

Library of Integrated Network-based Cellular Signatures

Proteomic Characterization Center for

Signaling and Epigenetics

Scientific Advisory Board Meeting

August 31, 2016

Jacob D. Jaffe – Broad Institute, PI

Li-Huei Tsai – MIT, co-investigator

Michael MacCoss – U. of Washington, co-investigator

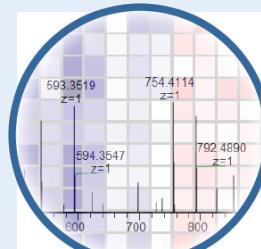
Agenda

- Introductions
- SAB Expectations and Guidance
- Center Overview – Jake Jaffe
- Neurobiology Focus – Li-Huei Tsai
- Next Generation MS – Mike MacCoss

Q & A is welcome at any point

LINCS Consortium Structure

DATA GENERATION

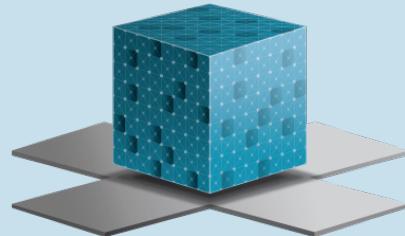


LINCS PCCSE



LINCS Center for
Transcriptomics

DATA COORDINATION



BD2K-LINCS
DATA COORDINATION AND
INTEGRATION CENTER

PROGRAM
OVERSIGHT



National Institutes of Health
Turning Discovery Into Health

The role of the PCCSE Scientific Advisory Board

- Scientific and logistical guidance
- Spreading the word to the right communities
- Helping us continuously improve
- Assistance with NIH “Mid-course Review”
 - Site visit: December 9th, 2016

Mid-course review criteria

1. Feedback on Data Generation & Analysis
2. Feedback on Data Release and Accessibility
3. Feedback on Community Outreach
4. Feedback on major adaptations going forward
5. Other comments/advice

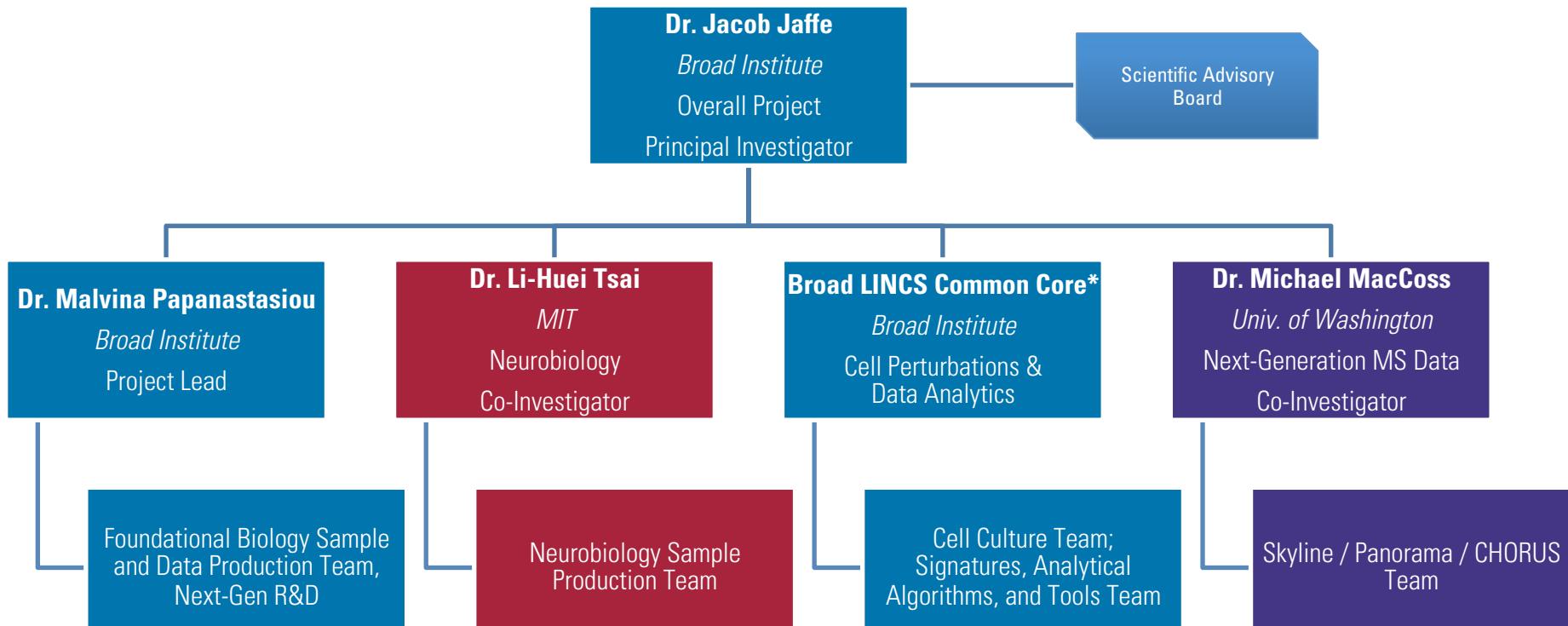
PCCSE Mission:

The LINCS Proteomic Characterization Center for Signaling and Epigenetics (PCCSE) is dedicated to understanding the therapeutic potential of drugs and unlocking the fundamental mechanisms of action of drugs, genes, and diseases through the lens of their cellular effects on phosphosignaling and epigenetic processes.

Why proteomics?

- Proteins are the targets of drugs
- Proteins mediate the actions of drugs
- Proteins are affected on time scales different than gene expression
- Proteins compose “pathways” and the bulk of molecular machinery
- Proteomics can complement other profiling methods

Organization of the Center:



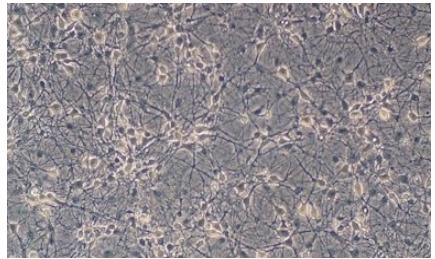
PCCSE Center Scientific Overview



Cell Lines



Drugs



Neural Lineages

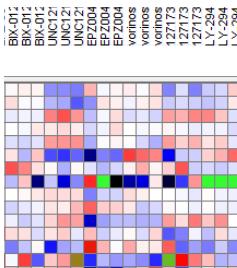
X



Genes



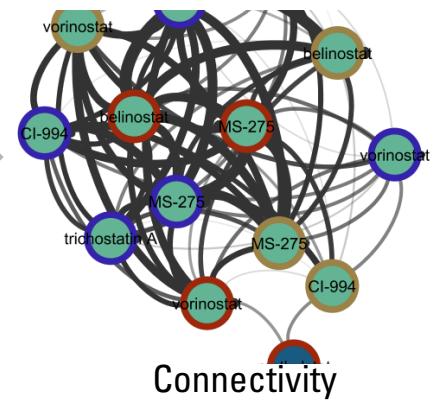
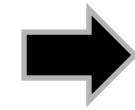
P100 / DIA
(phospho)



