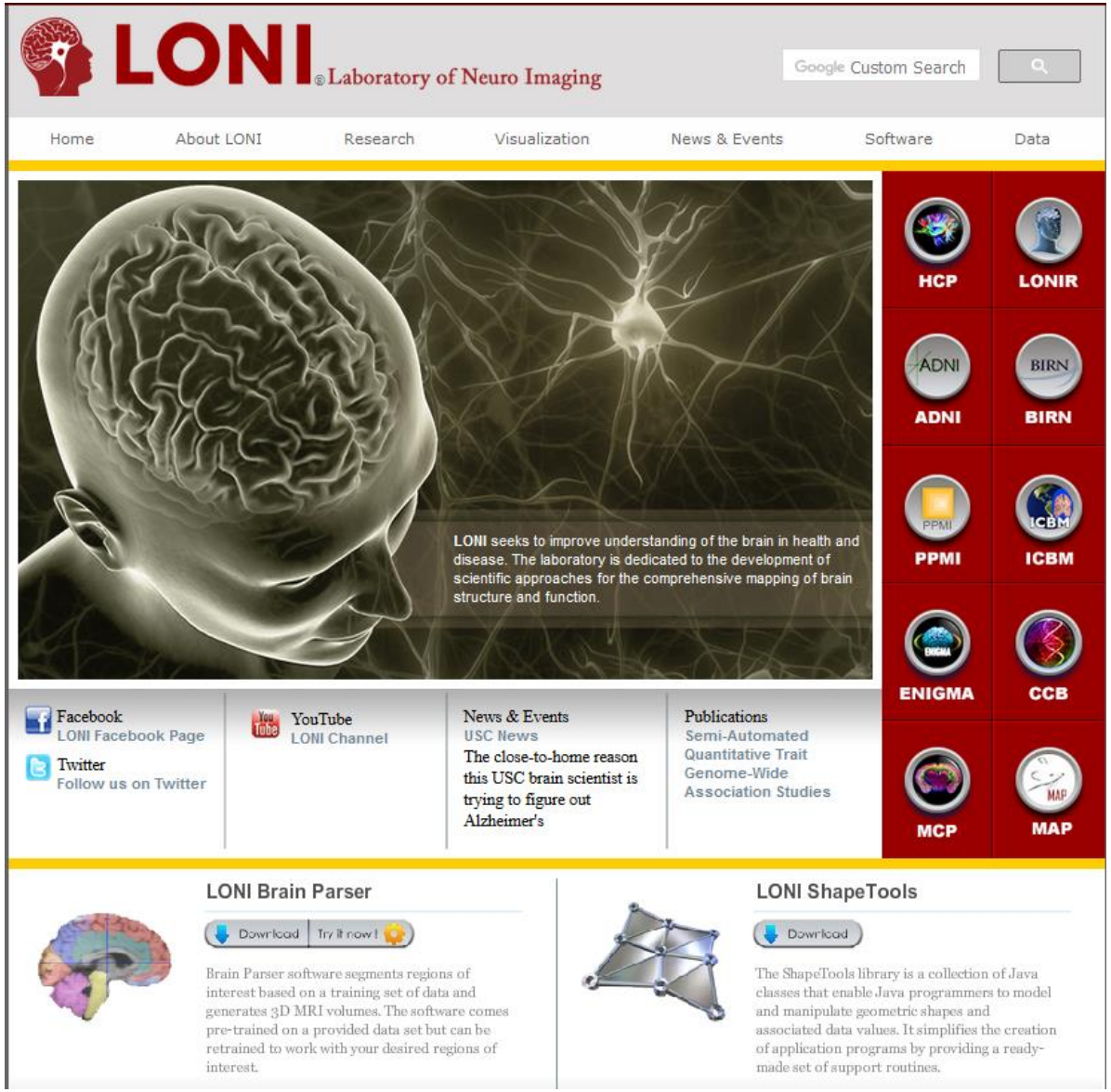
- R01 project,
- using skype-like video chats to improve cognitive function of socially isolated elderly.
- Each conversational session audio/video recorded for later analyses
- 30 minute video recording in mp4 format requires 300 megabyte of storage. 4 times per week = 1200 Mega byte of storage per week. 1200 X 180 subjects X 24 weeks require 5.2 terabyte of storage space (just for the 1st 6 months)

Video Chat

Systems and Data Storage

- Conversational sessions will be recorded for audio/visual analyses (mp4)
- 30 minutes of video chat = 300 megabyte data
- 300 megabyte X 4 times /week X 24 months X 180 subjects = 5.2 terabyte of data ! (for the 1st 6 months)
- Currently exploring storage options


