SageBionetworks

Community management and metadata

Sara Gosline, James Eddy

May 15th, 2018

What is Sage?

A non-profit research institute focused on finding ways to increase *collaboration* and *communication* in science

Better Science Together

Ongoing efforts to support collaborative science

- Mobile apps to connect patients within disease communities
- DREAM challenges to incentivize computational scientists to study novel biological datasets
- Work with granting agencies/foundations to support data sharing (and ultimately community building) across funded scientists

Computational Oncology team

Research scientists:

Sara Gosline, PhD, McGill
systems biology

James Eddy, PhD, UIUC
systems biology

Julie Bletz, PhD, Stanford
genetics

Brian White, PhD, Wash U
computational biology

Kristen Dang, PhD, UNC
computational biology & bioinformatics

Michael Mason, PhD, UCLA
statistics

Robert Allaway, PhD, Dartmouth
RAS signaling

Group leader:

Justin Guinney, PhD, Duke
computational biology & bioinformatics

Research associates:

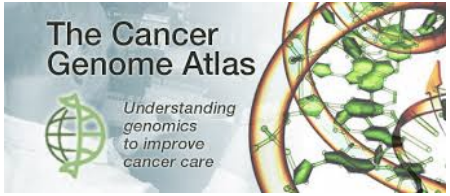
Thomas Yu, UW

Xindi Guo, UW

Andrew Lamb, Northeastern

Sage supports diverse communities across oncology

PARKER INSTITUTE
for CANCER IMMUNOTHERAPY



… and many others

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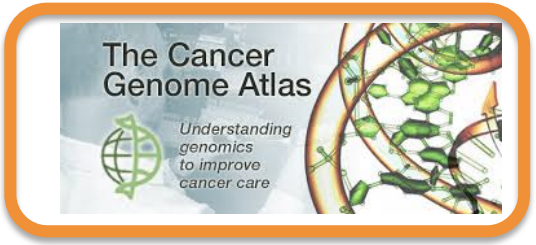
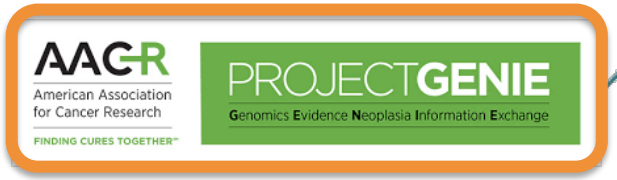
Some communities have unique metadata needs





What is Project GENIE?

- A collaboration of the AACR and cancer centers around the world.
- A data registry of clinical cancer sequencing results accompanied by clinical data.

By the numbers…

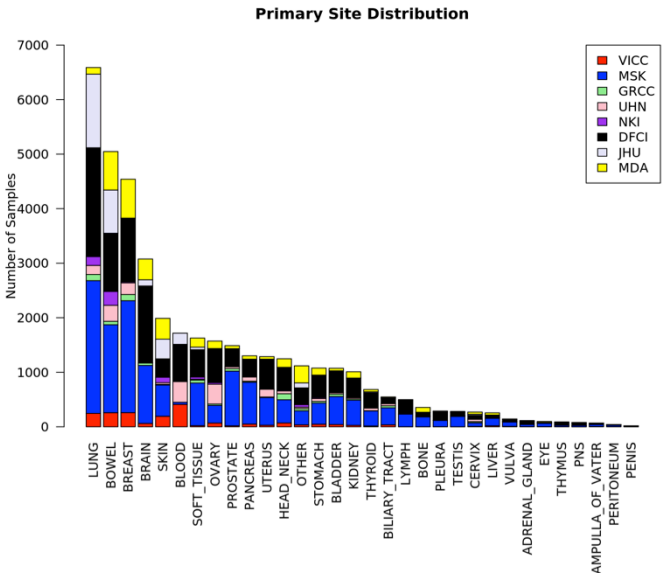
GENIE public release 3.0

39,600 samples

21 sequencing assays

8 cancer centers

15 primary sites with > 1000 samples



Sage serves as data harmonization intermediate

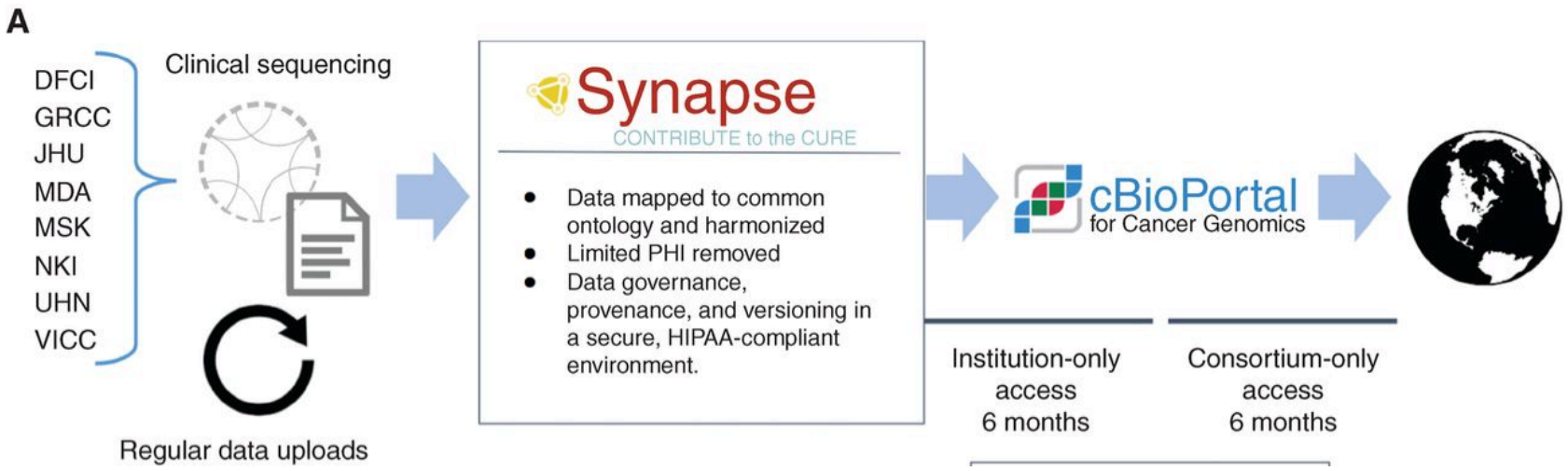


Figure 1. GENIE at a glance.
The AACR Project GENIE Consortium. Cancer Discovery. 2017

GENIE captures *clinical* and *genomic* data

Sample clinical
Sample ID
Oncotree code
Sample type
Seq assay ID
Age at seq report
Patient ID
Center
Seq Quarter

Patient clinical
Patient ID
Sex
Primary race
Secondary race
Tertiary race
Ethnicity
Center
Birth year

Genomic
Position
HUGO Symbol
Seq assay ID
Variant type
Sample ID
+ VEP annotations

GENIE's clinical data committee establishes data elements and agrees on definitions across all consortium members. External standards used:

- NAACCR (in use)
- NCI Thesaurus (under consideration)
- RxNorm (under consideration)