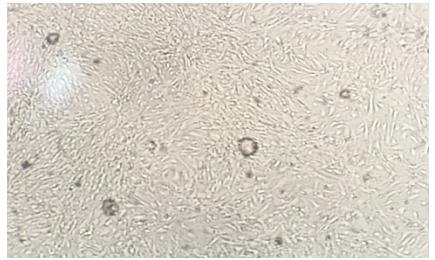
Signatures



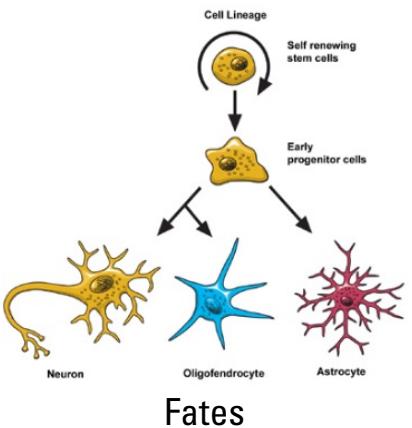
GCP
(histone marks)



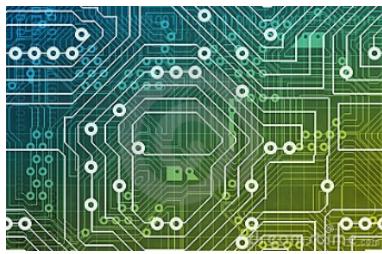
Connectivity



Primary Cells



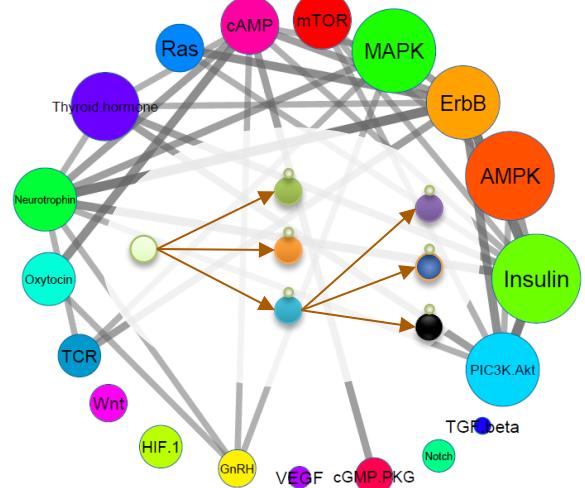
L1000
(mRNA)



Circuitry

Proteomic Signature Assays

P100 is a targeted proteomic assay against 96 phosphopeptide probes that are commonly observed and modulated in diverse cell types

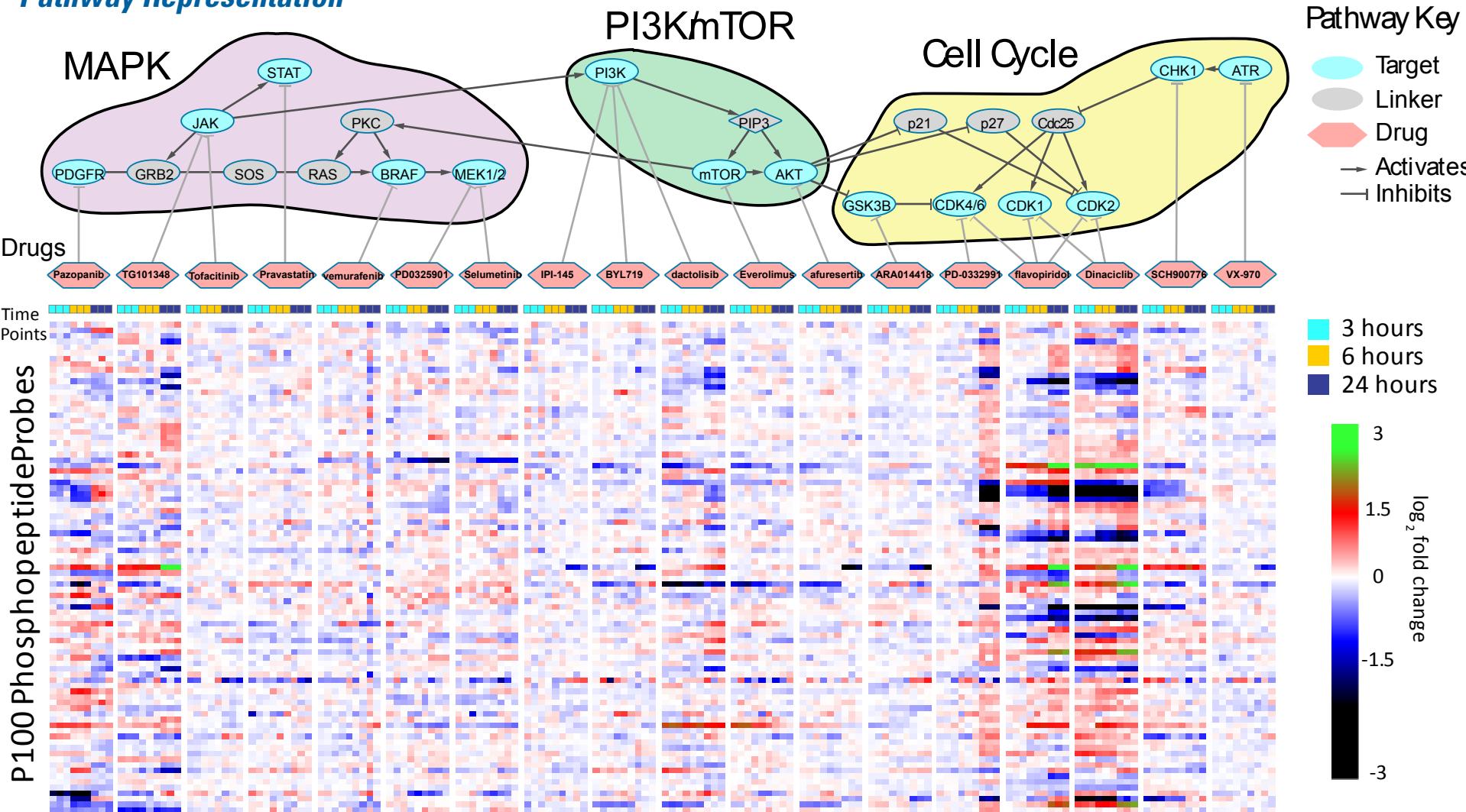


GCP is a targeted proteomic assay against ~ 60 probes that monitor combinations of post-translational modifications on histones