Secure | https://www.niagads.org/genomics/home.jsp
AGADS
GenomicsDB
Search
Strategies
Genome Browser
Documentation
gene, SNP, or reg
NIAGADS GenomicsDB
Search for a gene, variant, or region
SEARCH
Examples - Gene: APOE - Variant: rs6656401 - Region: chr19:45309039-45512650
The NIAGADS GenomicsDB is a searchable annotation resource that provides access to publicly available NIAGADS summary statistics datasets for Alzheimer's Disease and related neuropathologies. These data are curated along with variant and gene annotations and AD-revelant functional genomics datasets, allowing AD researchers to easily identify and interpret interesting genomic regions via interactive search strategies and the NIAGADS genome browser.
What would you like to do?
What's New?
Explore the region around a gene or SNP on the genome browser.
e.g., APOE
VIEW
Perform pathway or functional enrichment analysis on a list of genes.
Find SNPs with genome-wide significance in NIAGADS datasets.
Get a list of beta-amyloid binding genes.
Explore gene-pathway memberships.
Find SNPs associated with Alzheimer's Disease in the NHGRI GWAS Catalog.
Upload genomic locations from a BED file to compare against curated feature annotations.
Build your own query.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LONI seeks to improve understanding of the brain in health and disease. The laboratory is dedicated to the development of scientific approaches for the comprehensive mapping of brain structure and function.
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BIRN
PPMI
ICBM
ENIGMA
CCB
MCP
MAP
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News & Events
USC News
The close-to-home reason this USC brain scientist is trying to figure out Alzheimer's
Publications
Semi-Automated Quantitative Trait Genome-Wide Association Studies
LONI Brain Parser
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Try it now!
Brain Parser software segments regions of interest based on a training set of data and generates 3D MRI volumes. The software comes pre-trained on a provided data set but can be retrained to work with your desired regions of interest.
LONI ShapeTools
Download
The ShapeTools library is a collection of Java classes that enable Java programmers to model and manipulate geometric shapes and associated data values. It simplifies the creation of application programs by providing a ready-made set of support routines.

FEATURED STUDIES

The IDA contains data on 35,589 subjects from 106 studies

4RTNI
129
APPLY
BIO CLINIC CT dMRI fMRI
GENE sMRI SPECT PET OTHER

ABIDE
1,112
OPEN USE
BIO CLINIC CT dMRI fMRI
GENE sMRI SPECT PET OTHER

ABVIB
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ACE
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GENE sMRI SPECT PET OTHER

ADNI
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MAPP
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NAPLS
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BIO CLINIC CT dMRI fMRI
GENE sMRI SPECT PET OTHER

NAPLS3
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BIO CLINIC CT dMRI fMRI
GENE sMRI SPECT PET OTHER

NIAD
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PRIVATE
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GENE sMRI SPECT PET OTHER

NIFD
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APPLY
BIO CLINIC CT dMRI fMRI
GENE sMRI SPECT PET OTHER

SYSTEMS APPROACHES FOR TARGET DISCOVERY AND VALIDATION

Suzana Petanceska PhD

Accelerating Medicines Partnership Alzheimer's Disease Program

https://www.nia.nih.gov/alzheimers/amp-ad

Government

Industry

Non-profit

AMP-AD Partners

NIH National Institute on Aging

NIH National Institute of Neurological Disorders and Stroke

FDA

abbvie

Biogen

gsk GlaxoSmithKline

Lilly

alzheimer's association

Alzheimer's Drug Discovery Foundation

GEOFFREY BEENE

US Against Alzheimer's

Managing Partner → FNIH Foundation for the National Institutes of Health

ACCELERATING MEDICINES PARTNERSHIP (AMP)

ALZHEIMER'S DISEASE - Target Discovery and Preclinical Validation Project

- **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.**

- **Enable rapid and broad sharing of data.**

ACCELERATING MEDICINES PARTNERSHIP (AMP)

ALZHEIMER'S DISEASE - Target Discovery and Preclinical Validation Project

- **The project is a consortium of 6 multi-institutional, multidisciplinary research teams supported by NIA grants.**

- **The teams are applying cutting-edge systems and network biology approaches to integrate multidimensional human "omic" data (genomic, proteomic, metabolomic) from ~2,500 human brains/~1000 blood samples from all stages of the disease with clinical and pathological data to:**
  - **discover and select novel therapeutic targets for Alzheimer's disease**
  - **gain a systems-level understanding of the gene, protein, and metabolic networks within which these targets operate**
  - **evaluate their druggability in cell-based and animal models**