Others communities work with Sage to adopt standards

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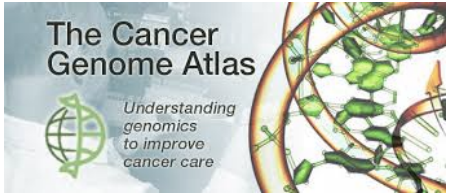
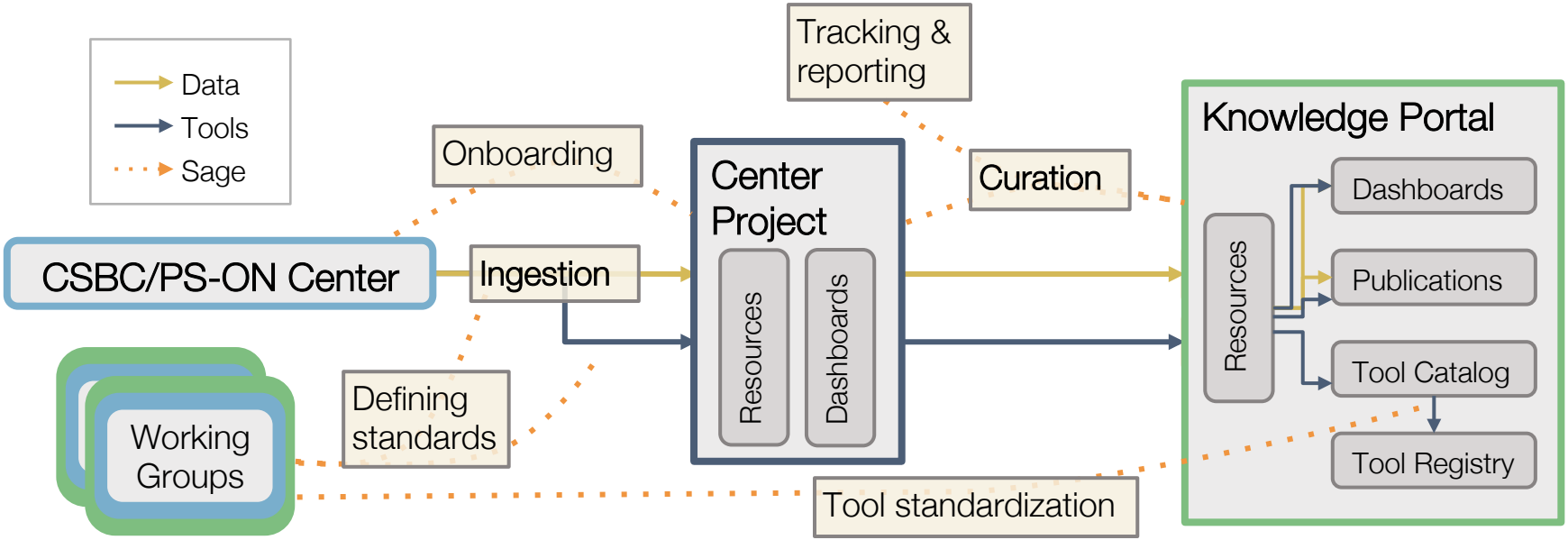
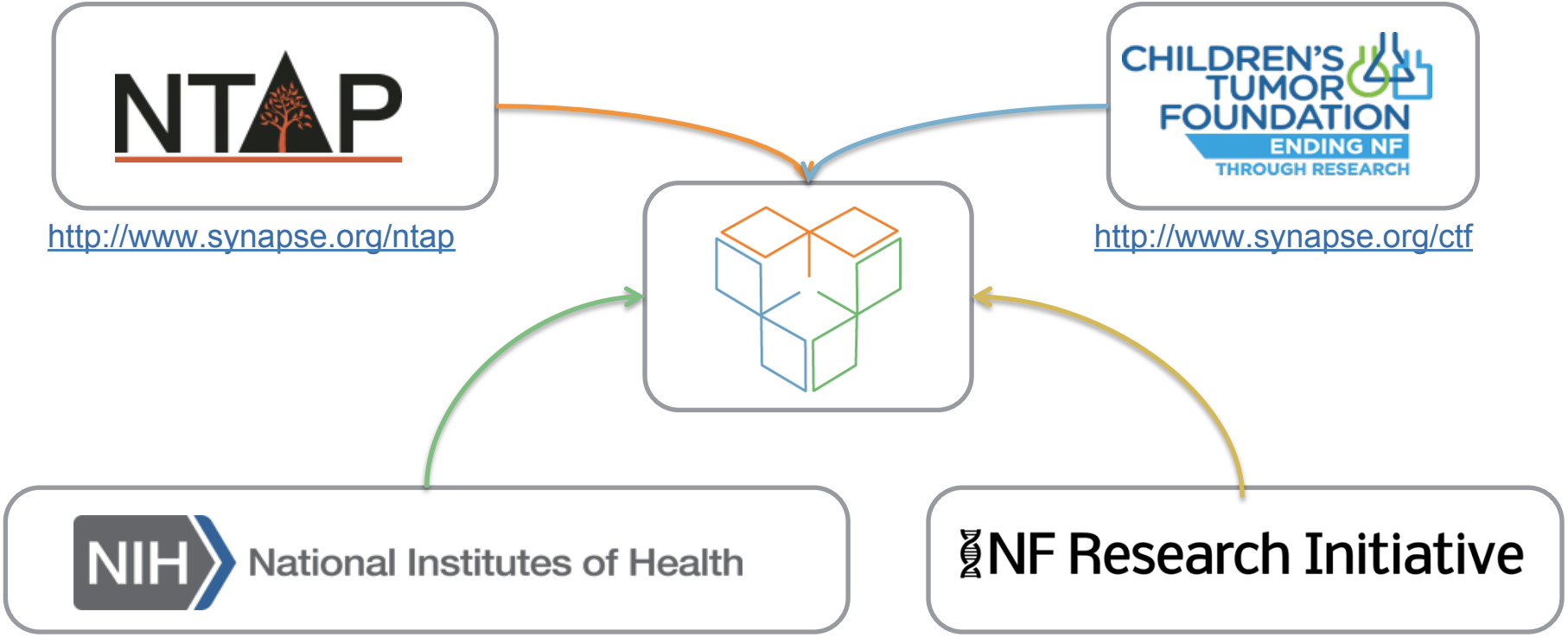
for CANCER IMMUNOTHERAPY



CSBC/PS-ON: thematic organization of publicly shared data

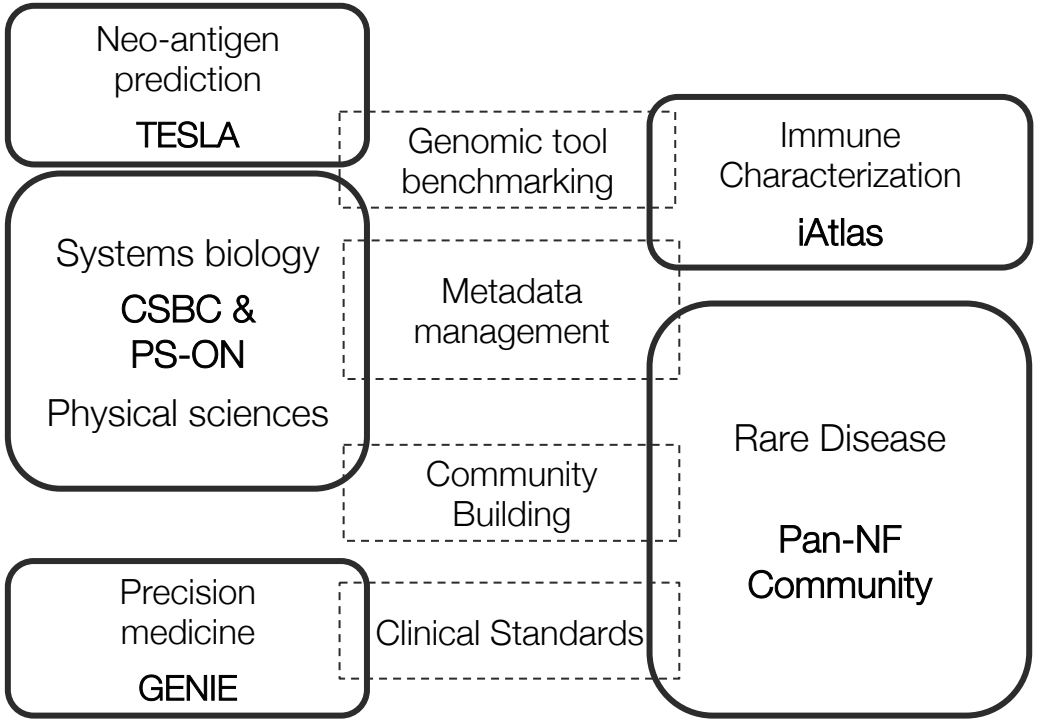


Neurofibromatosis: sharing big data across a small set of patients



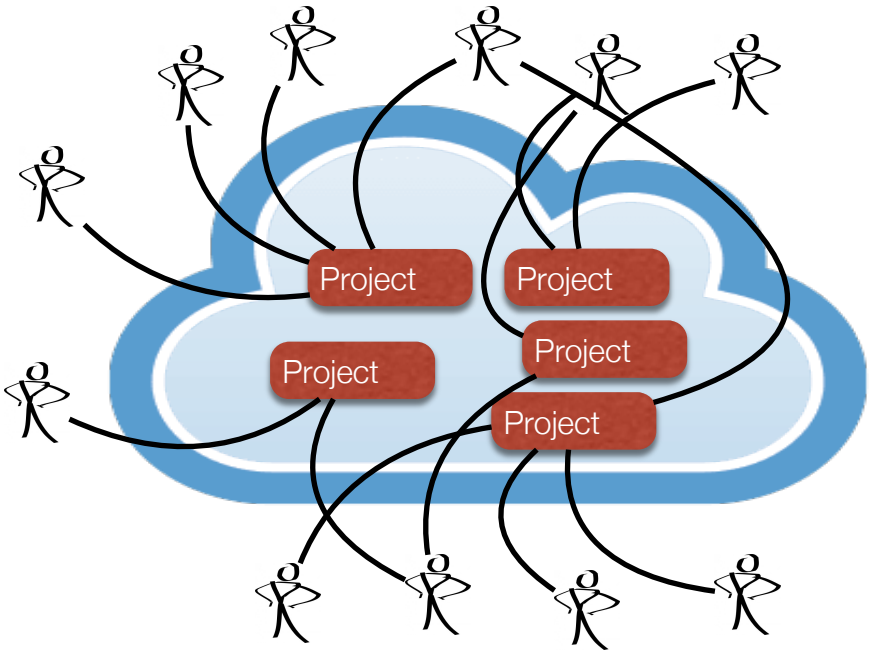
http://www.synapse.org/dhart

Despite diversity we can solve *common* problems



Projects share common processes & infrastructure: Synapse

- Typical data ingest
  - Linked from federated ecosystem site, e.g. GDC, GEO
  - Uploaded to Synapse
- Resource management in Synapse
  - Cloud-based resource
  - Centrally located projects
  - Scientists can interact with individual projects