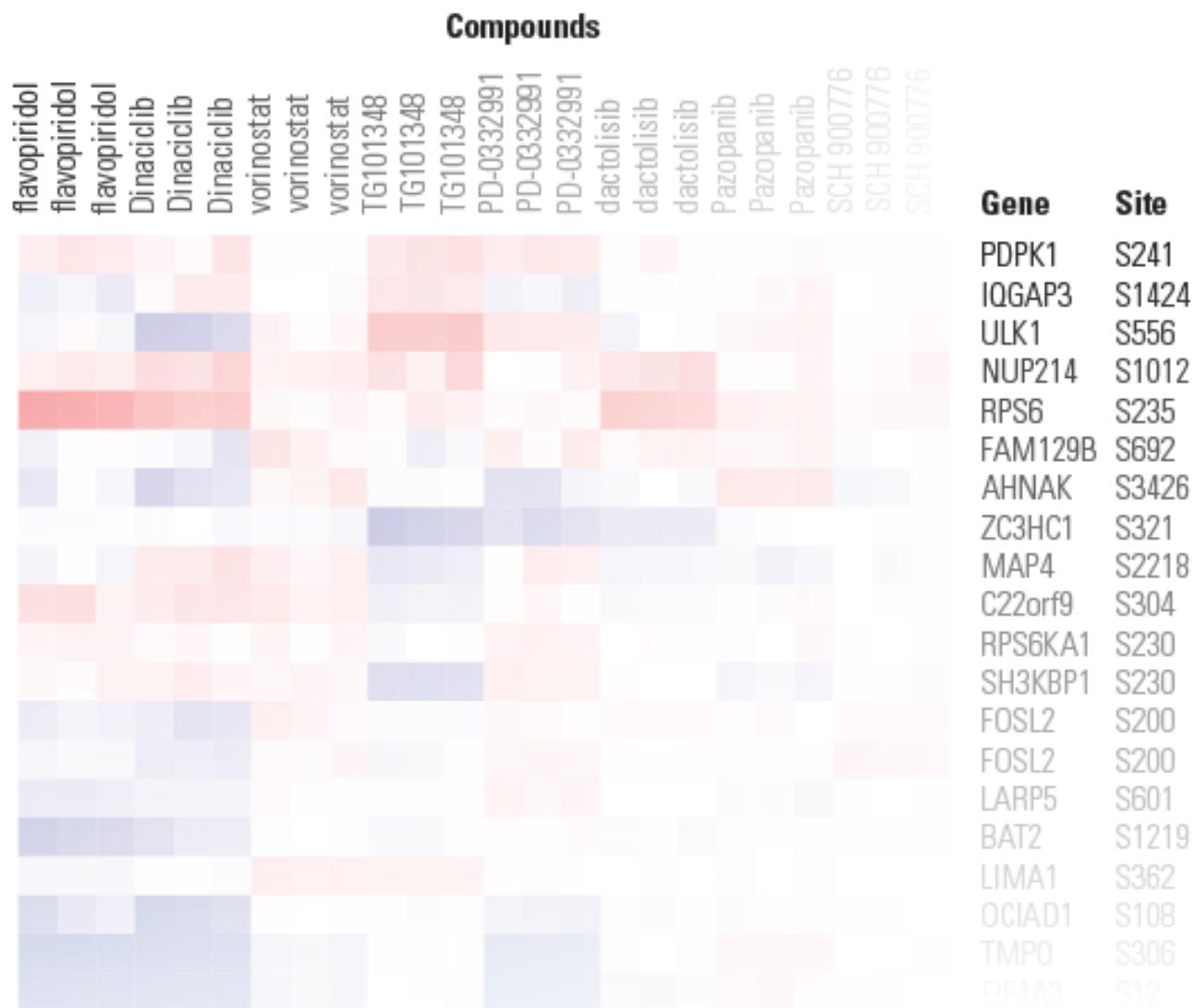
Reference signatures of drugs and pathways