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 –

www.synapse.org.ampad

Data
Network models
Code

AMP-AD Knowledge Portal

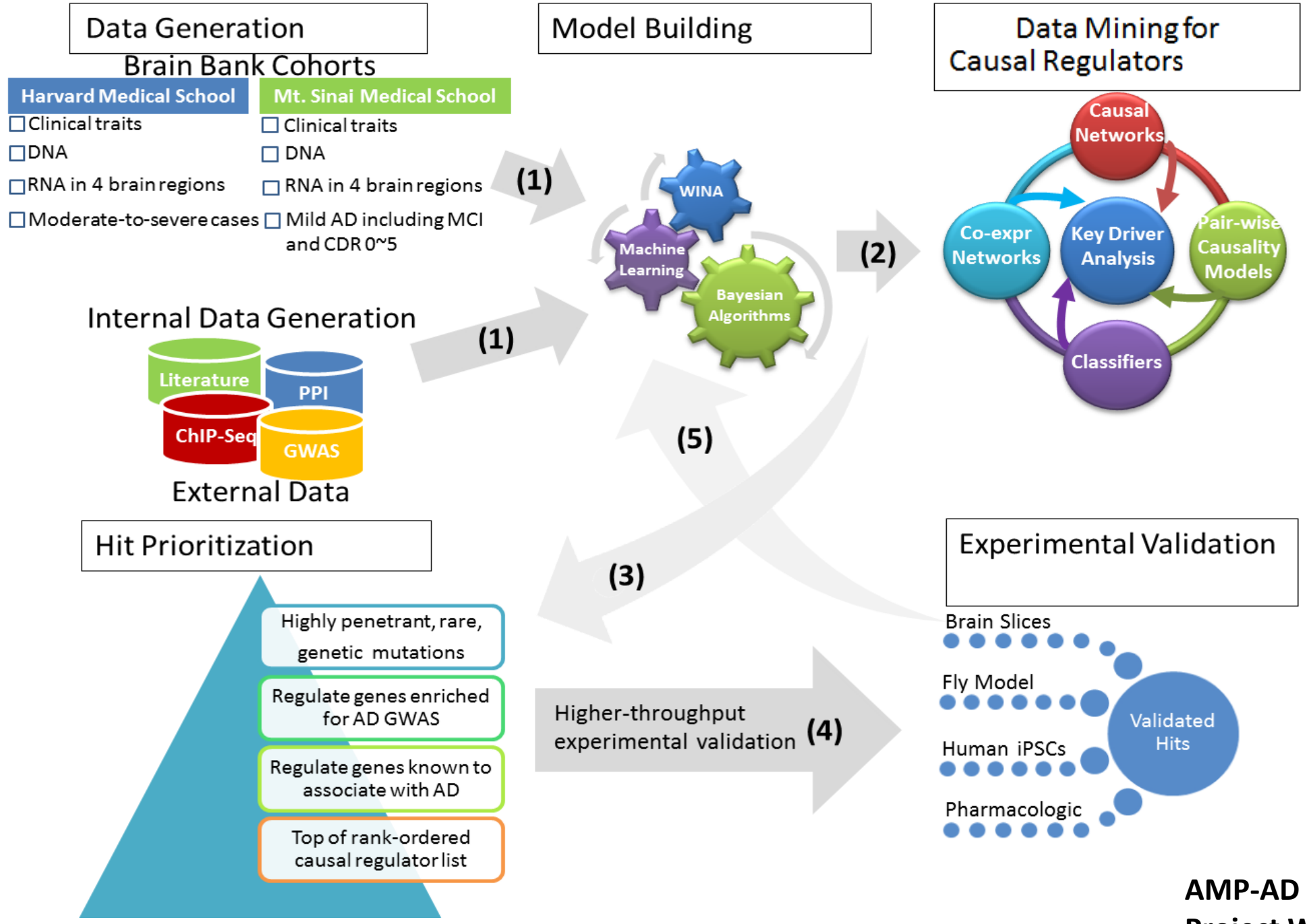
Sage BIONETWORKS Synapse

ACCELERATING MEDICINES PARTNERSHIP (AMP)

ALZHEIMER'S DISEASE - Target Discovery and Preclinical Validation Project

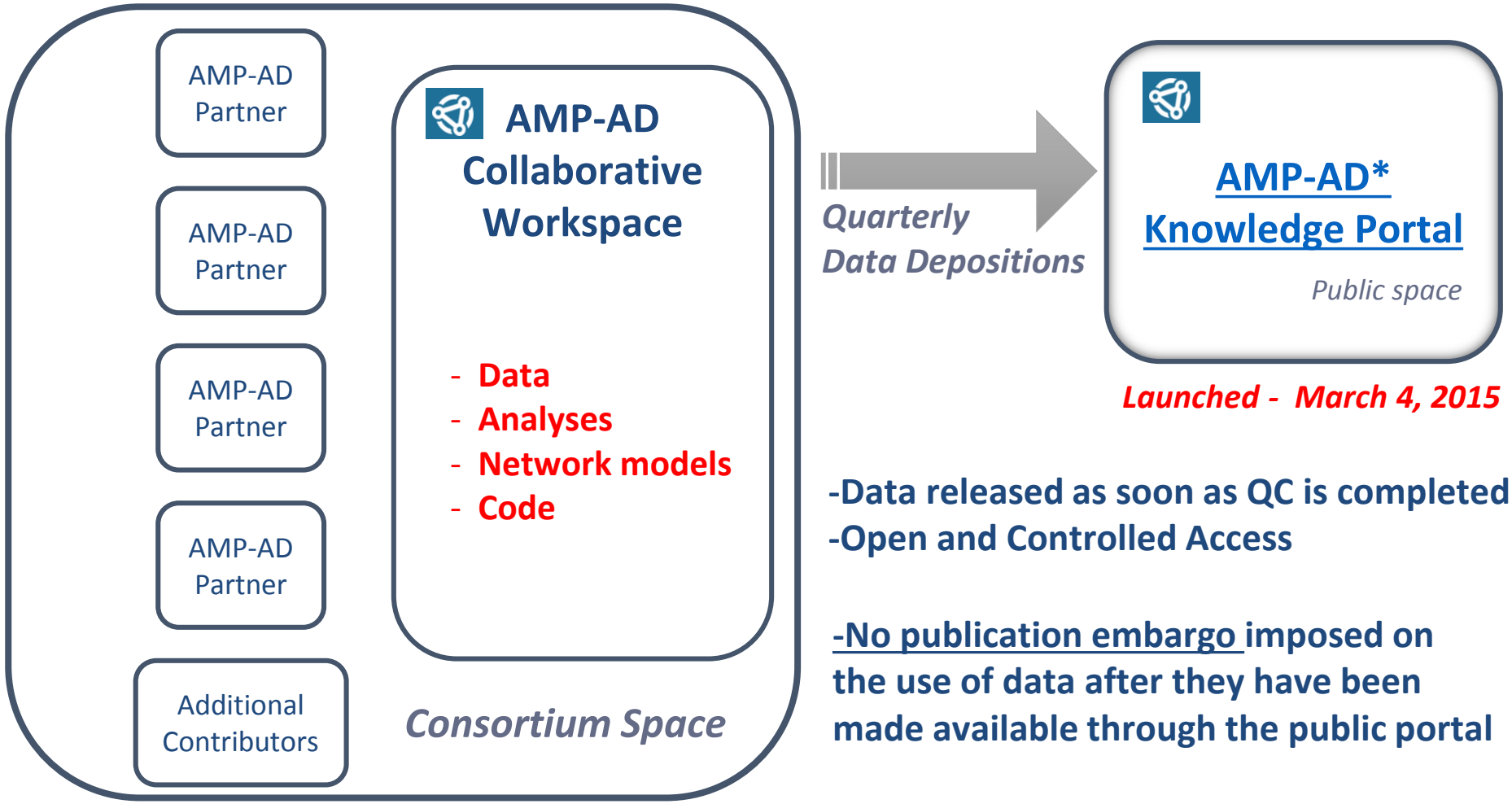
Academic Teams	Broad-Rush	Mt Sinai	UFL/ISB /Mayo	Emory	Duke	Harvard/ MIT
Principal Investigators	De Jager, Bennett	Schadt, Zhang	Golde, Price, Taner	Levey	Kaddurah-Daouk	Yankner, Tsai
Human Data source	ROSMAP	Mt Sinai Brain Bank	Mayo Brain Bank	All	ADNI	ROSMAP
Molecular Data Types	RNAseq	RNAseq Whole 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