Synapse projects create collaborative space

Wiki describes project

File browser

Structured data

Discussion

Center for Modeling Tumor Cell Migration Mechanics

Search | Sara Gosline (sgosline) | Help

Synapse ID: syn7349745 | Storage Location: Synapse Storage | Project Settings | Tools

Wiki | Files | Tables | Discussion | Docker

Center for Modeling Tumor Cell Migration Mechanics

- Center Investigators
- Research Projects and Core Facilities
- Data and Tools
  - Cell Migration Simulator (CMS)
  - Controlling the Cellular Microenvironment
  - Sleeping Beauty (SB) Transposon

Edit Order

The PSON U54 Research Center @ University of Minnesota

Center Title

Center for Modeling Tumor Cell Migration Mechanics

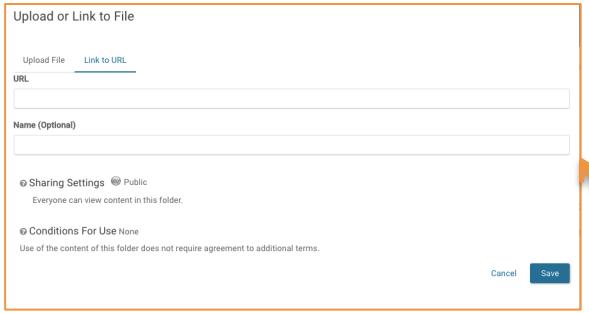
Overall Project Title

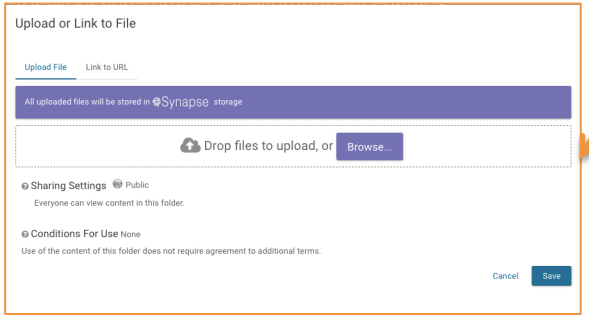
Simulating Tumor Cell Migration

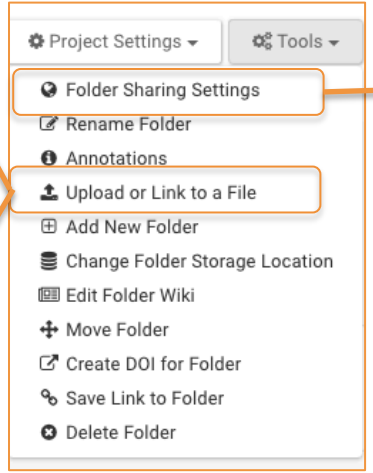
Center Website

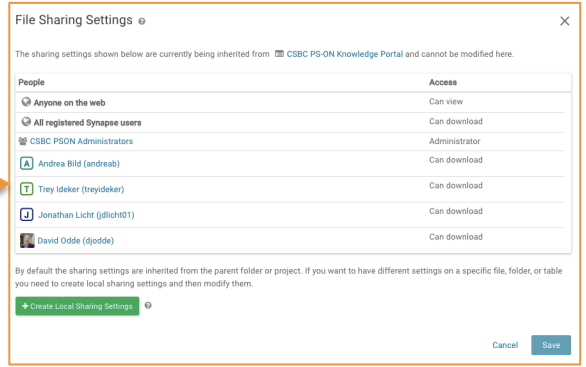
http://psoc.umn.edu/

Synapse enables flexible data ingestion & governance









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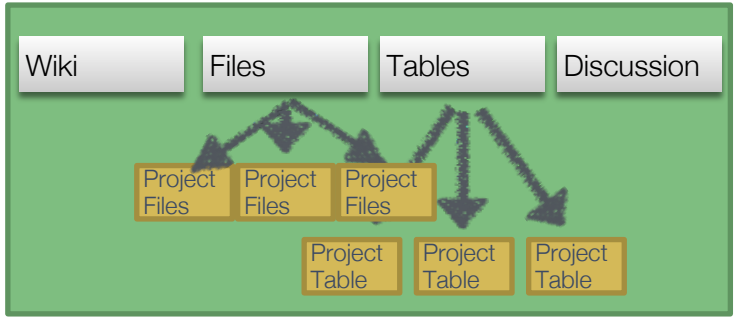
Synapse provides protected way to store & share data



Individual projects allow individual contributors to:

- Upload/annotate files ahead of release
- Analyze files
- Share individual files or results with collaborators
- Contextualize data with wiki figures and text

Every file gets assigned distinct metadata

- Applied to each file
- Standardized descriptions of what is in the file
- Key-value pairs
- Same values used across *all* projects at Sage to facilitate cross-dataset analysis

Files » Gene Expression Data » PNF Cells (gencodeV24Ali... » C856CANXX_1_RNASeq_Kalli...

Share | Annotations | File History | Tools

C856CANXX_1_RNASeq_Kallisto_gencodev24_quants.h5 Download

other download options

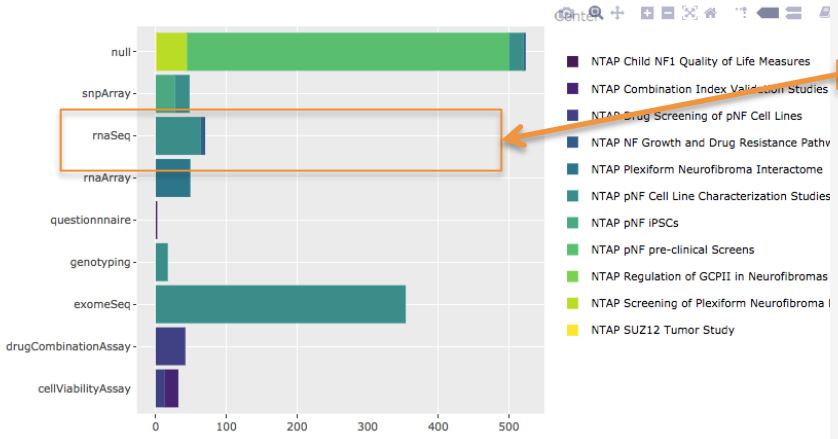
Download file as: C856CANXX_1_RNASeq_Kallisto_gencodev24_quants.h5 | 79.607 MB | Synapse Storage *md5*

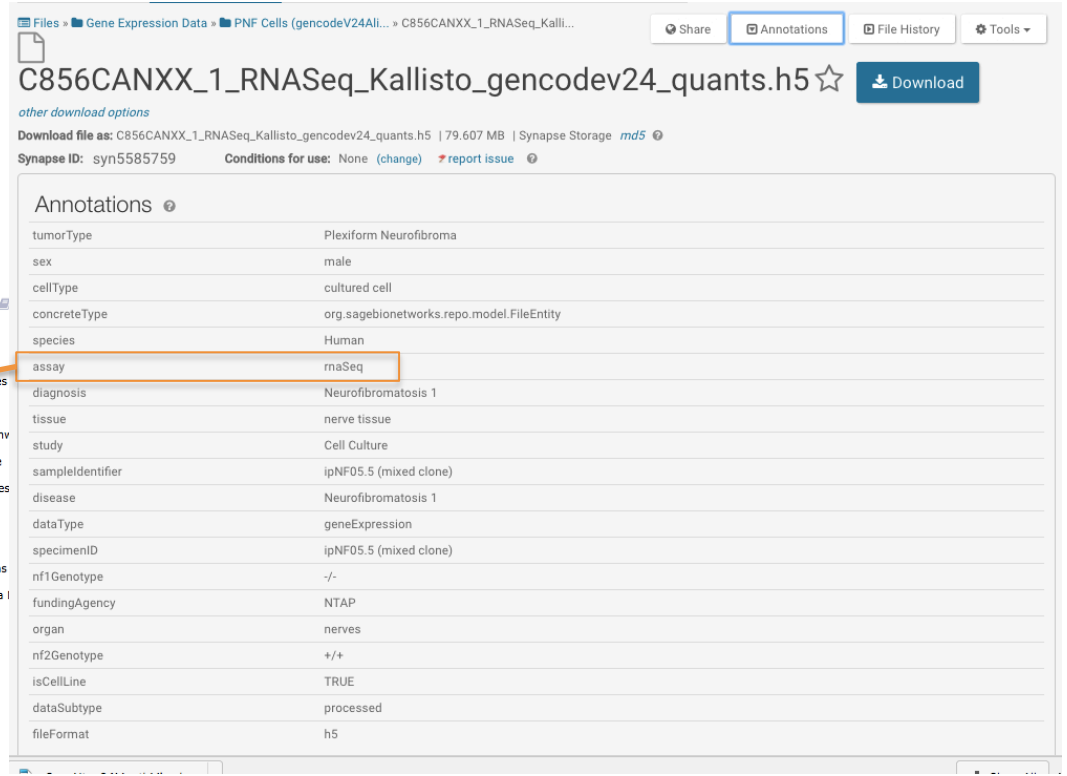
Synapse ID: syn5585759 **Conditions for use:** None (change) report issue