Pathway Representation



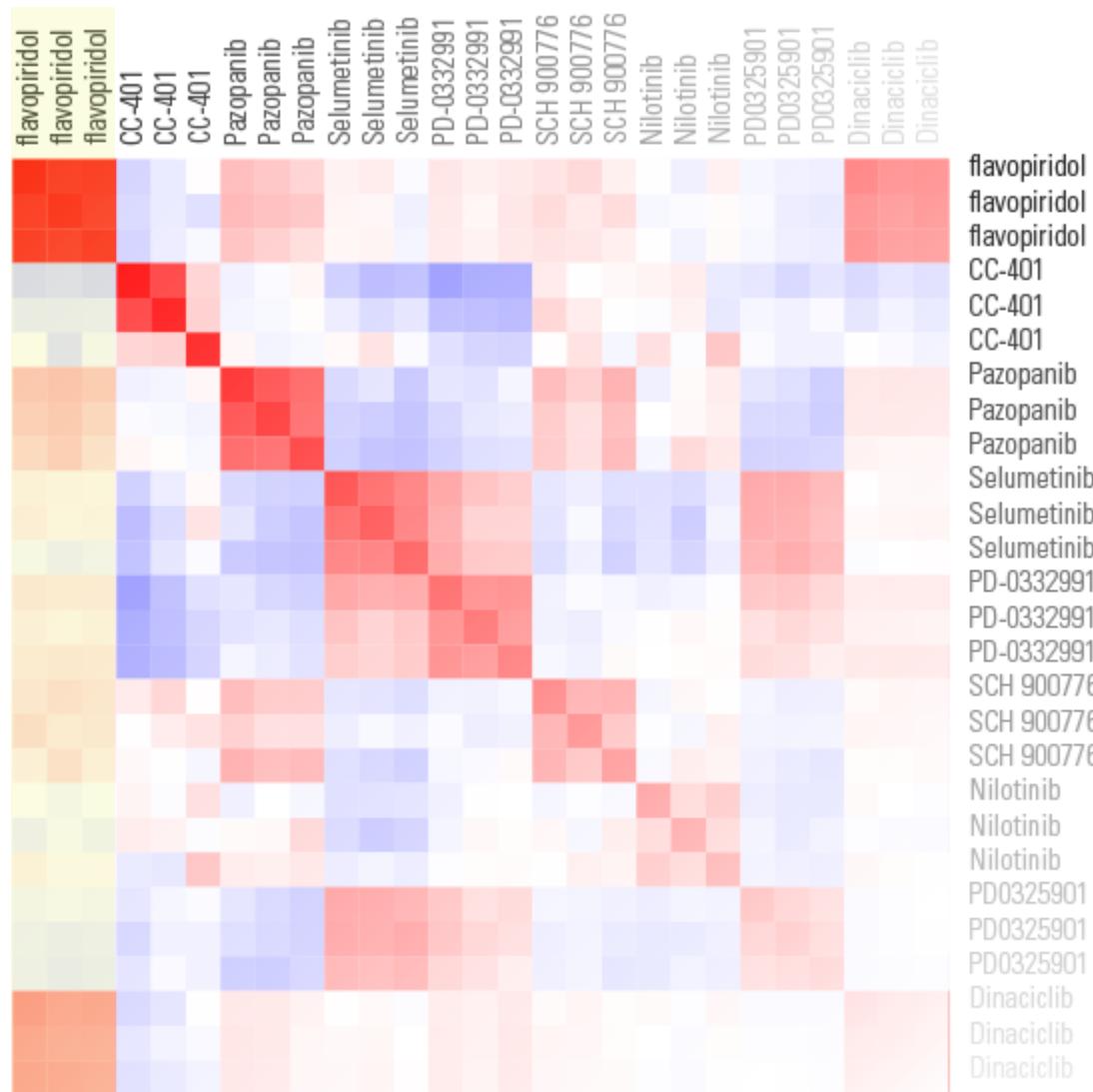
Turning signatures into connections

Signatures are groups of related profiles



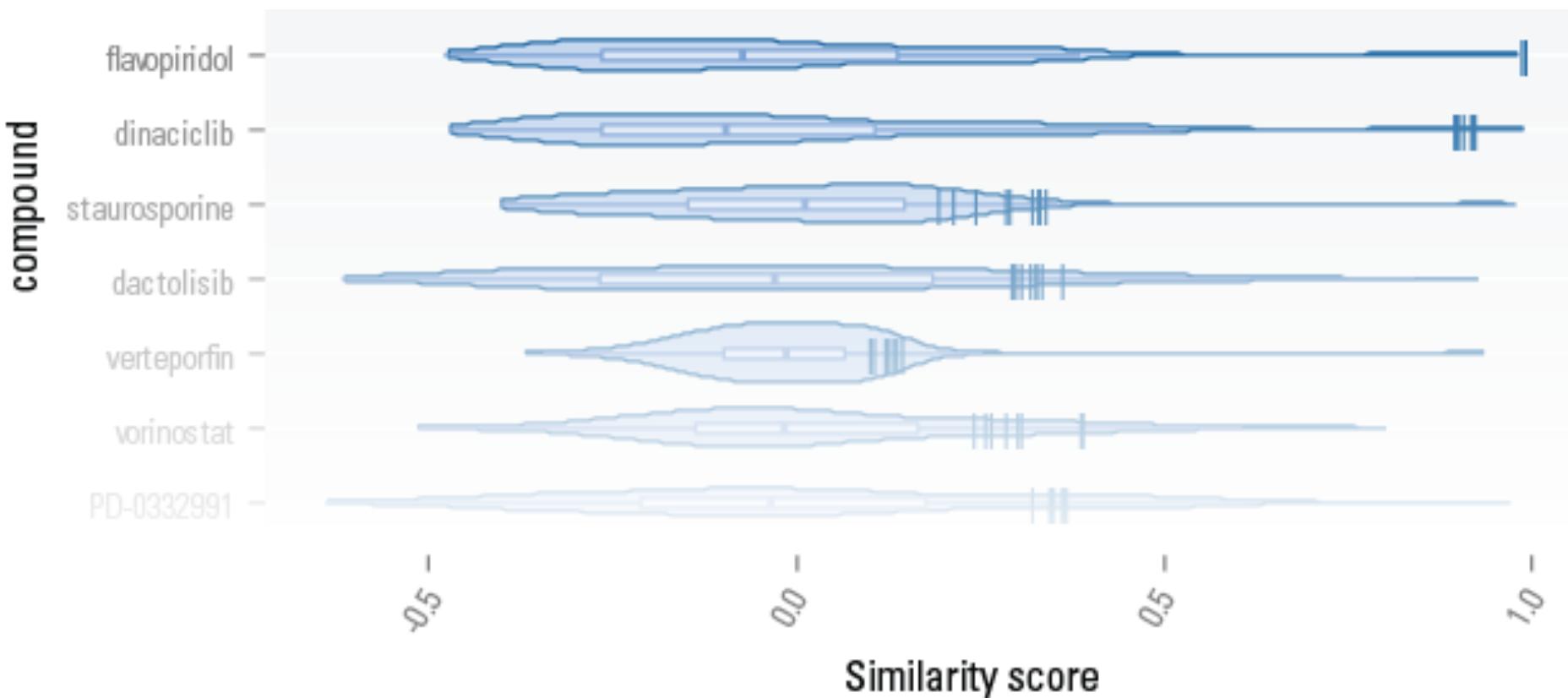
Turning signatures into connections

Similarities are correlations computed from signatures



Turning signatures into connections

Connectivity queries put correlations in context

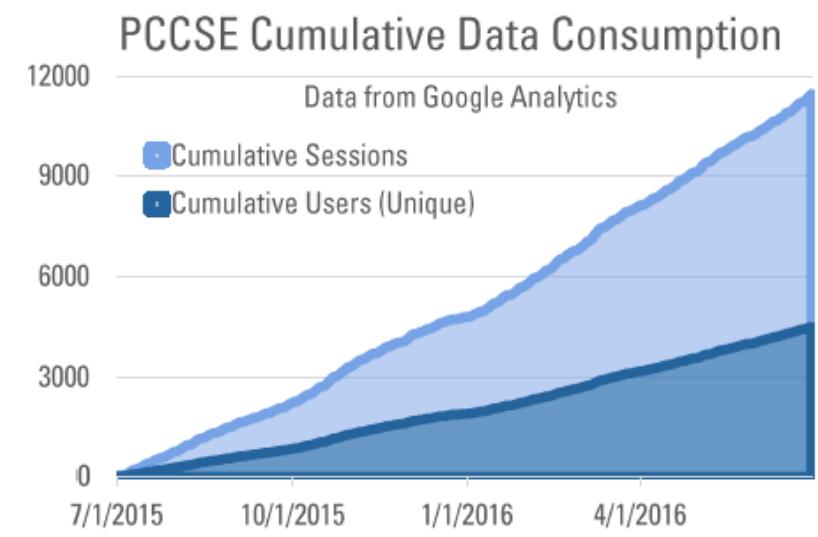
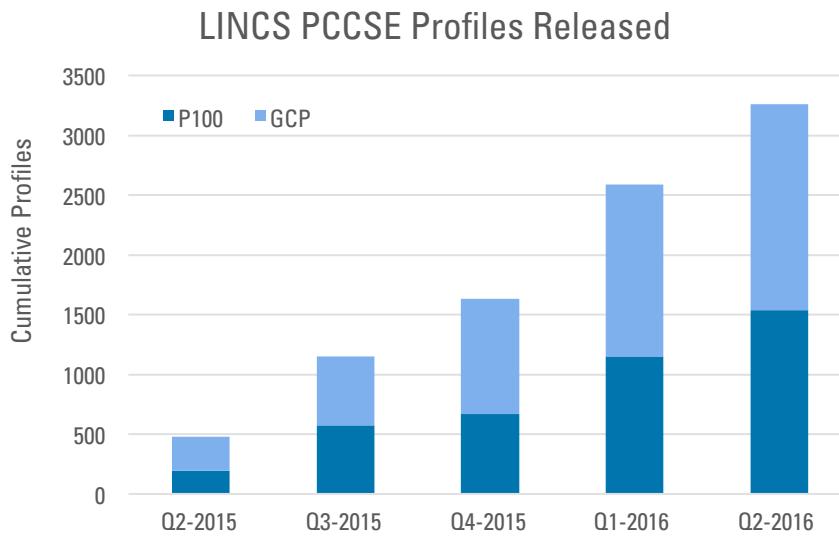


Use cases for connectivity

- What is the mechanism of action of a compound?
 - Through connectivity to drugs of known mechanism
 - Through connectivity to genetic perturbations
- Does a drug or gene's function depend on disease model or biological context?
 - Through connectivity of the same perturbation across cell types
- Does a drug activate signaling or epigenetic processes?
 - Through signature strength relative to known examples
- Are there potentially novel or unrecognized therapeutic opportunities?
 - Through *anti*-connectivity of a drug to a genetic model of disease