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



AMP-AD Mt.Sinai team: Project Workflow

Sage BIONETWORKS Synapse



Launched - March 4, 2015

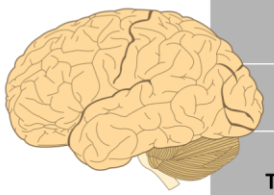
-Data released as soon as QC is completed
-Open and Controlled Access

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

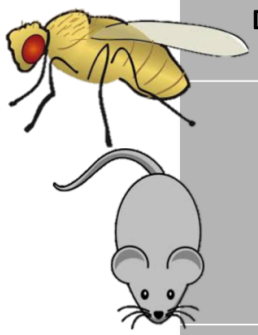
***AMP-AD Knowledge Portal –** https://www.synapse.org/#!Synapse:syn2580853/wiki/409840

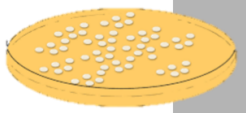
Sage BIONETWORKS Synapse

AMP-AD Knowledge Portal



HUMAN TISSUE	Diagnosis	Assay
Prefrontal Cortex	• Alzheimer's Disease • Mild Cognitive Impairment • Parkinson's Disease • Amyothrophic Lateral Sclerosis • Corticobasal Degeneration • Frontotemporal Dementia • Dementia with Lewy Bodies	• RNAseq • Gene Expression array • miRNA array • ChIPseq • DNA Methylation array • Proteomics • Confocal Imaging • SNP genotypes • Proteomics • Whole Exome Seq
Visual Cortex	• Alzheimer's Disease	• Gene Expression Array • SNP genotypes
Temporal Cortex	• Alzheimer's Disease • Progressive Supranuclear Palsy • Parkinson's Disease	• RNAseq • SNP genotypes
Cerebellum	• Alzheimer's Disease • Progressive Supranuclear Palsy • Parkinson's Disease	• RNAseq
Superiour Temporal Gyrus	• Alzheimer's Disease	• RNAseq • Whole Exome Seq
Parahippocampal Gyrus	• Alzheimer's Disease	• RNAseq
Serum	• Alzheimer's Disease • Mild Cognitive Impairment	• Metabolomics





MODELS	Type	Assay
Drosophila	• TAU • TYROBP • TREM2	• Proteomics • RNAseq
Mouse	• APP • TAU • PSEN1 • HDAC1 • db/db • Stroke	• RNAseq • Gene Expression array • Behavioral analysis • Electrophysiology
CELLULAR MODELS - Human - Rat	• iPSC • iPSC derived organoids • Microglia • Macrophages • Astrocytes • APP/PSEN1, SNRNP70 transduced neurons • SH-SY5Y	• RNAseq • ChIPseq • ELISA (Aβ) • Proteomics

Religious Orders Study and Rush Memory and Aging Project

- Two cohort studies of aging and AD ongoing for 20+ years
- >3,000 older persons without [known] dementia from across the USA
- All agreed to annual detailed clinical evaluation for common chronic conditions of aging with detailed evaluation of risk factors, and blood donation
- All agreed to organ donation at death
- > 900 cases incident MCI
- > 700 cases incident AD dementia
- > 1,200 autopsies