Annotations

tumorType	Plexiform Neurofibroma
sex	male
cellType	cultured cell
concreteType	org.sagebionetworks.repo.model.FileEntity
species	Human
assay	rnaSeq
diagnosis	Neurofibromatosis 1
tissue	nerve tissue
study	Cell Culture
sampleIdentifier	ipNF05.5 (mixed clone)
disease	Neurofibromatosis 1
dataType	geneExpression
specimenID	ipNF05.5 (mixed clone)
nf1Genotype	-/-
fundingAgency	NTAP
organ	nerves
nf2Genotype	+/+
isCellLine	TRUE
dataSubtype	processed
fileFormat	h5

These metadata enable summaries across projects





http://www.synapse.org/pnfCellCulture

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Diverse metadata needs require collective efforts

- Standardized terms and vocabulary for community resources
  - Pulled from known ontologies
  - Updated with missing terms
- Tooling & processes to ascribe resource annotations
- Need to provide standards across Sage-led communities but also flexibility

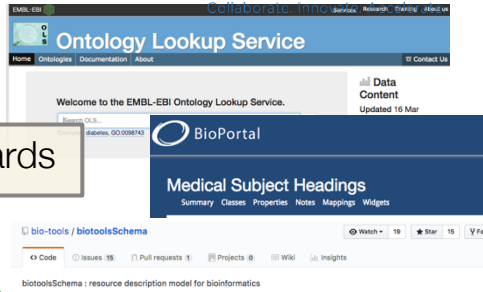
Organically evolving metadata and SOPs

Global Alliance for Genomics & Health

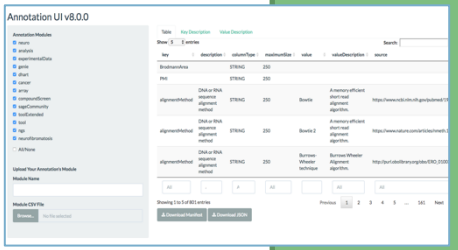
Define Use Cases

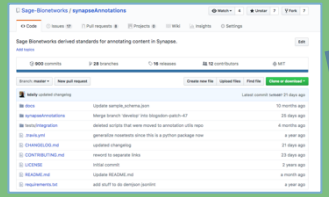
Users, Working Groups

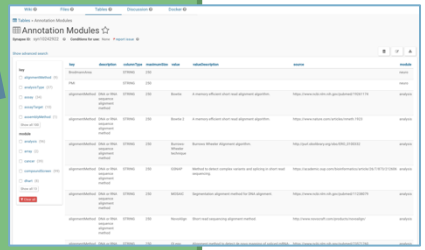
Search Standards



GitHub Site







Sage Annotations Team

Annotation Browser

Synapse Table

SageBionetworks

Reviewed by Sage-wide team via GitHub

Sage-Bionetworks / synapseAnnotations

Code | Issues 19 | Pull requests 5 | ZenHub | Projects 0

Sage Bionetworks derived standards for annotating content in Synapse.

Add topics

900 commits | 30 branches | 16 releases

Branch: master | New pull request

kdaily updated changelog

docs	Update sample_schema.json
synapseAnnotations	Merge branch 'develop' into blogsdon-patch-47
tests/integration	deleted scripts that were moved to annotation util
.travis.yml	generalize nosetests since this is a python packag
CHANGELOG.md	updated changelog
CONTRIBUTING.md	reword to separate links
LICENSE	Initial commit
README.md	Update README.md
requirements.txt	add stuff to do demjson jsonlint

Filters | is:issue is:open | Labels | Milestones | New issue

19 Open | 88 Closed | Author | Labels | Projects | Milestones | Assignee | Sort

- Need to find solution to cancer subtype — #366 opened 22 days ago by sgosline | New Issues — 4
- Add multi-sample/individual SOP to contributing.md — #365 opened on Mar 21 by sgosline | New Issues
- Get serious about tool/model annotations — #364 opened on Mar 20 by jaeddy | New Issues — 2
- Mouse Strain key [question] — #362 opened on Mar 9 by amapeters | New Issues — 1
- Think more and come to some conclusion about JSON-LD — #351 opened on Feb 27 by kdaily | 2018-05-08 | New Issues — 8
- Discussion about mouse behavioral analysis annotations — #341 opened on Feb 21 by ychae | 2018-02-28 | New Issues — 3
- should keys have sources? [question] — #301 opened on Dec 12, 2017 by kdaily | New Issues — 1
- Recommended annotations for QC files [help wanted] — #292 opened on Nov 28, 2017 by xindiguo | New Issues — 2
- Synonyms/aliases for annotation values [enhancement] — #270 opened on Oct 24, 2017 by jaeddy | New Issues — 2
- add cellType: monocyte derived microglia [AMP-AD sprint] [create value] — #260 opened on Oct 19, 2017 by ychae | New Issues — 1
- add cellType: iPSC-derived neurons [AMP-AD sprint] [create value] — #258 opened on Oct 19, 2017 by ychae | New Issues — 2

https://github.com/Sage-Bionetworks/synapseAnnotations

SageBionetworks

Metadata dictionary is always evolving

- Want to get as many terms needed for analysis, but no burden researchers
- Adding weekly to satisfy specific use cases

Challenges

Synapse-based limitations

- Metadata requires key-value pairs, no hierarchy
- Metadata are tied to file
- Very flexible, can annotate with *anything*

- We're working on these things!

Diverse requirements within and across projects

- Most projects are not *data generation* projects, require on-the-fly identification of metadata terms
- Some projects require more depth than others, for example:
  - Is this cancer or not?
  - What is the organ of origin?
  - What subtype of cancer?
- Not just data:
  - Tools
  - Analysis

In the community: lack of single standard

- Ontologies are limited to a single domain
  - Defining disease and clinical parameters
  - Defining computational analysis or experimental protocols
  - Defining tools
- We like to balance using existing terms with what is provided
  - For example: ChIP-Seq can be applied to transcription factor or histone mark, do we:
    - Create TF ChIP-Seq and histone ChIP-Seq?
    - Create a new term called assayTarget and define there?

Dearth of tools in the field

- How can we validate that metadata is correct?
- Schema are still very hard to visualize, select in piecemeal
- Semi-automated metadata assignment
- Mapping between ontologies

Summary

- Sage has a diverse set of projects/communities
- We work to standardize metadata and tools across these communities
- Adhere to standards whenever possible

Questions?

Extra slides

Select metadata dictionary

- Online tool enables download of manifest or JSON file

Annotation UI v8.0.0

Annotation Modules

- neuro
- analysis
- experimentalData
- genie
- dhart
- cancer
- array
- compoundScreen
- sageCommunity
- toolExtended
- tool
- ngs
- neurofibromatosis
- All/None

Upload Your Annotation's Module

Module Name

Module CSV File

Browse... No file selected

Table | Key Description | Value Description

Show 50 entries Search:

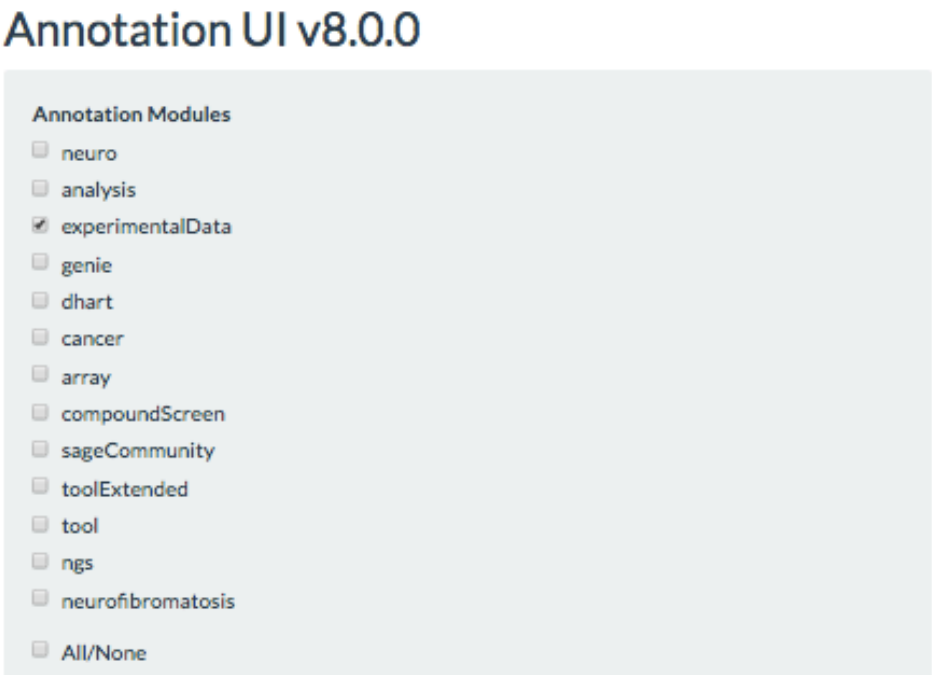
key	description	columnType	maximumSize	value	valueDescription	source
assay	The technology used to generate the data in this file	STRING	250	ATACSeq	Open chromatin regions measured by sequencing DNA after assay for transposase-accessible chromatin (ATAC) treatment	http://purl.obolibrary.org/obo/OBI_0002039
assay	The technology used to generate the data in this file	STRING	250	ChIPSeq	Chromatin immuno-precipitation followed by sequencing	http://purl.obolibrary.org/obo/OBI_0000716
assay	The technology used to generate the data in this file	STRING	250	FIA-MSMS	Flow injection analysis - tandem mass spectrometer	https://www.ncbi.nlm.nih.gov/pubmed/28667829
assay	The technology used to generate the data in this file	STRING	250	HI-C	Chromatin interactions detected by HI-C protocol	http://www.ebi.ac.uk/efo/EFO_0007693
assay	The technology used to generate the data in this file	STRING	250	ISOSeq	Full isoform sequencing	
assay	The technology used to generate the data in this file	STRING	250	LC-MS	A method where a sample mixture is first separated by liquid chromatography before being converted into ions which are characterised by their mass-to-charge ratio and relative abundance	http://purl.obolibrary.org/obo/CHMO_0000524

https://shiny.synapse.org/users/nsanati/annotationUI/

SageBionetworks

Select metadata dictionary

- Select module of interest
  - experimentalData
  - cancer
  - sageCommunity
  - ngs



https://shiny.synapse.org/users/nsanati/annotationUI/

Select metadata dictionary

- Learn about keys/values

Table | Key Description | Value Description

Show 50 entries

Search:

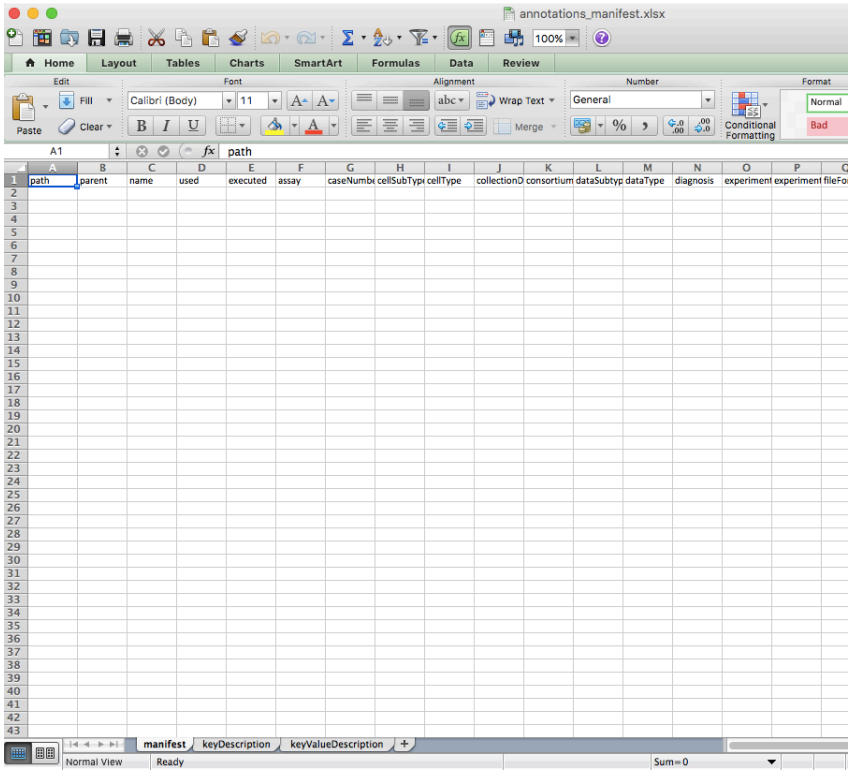
key	description	columnType	maximumSize	value	valueDescription	source
assay	The technology used to generate the data in this file	STRING	250	ATACSeq	Open chromatin regions measured by sequencing DNA after assay for transposase-accessible chromatin (ATAC) treatment	http://purl.obolibrary.org/obo/OBI_0002039
assay	The technology used to generate the data in this file	STRING	250	ChIPSeq	Chromatin immuno-precipitation followed by sequencing	http://purl.obolibrary.org/obo/OBI_0000716

https://shiny.synapse.org/users/nsanati/annotationUI/

SageBionetworks

Download terms as manifest, fill out

- Identify files of interest
- Browse keys/values
- Upload to file view programmatically or via web UI



SageBionetworks

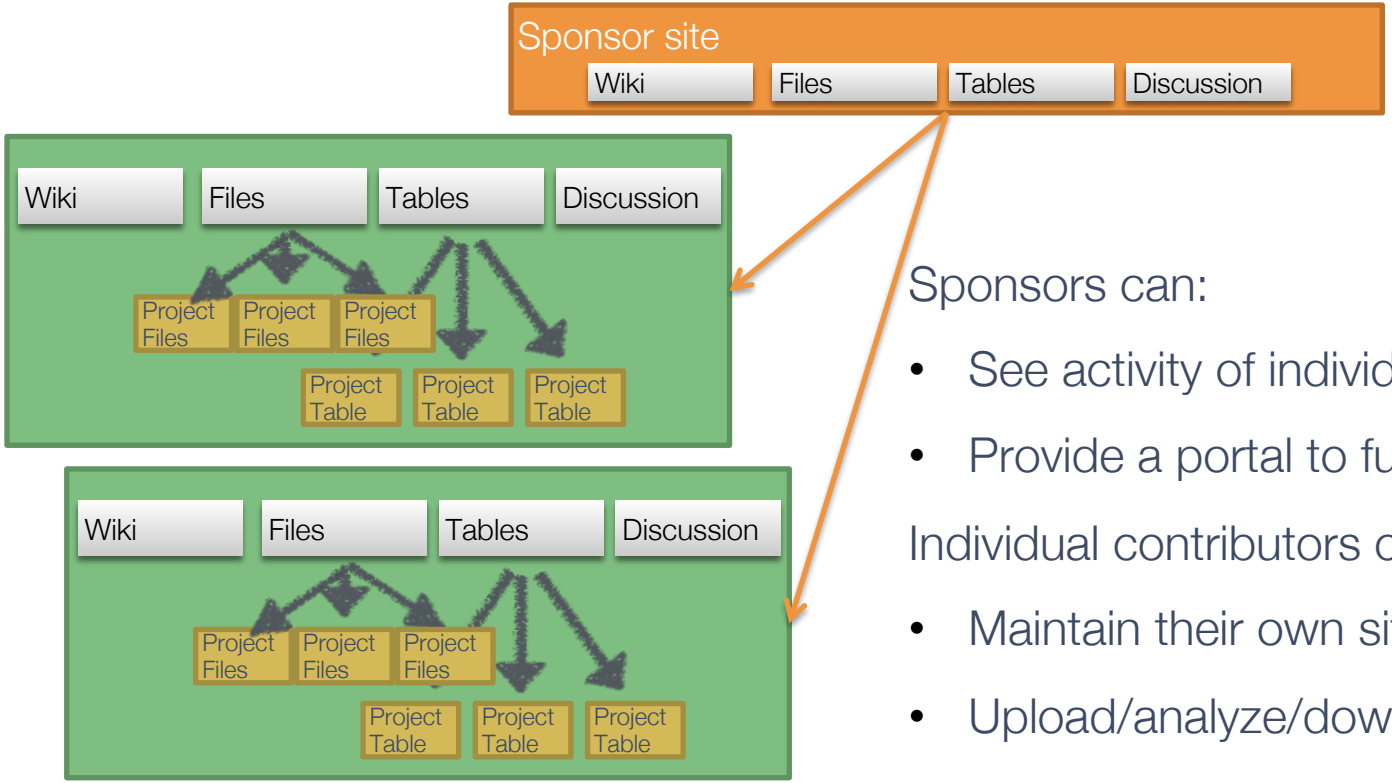
Can be applied via command line or file view