Extensive progress building the library

- 3400+ biological samples generated spanning:
 - 92 compounds in triplicate
 - Beginning CRISPR/Cas9-based gene disruptions
 - 6 cellular models (breast, lung, skin, prostate, and pancreatic cancers; neuronal precursors)
 - 2 assay platforms
- Key infrastructure:
 - Public data repository with built-in signature visualization (bit.ly/PCCSEData)
 - Documented workflows; automated analytical pipeline for reproducibility



Outreach activities

- Signatures of cardiovascular hypertension induced by chemotherapeutic drugs
 - Molecular Cardiology Research Institute, Tufts Medical Center
- Signatures of neuropsychiatric phenotypes and their responses to drugs in patient-isolated iPS-derived neurons
 - Massachusetts General Hospital
- Mapping of P100 probe-sets onto known pathway networks
 - Georgetown University and University of Delaware
 - Together with DCIC through LICNS EDSR
- Substrates to promote neuronal fates and phenotypes
 - Intra-LINCS with OHSU MEP LINCS Center

Focus areas and challenges

- Extending further into the neurobiology space
 - Li-Huei Tsai and her team will lead the way
- Unlocking Next-gen MS data
- Data: primary use, sharing, and re-use
 - What are the tools that we need to build?
 - How do we get people to utilize these data?
 - Are there audiences to be targeted and engaged?

Progress and challenges in the neurobiology space



Cell Lines



Drugs



Neural Lineages

X

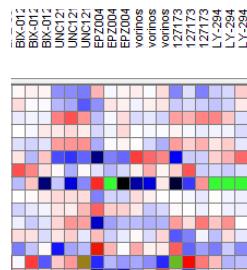


Genes

X



P100 / DIA
(phospho)

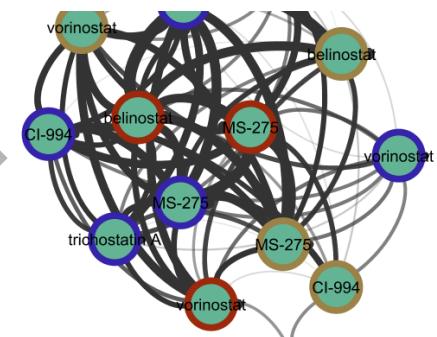
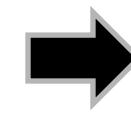


Signatures

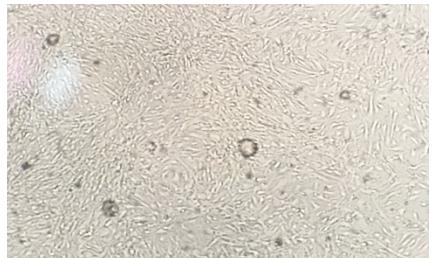
id
10011 DYRK Y3221
1024 ISPK1 S369
1078 ARM2 S87 R
1130 HSPC216 S32
1142 CTG26 S956
12 KIF3B01 S935
1468 OG48 S104 L
1501 PDK1 S241 A
1511 ABP1 S184 T N
1797 WDR20 S465
1811 MAP4 S2218
1953 RBM17 S222
2328 IQGAP3 S142
2577 C9orf68 S69



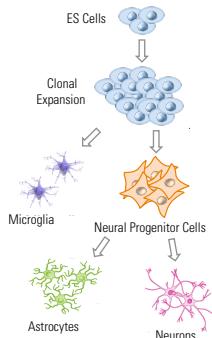
GCP
(histone marks)



Connectivity



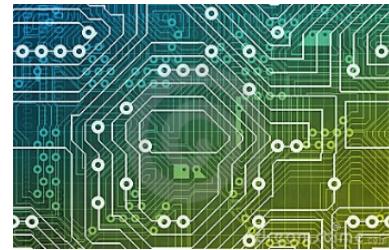
Primary Cells



Fates



L1000
(mRNA)