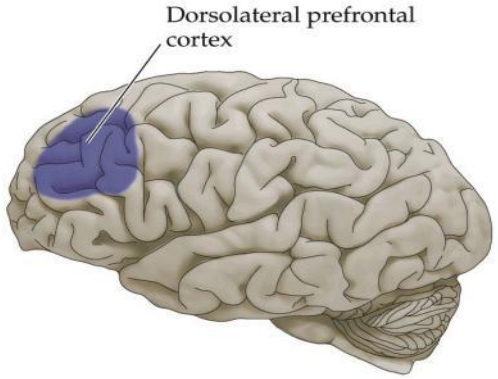
Risk Factors: Medical, Psychological, Experiential, and genome-wide genotyping

Genotypes
Affy 6.0/Illumina Quad
1000G imputation

Genotypes
Whole Exome Sequencing

DNA methylation, histone acetylation

DNA Methylation Illumina 450K
Histone H3K9Ac
ChIP-Seq



Next generation RNAseq, miRNA

RNA profile
mIRNA & RNAseq

MS Proteomic and metabolomic

LC/MS profile
Lipids, proteins

Quantitative neurobiology

Neuropathology
AD, CVD, LBD, HS, TDP

Resilience Markers
Synaptic proteins, LC

Structural and functional MRI

Flair, MP Rage, DTI, SWI, rsfMRI

post-mortem MRI
DTI, MP Rage, T2

Quantitative clinical phenotype

Cognitive Function
19 tests annually

Motor Function
Disability BMI,
Actigraphy

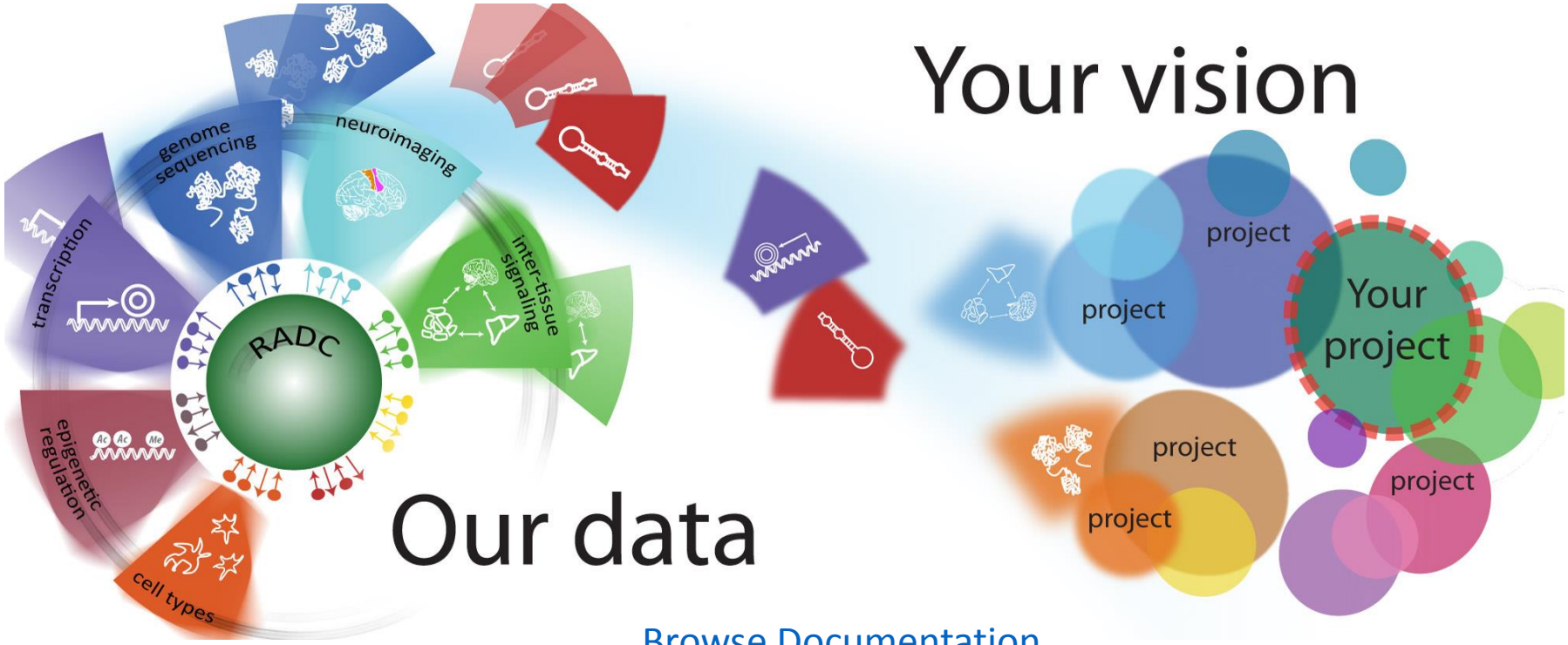
Dynaport – Gait, Sleep, circadian rhythms, Behavioral Economics, Olfaction,