- Results are viewed on web
- Can be edited/updated

diagnosis	egfrStatus	fileFormat	fundingAgency	idh1Status	individualID	isMultiIndividual	isMultiSpecimen	location	organ	platform	resourceType	sex	species	specimenID	study	tissue	tumorType	geoAccession	libraySource	molecule
Brain Cancer		csv				False	False		brain	NextSeq500	experimentalData		Human					GSE84465		
Brain Cancer		csv	NIH-NCI			True	True		brain	NextSeq500	experimentalData				scRNA		Glioblastoma	GSE84465	transcriptomic	polyA RNA
Breast Cancer		html							breast											
Breast Cancer		SRA			BC11	False	False			HiSeq2500	experimentalData		Human	BC11_88	scRNA	primary tumor	breast cancer	GSM2392141	transcriptomic	total RNA
Breast Cancer		SRA			BC11	False	False			HiSeq2500	experimentalData		Human	BC11_81	scRNA	primary tumor	breast cancer	GSM2392140	transcriptomic	total RNA
Breast Cancer		SRA			BC11	False	False			HiSeq2500	experimentalData		Human	BC11_78	scRNA	primary tumor	breast cancer	GSM2392139	transcriptomic	total RNA
Breast Cancer		SRA			BC11	False	False			HiSeq2500	experimentalData		Human	BC11_70	scRNA	primary tumor	breast cancer	GSM2392138	transcriptomic	total RNA
Breast Cancer		SRA			BC11	False	False			HiSeq2500	experimentalData		Human	BC11_69	scRNA	primary tumor	breast cancer	GSM2392137	transcriptomic	total RNA
Breast Cancer		SRA			BC11	False	False			HiSeq2500	experimentalData		Human	BC11_56	scRNA	primary tumor	breast cancer	GSM2392136	transcriptomic	total RNA

SageBionetworks

Summaries can be aggregated across projects workspaces



Sponsors can:

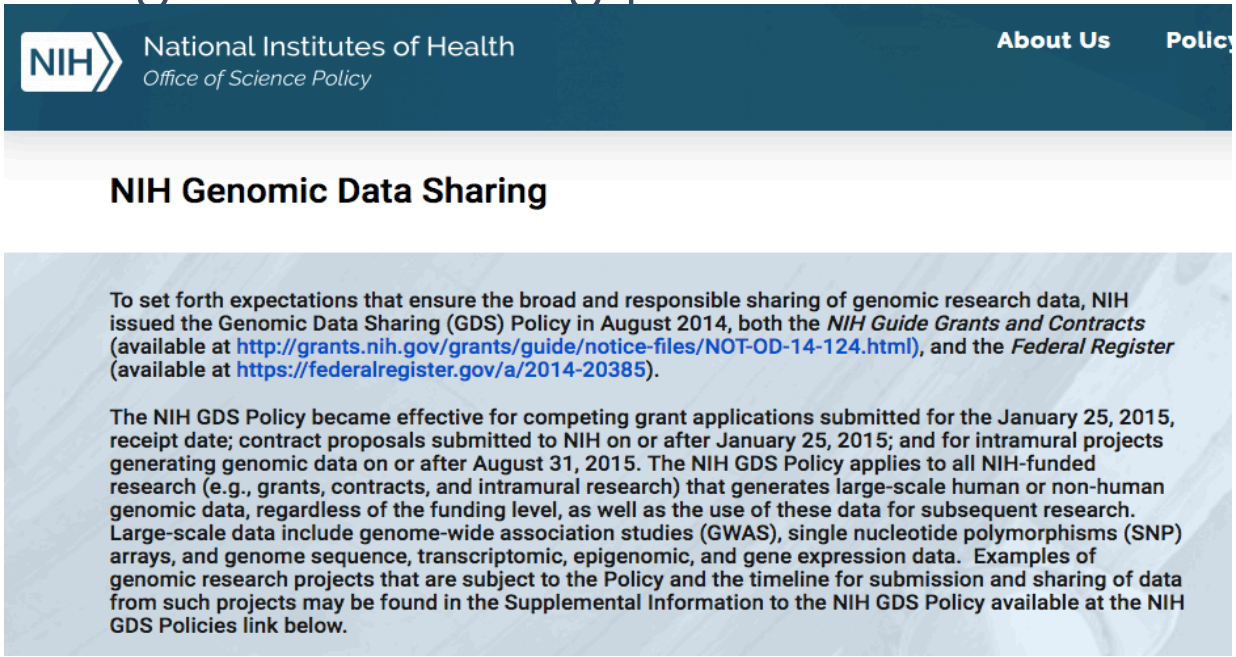
- See activity of individual projects
- Provide a portal to funded research

Individual contributors can:

- Maintain their own site
- Upload/analyze/download files as needed

Building **data repositories:** a way to encourage data sharing

- Journals and the NIH are more actively monitoring - and enforcing - data sharing policies.



National Institutes of Health
Office of Science Policy

About Us Policy

NIH Genomic Data Sharing

To set forth expectations that ensure the broad and responsible sharing of genomic research data, NIH issued the Genomic Data Sharing (GDS) Policy in August 2014, both the *NIH Guide Grants and Contracts* (available at http://grants.nih.gov/grants/guide/notice-files/NOT-OD-14-124.html), and the *Federal Register* (available at https://federalregister.gov/a/2014-20385).

The NIH GDS Policy became effective for competing grant applications submitted for the January 25, 2015, receipt date; contract proposals submitted to NIH on or after January 25, 2015; and for intramural projects generating genomic data on or after August 31, 2015. The NIH GDS Policy applies to all NIH-funded research (e.g., grants, contracts, and intramural research) that generates large-scale human or non-human genomic data, regardless of the funding level, as well as the use of these data for subsequent research. Large-scale data include genome-wide association studies (GWAS), single nucleotide polymorphisms (SNP) arrays, and genome sequence, transcriptomic, epigenomic, and gene expression data. Examples of genomic research projects that are subject to the Policy and the timeline for submission and sharing of data from such projects may be found in the Supplemental Information to the NIH GDS Policy available at the NIH GDS Policies link below.

New terms are gleaned from existing ontologies

EMBL-EBI

Services | Research | Training | About us

Ontology Lookup Service

Home | Ontologies | Documentation | About | Contact Us

Welcome to the EMBL-EBI Ontology Lookup Service.

Search OLS...

Examples: diabetes, GO:0098743

Looking for a particular ontology?

About OLS

The Ontology Lookup Service (OLS) is a repository for biomedical ontologies that aims to provide a single point of access to the latest ontology versions. You can browse the ontologies through the website as well as programmatically via the OLS API. OLS is developed and maintained by the Samples, Phenotypes and Ontologies Team (SPOT) at EMBL-EBI.

Related Tools

In addition to OLS the SPOT team also provides the OxO, Zooma and Webulous services. OxO provides cross-ontology mappings between terms from different ontologies. Zooma is a service to assist in mapping data to ontologies in OLS and Webulous is a tool for building ontologies from spreadsheets.

Contact Us

For feedback, enquiries or suggestion about OLS or to request a new ontology please contact ols-support @ ebi.ac.uk. For bugs or problems with the code or API please report on GitHub issue For announcements relating to OLS, such as new releases and new features sign up to the OLS announce mailing list

Data Content

Updated 25 Apr 2018 03:03

- 207 ontologies
- 5,376,937 terms
- 17,811 properties
- 479,385 individuals

Tweets by @EBIOLS

EBISPOT OLS
@EBIOLS
Our new Ontology mapping service (OxO) will be integrated into OLS in 2018 ebi.ac.uk/spot/oxo/
Dec 18, 2017

EBISPOT OLS
@EBIOLS
OLS hits 200 #ontologies!

Sage approach: build community, not just a repository

- **Platform** is the foundation of a community

Sage approach: build community, not just a repository

- **Platform** is the foundation of a community
- Engaging the **people** in the community

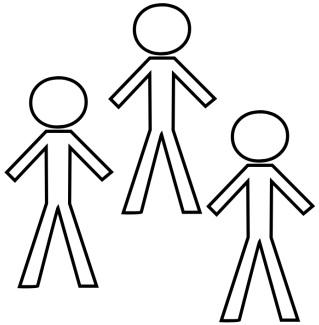
Sage approach: build community, not just a repository

- **Platform** is the foundation of a community
- Engaging the **people** in the community
- Shared **principles** build trust across community

Sage is built on these three pillars

Platform

People



Principles

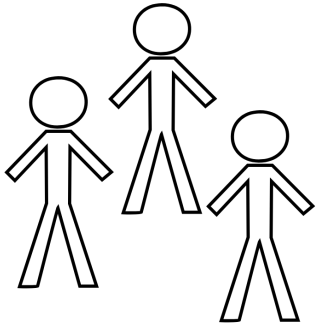
Sage is built on these three pillars

Platform

Synapse

Bridge

People



Principles

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Platform

Synapse

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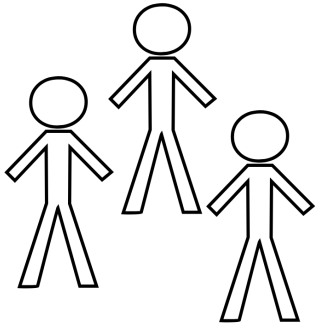
People