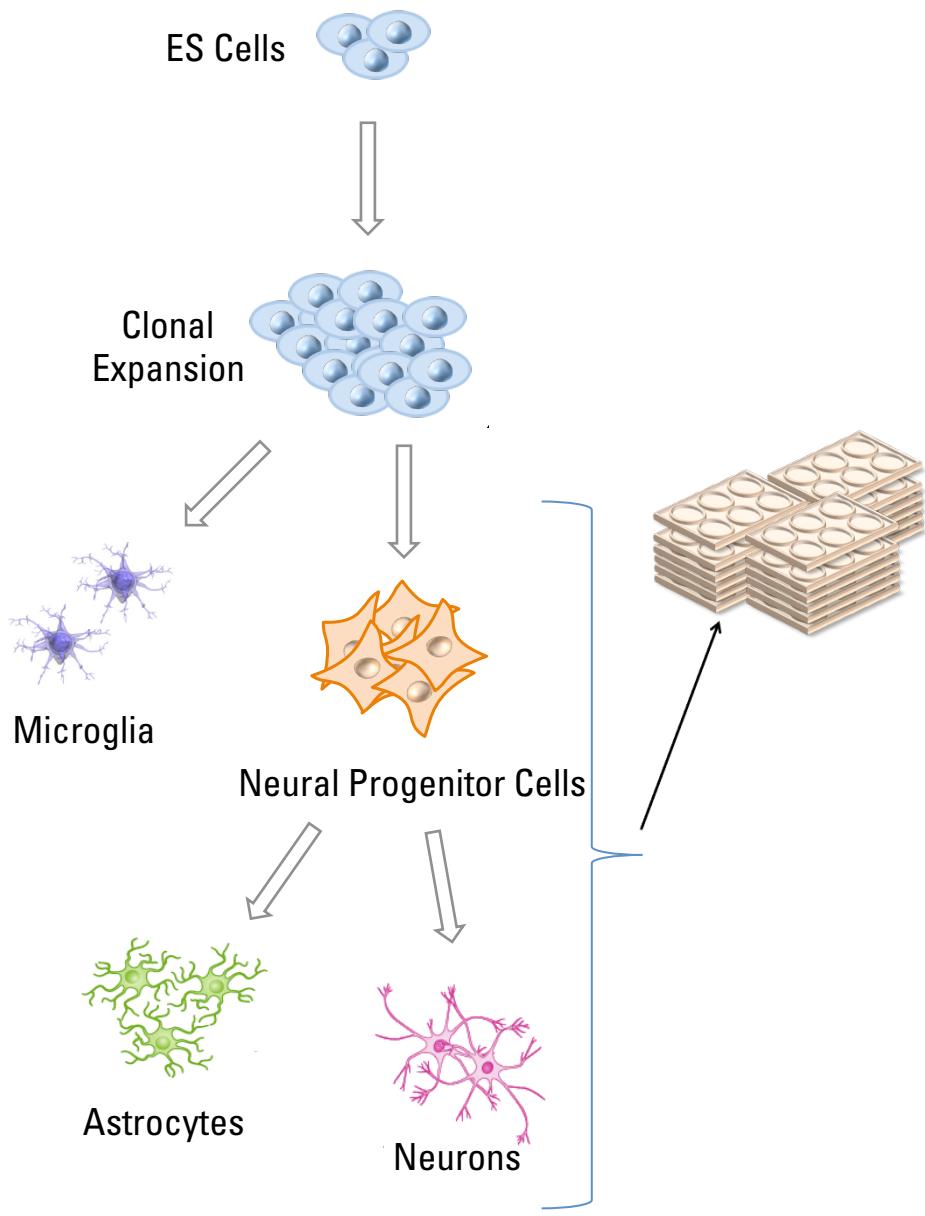


Circuitry

Neurobiology focus

- Epigenetic processes are disrupted in neurological disorders such as autism spectrum disorders (ASDs)
- Causal mutations have been found in chromatin-associated enzymes in ASD patients
- Study neural cells during development and across cellular subtypes:
 - establish epigenetic and phosphosignaling signatures
 - study effects of knocking down chromatin-modifying enzymes
 - re-create perturbations in ASD risk genes

Differences in neural cell types



P100 / DIA
(phospho)



GCP
(histone marks)



Compound Treatment

Genes to perturb neural cell types

Core Epigenetic Reference Genes

CHD8	HDAC2	KDM2A	KMT2A	SIRT6	BRD9
DNMT1	HDAC3	KDM2B	KMT2D	SIRT7	CBX1
DNMT3A	HDAC4	KDM3A	KMT2C	SUV39H1	CBX2
DNMT3AP1	HDAC5	KDM3B	KMT2E	SUV39H2	CBX3
DNMT3B	HDAC6	KDM4A	SETD1A	SUV420H1	CBX4
DNMT3L	HDAC7	KDM4B	SETD1B	SUV420H2	CBX5
DOT1L	HDAC8	KDM4C	SETD2	WHSC1	CBX6
EHMT1	KAT2A	KDM4D	SETD7	WHSC1L1	CBX7
EHMT2	KAT2B	KDM4E	SETD8	NELFA	CBX8
EZH1	KAT5	KDM5A	SETDB1	ASXL1	EED
EZH2	KAT6A	KDM5B	SETDB2	BRD1	EP300
HAT1	KAT6B	KDM5C	SIRT1	BRD2	NSD1
HDAC1	KAT7	KDM5D	SIRT2	BRD3	SMYD1
HDAC10	KAT8	KDM6A	SIRT3	BRD4	SMYD2
HDAC11	KDM1A	KDM6B	SIRT4	BRD7	SMYD3
SUZ12	KDM1B	KDM8	SIRT5	BRD8	CLOCK

Autism-Spectrum Disorder & Other Neurobiology Genes

ADNP	DYRK1a	MECP2	SEMA5A
ARID1B	EHMT1	NLGN3	SHANK3
CACNA1C	EIF4G1	NLGN4X	SYNGAP1
CNTN4	EPC2	NRXN1	TLK2
CNTNAP2	FMR1	PTCHD1	TSC1
CREBBP	GRIN2B	PTEN	TSC2
CTCF	GRIP1	SCN1A	UBE3a
CTNNB1	GRM5	SCN2a	UBE3b

Neural Cell Differentiation

Lentivirus Transduction & Selection



+Blasticidin
Inducible Cas9 (iCas9)

Neural Progenitor Cell Induction

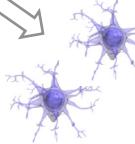
Shi et al., Nat. Protocols, 2012



Neurons

Zhang et al., Neuron, 2013

Clonal Expansion



Microglia



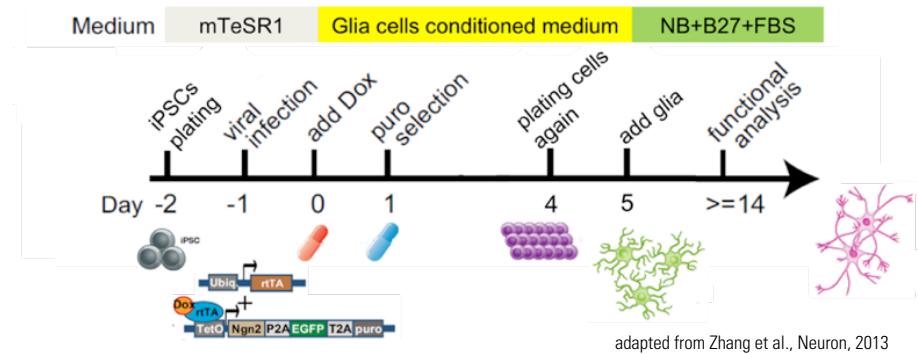
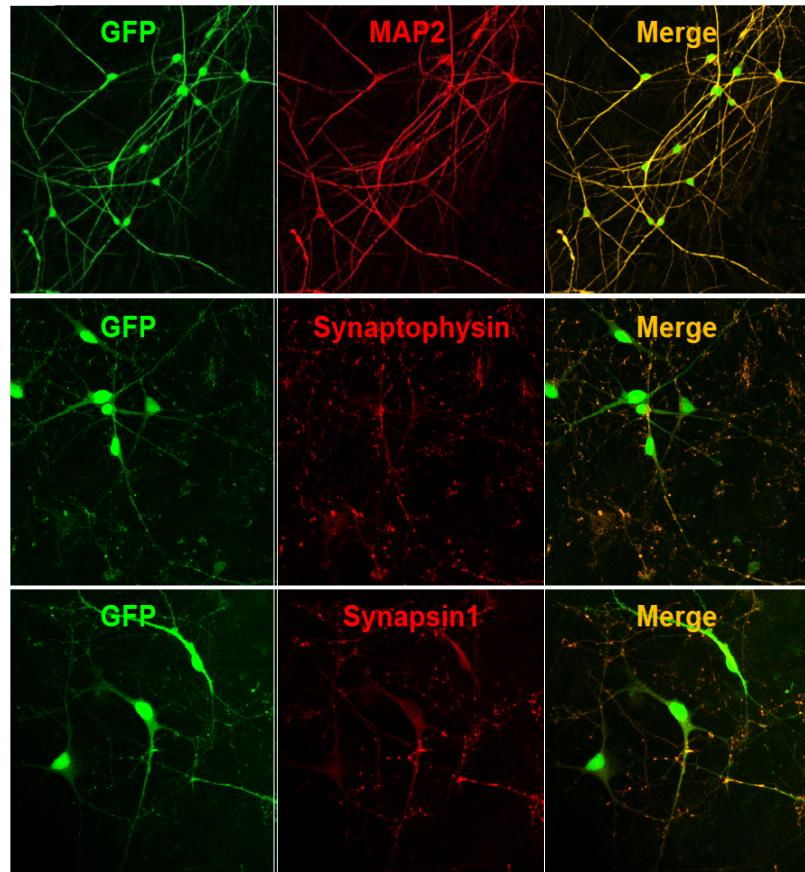
Astrocytes