Syndromic phenotype

Clinical Diagnoses
AD, Stroke, PD,

RADC Research Resource Sharing Hub

https://www.radc.rush.edu



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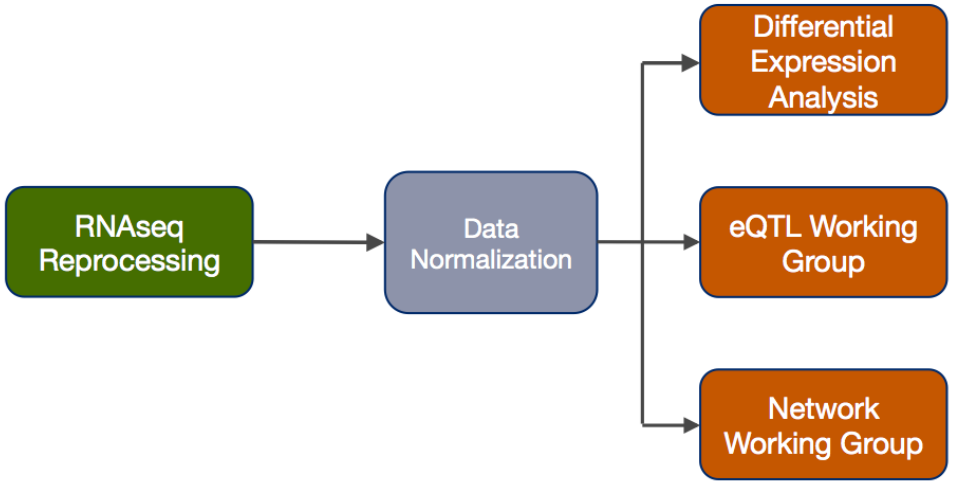
AMP-AD RNASeq Reprocessing WG: Goals and Deliverables

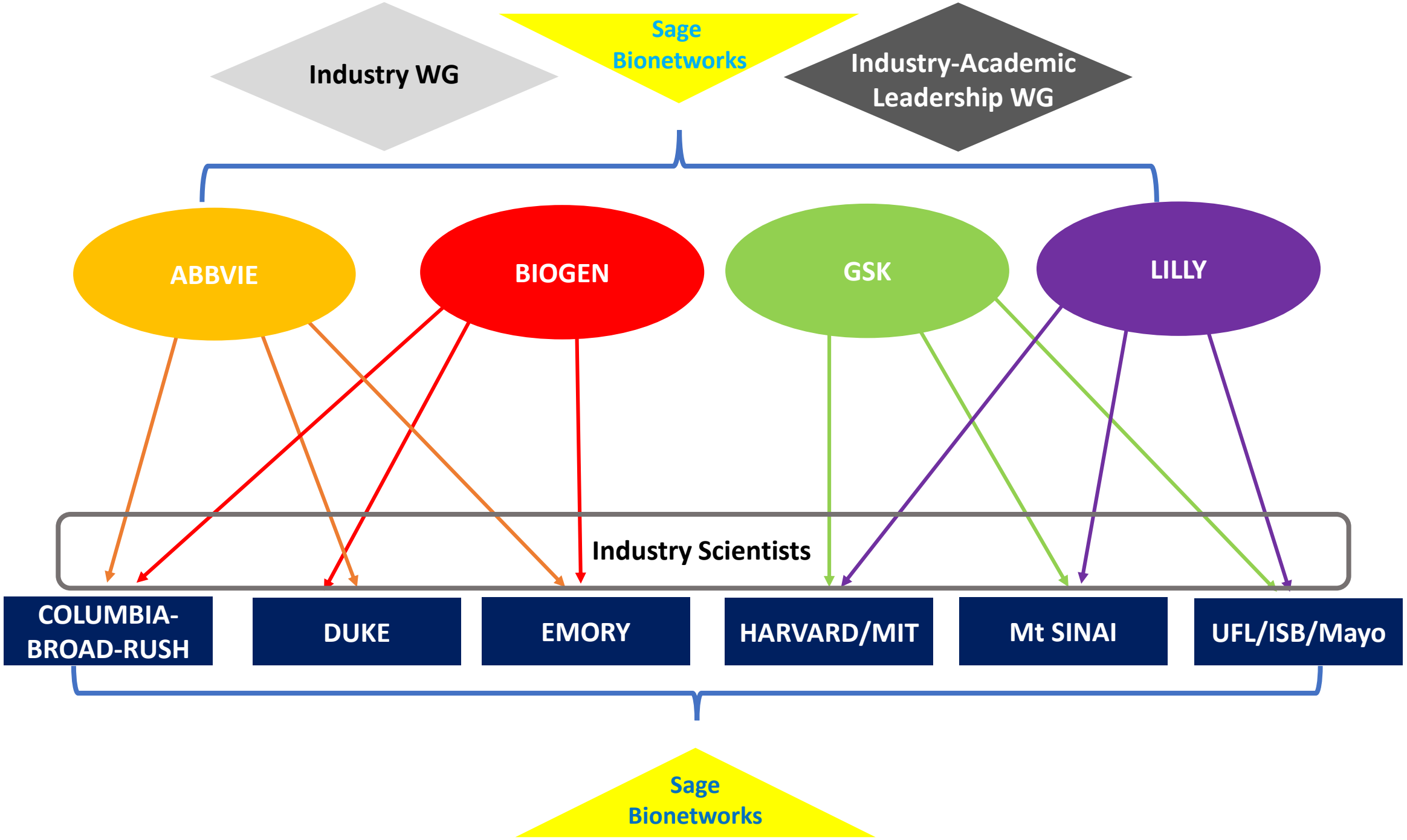
- **Enable joint analysis through uniform reprocessing to reduce technical variation across Human RNAseq datasets**
- **Meta-analysis to inform internal AMP-AD projects and support target selection processes**
- **Development of a standardized resource for external users**