Principles

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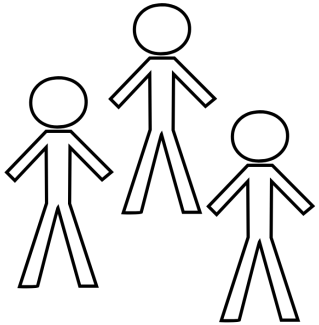
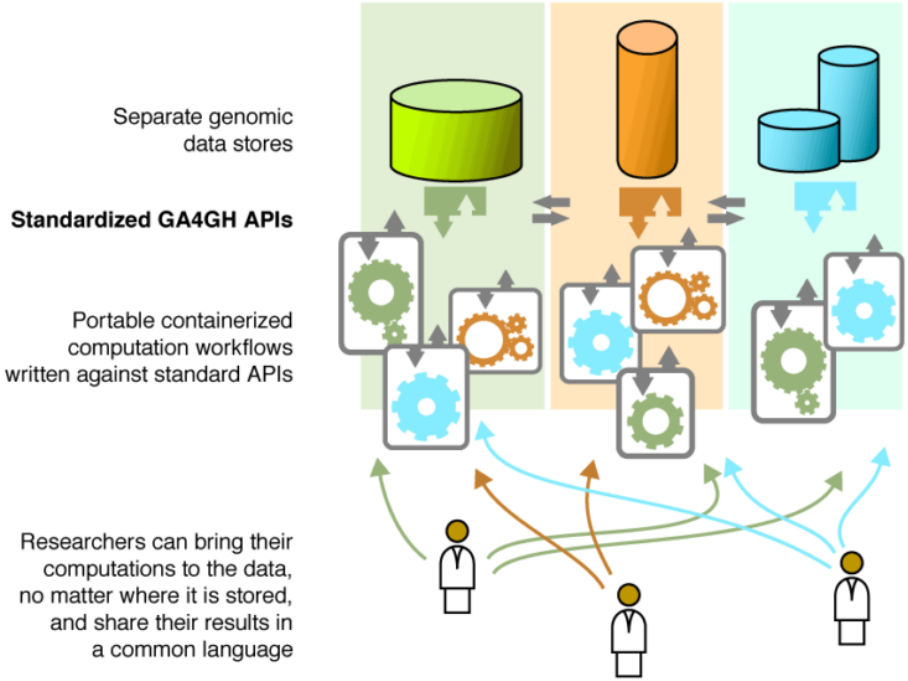


Principles

Findable Interoperable
Accessible Reusable

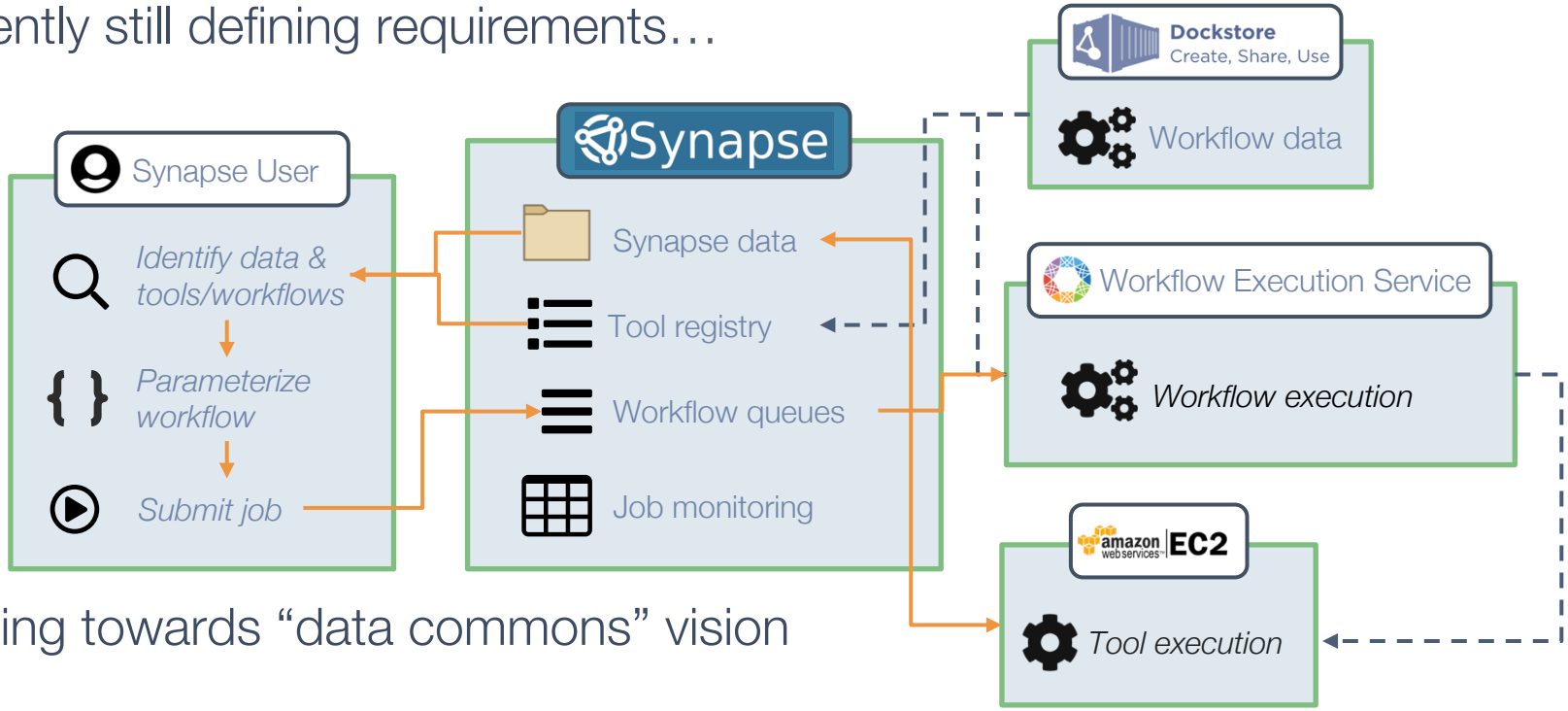
Workflows on Synapse: Emerging Requirements

- Workflow use cases for Sage and Synapse communities:
  - Challenges, benchmarking
  - Data coordination, curation, & validation
  - Mobile data processing
  - Scientific computation
- Solutions and standards developed by communities like GA4GH, BD2K aim to make writing, sharing, and running workflows easier



Reproducible analysis ecosystem through Synapse

- Currently still defining requirements…



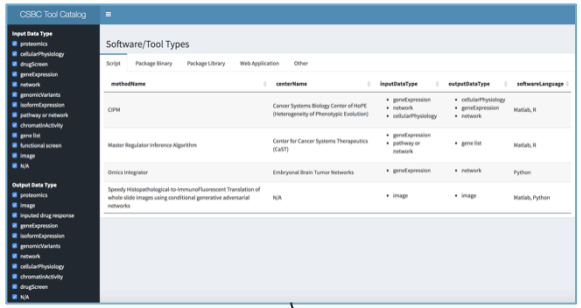
- Building towards "data commons" vision

Future: “Communities” and Real-Time Insights

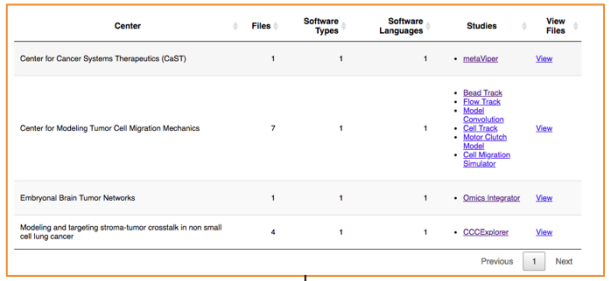
- Vision: Synapse as an interoperable platform/commons
- Native support for concept of a “**community**” comprised of multiple projects/teams
- **Activity feeds** for project/community insight
- Platform-driven **notifications** of key activity
- **Dashboards** for key community metrics

Share Annotated, Standardized Tools through Unified Portal

Tool Catalog:
retrospective, in development



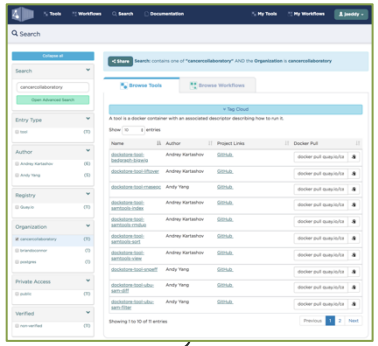
Tools on Synapse:
in development, published



Center	Files	Software Types	Software Languages	Studies	View Files
Center for Cancer Systems Therapeutics (CaST)	1	1	1	• metaViper	View
Center for Modeling Tumor Cell Migration Mechanics	7	1	1	• Bead Track • Flow Track • Model Convolution • Cell Track • Motor Clutch Model • Cell Migration Simulator	View
Embryonal Brain Tumor Networks	1	1	1	• Omics Integrator	View
Modeling and targeting stroma-tumor crosstalk in non small cell lung cancer	4	1	1	• CCCExplorer	View