Chen et al., Nat. Commun., 2014

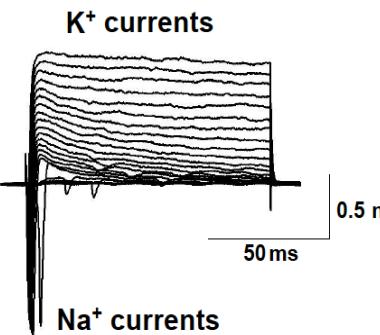
HUES8 iCas9-13
Clone #1

Creating neurons for high-content proteomics assays

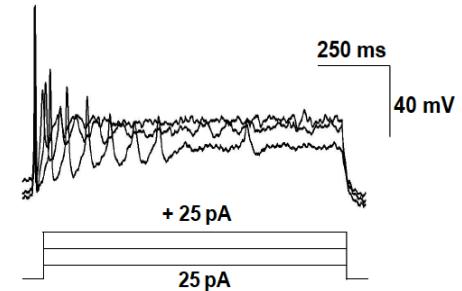
OPTION 1: Neurogenin-2 (Ngn2) induction to force excitatory cortical neuron production



Whole-cell voltage clamp

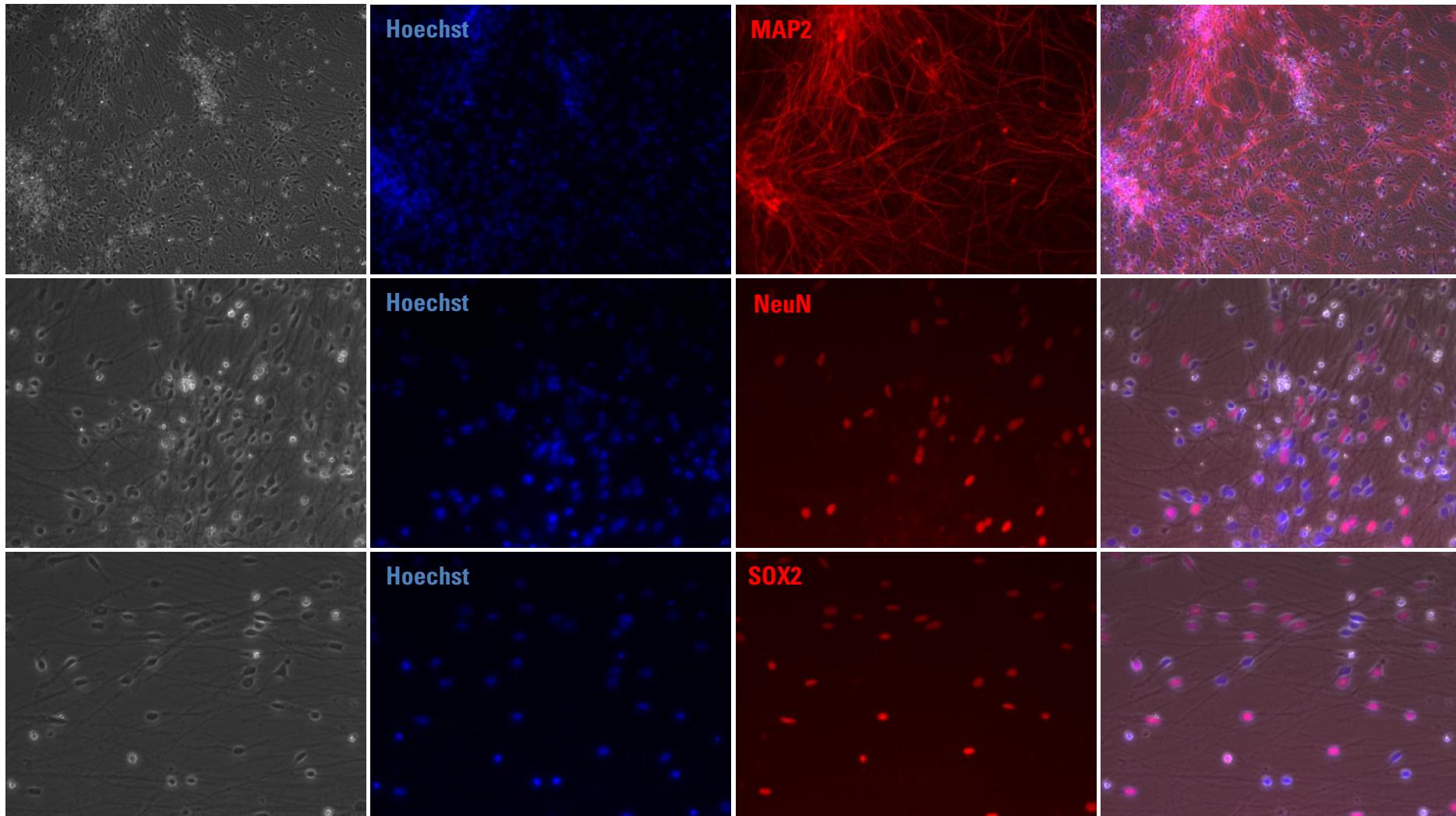


Action potential



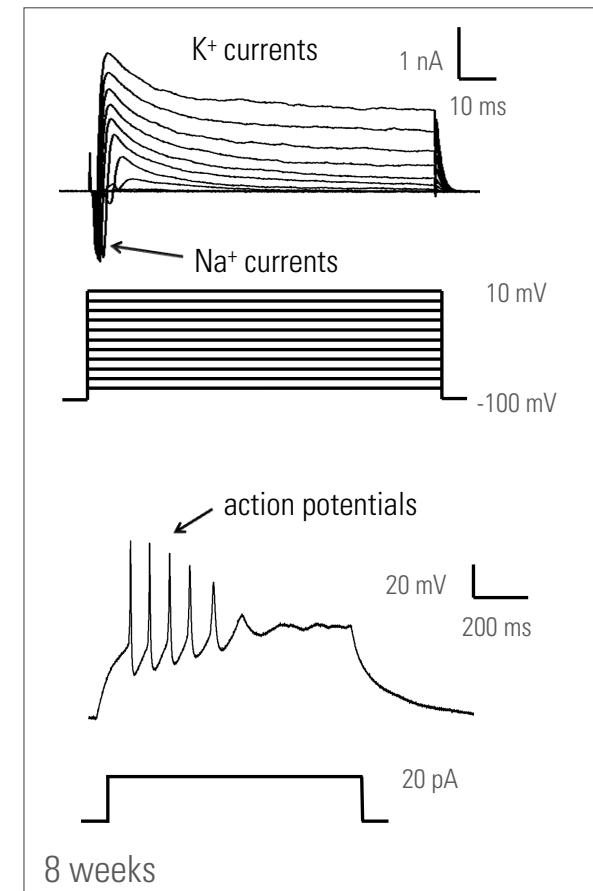
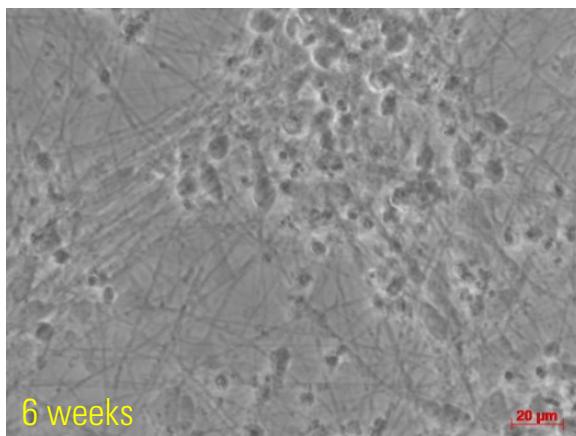