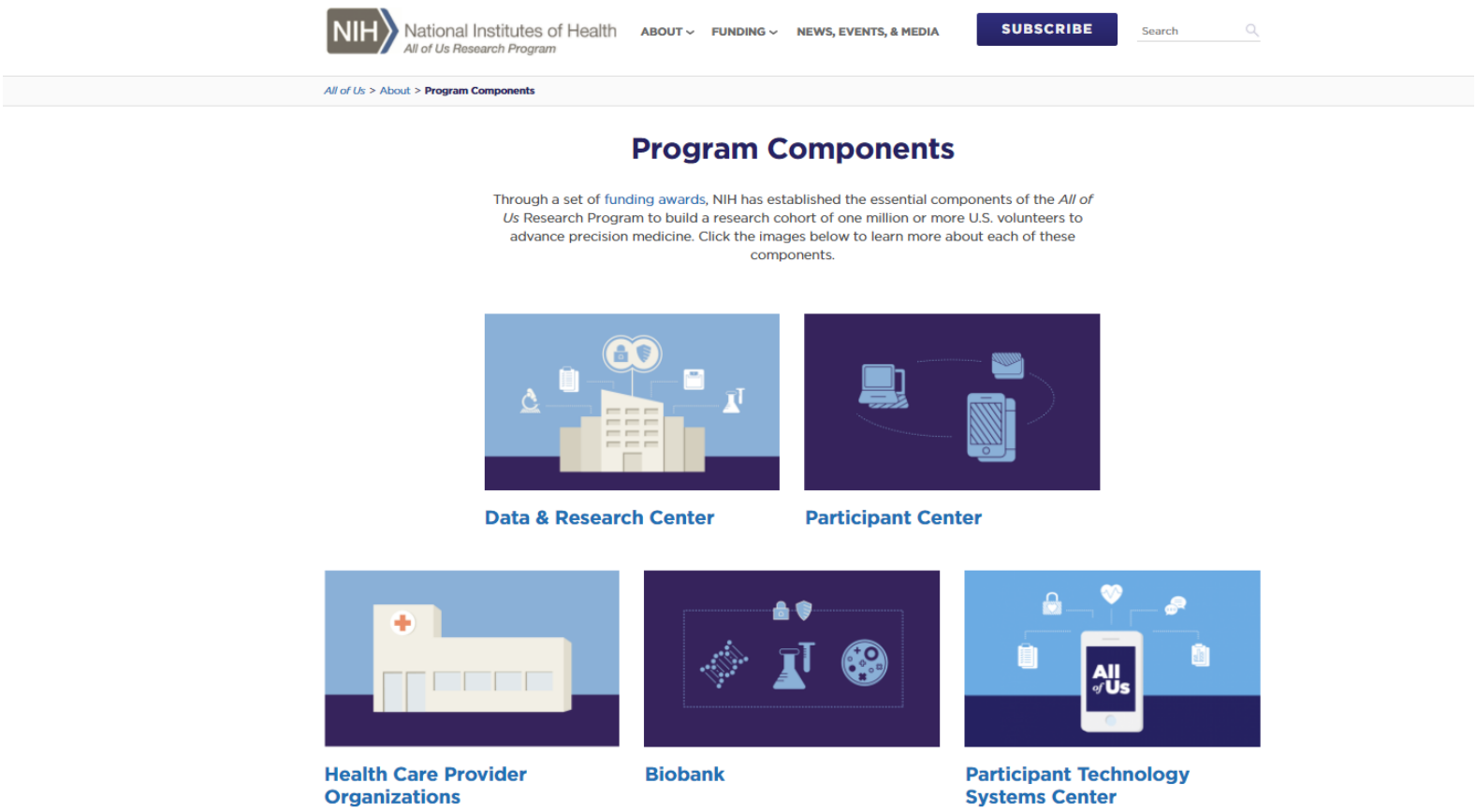
RNAseq reprocessing working group

29 members representing 5 AMPAD academic teams and all 4 industry partners

Contacts: kristen.dang@sagebase.org & thanneer.perumal@sagebase.org


Industry WG
Sage Bionetworks
Industry-Academic Leadership WG
ABBVIE
BIOGEN
GSK
LILLY
Industry Scientists
COLUMBIA-BROAD-RUSH
DUKE
EMORY
HARVARD/MIT
Mt SINAI
UFL/ISB/Mayo
Sage Bionetworks

NIH's All of Us Initiative



Data & Research Center

The Data and Research Support Center will acquire, organize, and provide secure access to what will be one of the world's largest and most diverse datasets for precision medicine research. The center will also provide research support for the scientific data and analysis tools for The Program, helping to build a vibrant community of researchers from community colleges to top health care research institutions and industries, as well as citizen scientists, who can propose studies using this information.