Previous 1 Next

Tool Registry:
published, searchable



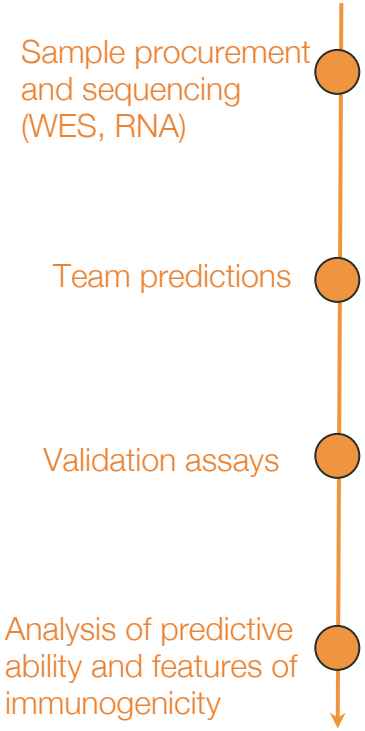
Tool Portal

Future tool catalog will link to all tool resources

SageBionetworks

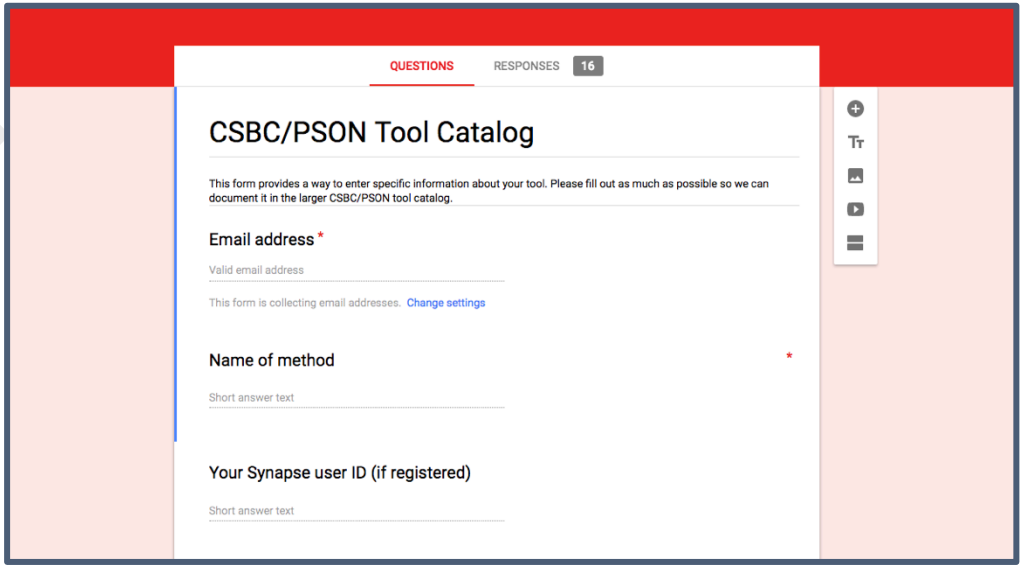
Precision Immunology: Tumor Neoantigen Selection Alliance (TESLA)

- Began in 2017 with Parker Institute and CRI
- A benchmarking exercise in predicting immunogenic (neo)epitopes.
- Multiple validation assays (MHC binding, TCR binding by flow and nanoparticles, T cell reactivity)
- >25 teams participating
- Multiple cancer types: melanoma, breast cancer, NSCLC, CRC (MSI-high, MSS)



Tool Catalog Collates Submissions from Centers

Individual centers submit data to survey



Single Interface Combines All Tools and Provides Links

CSBC Tool Catalog

Input Data Type
- proteomics
- cellularPhysiology
- drugScreen
- geneExpression
- network
- genomicVariants
- isoformExpression
- pathway or network
- chromatinActivity
- gene list
- functional screen
- image
- N/A

Output Data Type
- proteomics
- image
- inputed drug response
- geneExpression
- isoformExpression
- genomicVariants
- network
- cellularPhysiology
- chromatinActivity
- drugScreen
- N/A

Software/Tool Types

Script | Package Binary | Package Library | Web Application | Other

methodName	centerName	inputDataType	outputDataType	softwareLanguage
CIPM	Cancer Systems Biology Center of HoPE (Heterogeneity of Phenotypic Evolution)	• geneExpression • network • cellularPhysiology	• cellularPhysiology • geneExpression • network	Matlab, R
Master Regulator Inference Algorithm	Center for Cancer Systems Therapeutics (CaST)	• geneExpression • pathway or network	• gene list	Matlab, R
Omics Integrator	Embryonal Brain Tumor Networks	• geneExpression	• network	Python
Speedy Histopathological-to-ImmunoFluorescent Translation of whole slide images using conditional generative adversarial networks	N/A	• image	• image	Matlab, Python

Single Interface Combines All Tools and Provides Links

Filter by data type

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Filter by data type

Broken down by type of tools

Single Interface Combines All Tools and Provides Links

Abstract and information

CSBC Tool Catalog

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Omics Integrator

Center
Embryonal Brain Tumor Networks

Synapse Site
syn9898746

Website
http://fraenkel-nsf.csbi.mit.edu/omicsintegrator/

Abstract

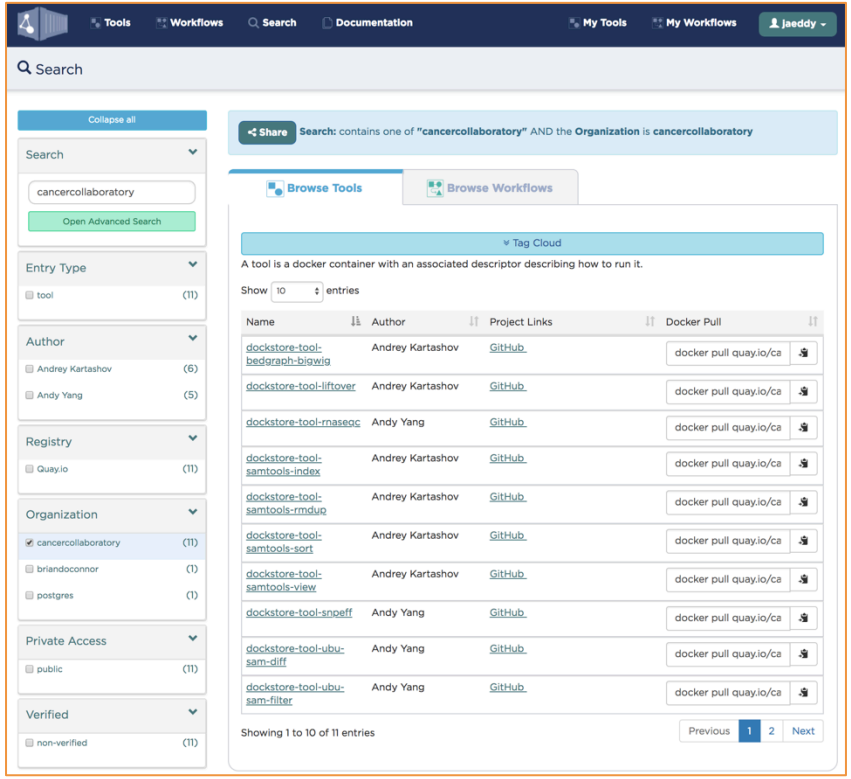
High-throughput, 'omic' methods provide sensitive measures of biological responses to per-turbations. However, inherent biases in high-throughput assays make it difficult to interpret experiments in which more than one type of data is collected. In this work, we introduce Omics Integrator, a software package that takes a variety of 'omic' data as input and identifies putative underlying molecular pathways. The approach applies advanced network optimiza-tion algorithms to a network of thousands of molecular interactions to find high-confidence, interpretable subnetworks that best explain the data. These subnetworks connect changes observed in gene expression, protein abundance or other global assays to proteins that may not have been measured in the screens due to inherent bias or noise in measurement. This approach reveals unannotated molecular pathways that would not be detectable by searching pathway databases. Omics Integrator also provides an elegant framework to incorporate not only positive data, but also negative evidence. Incorporating negative evidence allows Omics Integrator to avoid unexpressed genes and avoid being biased toward highly-studied hub pro- teins, except when they are strongly implicated by the data. The software is comprised of two individual tools, Garnet and Forest, that can be run together or independently to allow a user to perform advanced integration of multiple types of high-throughput data as well as create condition-specific subnetworks of protein interactions that best connect the observed changes in various datasets.

Close

aType	softwareLanguage
arPhysiology Expression ork	Matlab, R
list	Matlab, R
ork	Python
e	Matlab, Python

CSBC/PS-ON Tool Registry: Vision

- Dockerize/standardize tools and workflows in the CSBC/PS-ON Tool Catalog
- Register tools and workflows in Dockstore to enable findability and sharing
- Proposed Dockstore integration in Synapse would provide a way to view and access curated computational tools from CSBC/PS-ON investigators



SageBionetworks