Awardees:

- Vanderbilt University Medical Center, Nashville, Tennessee, working with the Broad Institute, Cambridge, Massachusetts, and Verily, Mountain View, California

Sub-awardees:

- Columbia University Medical Center, New York City
- Northwestern University Feinberg School of Medicine, Chicago, Illinois
- University of Michigan School of Public Health, Ann Arbor, Michigan
- University of Texas Health Science Center at Houston School of Biomedical Informatics, Houston, Texas

Introduction

BD2K funds research and training activities that support the use of Big Data to advance biomedical research and discovery. This includes efforts in enhancing training, resource indexing, methods and tools development, and other data science-related areas.

BD2K Centers

The BD2K Centers of Excellence program has established 11 Centers of Excellence for Big Data Computing and one Center that is a collaborative project with the NIH Common Fund LINCS program, the LINCS-BD2K Perturbation Data Coordination and Integration Center. The centers are located all across the United States. They are large-scale projects aiming to develop new approaches, methods, software tools, and related resources. The Centers will also provide training to advance Big Data science in the context of biomedical research. The 12 BD2K Centers function with the other BD2K grantees as a consortium and collaborate with one another, with the purpose of furthering every aspect of the field of biomedical data science research.

Read more about the BD2K Centers

Resource Indexing

To harness the full potential of Big Data scientists must be able to readily find, cite, and access existing data and other digital objects, such as software. There is no existing infrastructure or incentive that enables this. These basic goals maximize data use, enable sharing, limit duplication of effort, and allow areas of sparse research coverage to be more readily identified. To advance the infrastructure and policies needed to meet these goals, awards in this area address the challenges of resource discovery, citation, and access.

Read more about BD2K awards supporting Resource Indexing

Funding Opportunities

NIGMS

NIGMS Institutional Predoctoral Training Programs

- Behavioral-Biomedical Sciences Interface
- **Bioinformatics and Computational Biology**
- **Biostatistics**
- Biotechnology
- Cellular, Biochemical, and Molecular Sciences
- Chemistry-Biology Interface
- Genetics
- Medical Scientist Training Program (M.D.-Ph.D.)
- Molecular Biophysics
- Molecular Medicine
- **Pharmacological Sciences**
- **Systems and Integrative Biology**

NIGMS

Ruth L. Kirschstein National Research Service Award (NRSA)

- Awards honor Dr. Ruth L. Kirschstein, former Director of the National Institute for General Medical Sciences. Aside from Dr. Kirschsteins scientific accomplishments in polio vaccine development, she was a champion of research training and a strong advocate for the inclusion of underrepresented individuals in the scientific workforce
- **Individual Predoctoral MD/PhD or Other Dual-Doctoral Degree Fellowship** PA-14-150
- **Individual Predoctoral Fellowship** (PA-14-147)
- **Individual Predoctoral Fellowship to Promote Diversity in Health-Related Research** (PA-14-148)
- **Individual Senior Fellowship** (PA-14-151)

PAR 17-032

Translational Bioinformatics Approaches to Advance Drug Repositioning and Combination Therapy Development for Alzheimer's Disease (R01)

Award Budget - Annual direct costs are capped at $500K.

Award Project Period - The maximum project period is 5 years.

PROGRAMMATIC GOAL: Establish new research programs that will promote the use of systems-based, data-driven approaches to create a knowledge base needed for successful drug repositioning and combination therapy development for AD.

To this end this funding opportunity announcement is soliciting projects that use of existing or develop novel computational approaches to identify drugs or drug combinations currently used for other conditions with potential to be efficacious in AD and AD-related dementias.

This initiative encourages cross-disciplinary, team-science approach and academia-industry collaborations.

Research scope/Examples of responsive applications

- Purely computational research aimed at using existing methodology to analyze various types of molecular and clinical data to identify individual drugs or drug combinations with favorable efficacy and toxicity profiles as candidates for repositioning against AD or AD-related dementias.

- Studies proposing the use of translational bioinformatics approaches to integrate existing data with newly generated molecular data collected from biosamples from legacy trials for AD that have tested the efficacy of repurposed drugs (statins, NSAIDs etc.) for the purpose of identifying the molecular determinants of responder phenotypes.

Research scope/Examples of responsive applications

- Research that combines computational and experimental approaches to generate data-driven predictions on the efficacy of repurposed drugs or drug combinations, followed by efficacy testing in proof-of-principle animal studies or in proof-of-principle human trials.

- Research that combines computational and experimental approaches to identify quantitative methods that can assess synergy/additivity of candidate therapeutics, including synergy between drugs and non-pharmacological perturbations.

- Of particular interest are projects that leverage the network concept of drug targets and the power of phenotypic screening to advance rational drug repurposing and data-driven development of drug combinations based on the ability of single or multiple therapeutic agents to perturb entire molecular networks away from disease states in cell-based and/or animal models.

- **The development and testing of new therapeutic agents is outside the scope of this funding opportunity.**

- ***Applicants are expected to adhere to NIH guidelines for rigorous study design and transparent reporting to maximize the reproducibility and translatability of their findings.***