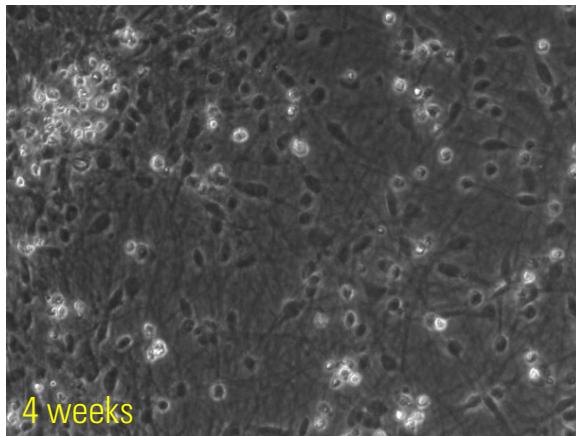
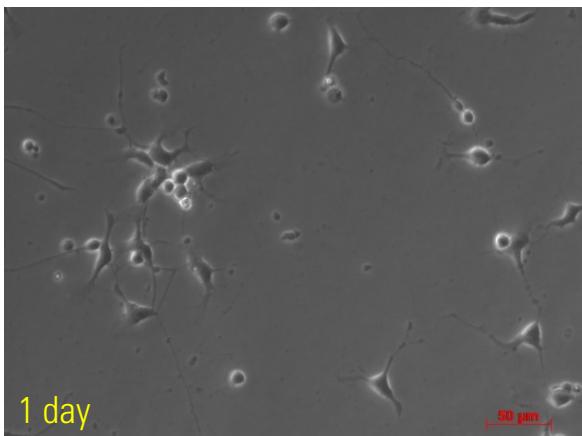
Creating neurons for high-content proteomics assays

OPTION 2: Passive differentiation via growth factor withdrawal (GFW)



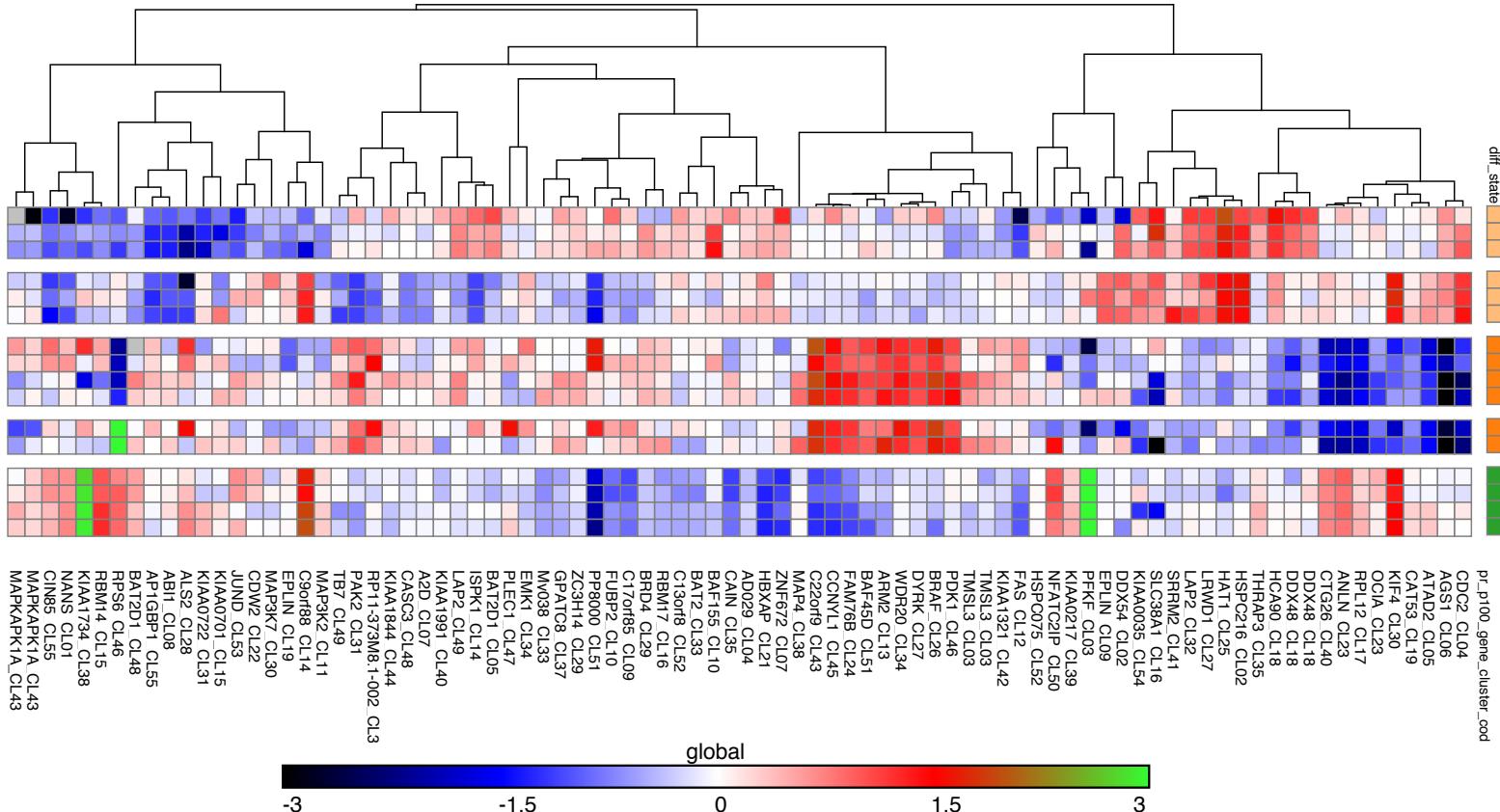
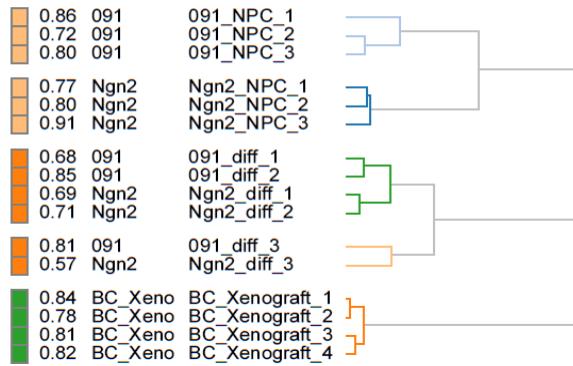
Creating neurons for high-content proteomics assays

OPTION 2: Passive differentiation via growth factor withdrawal (GFW)



P100 comparison of different cell types

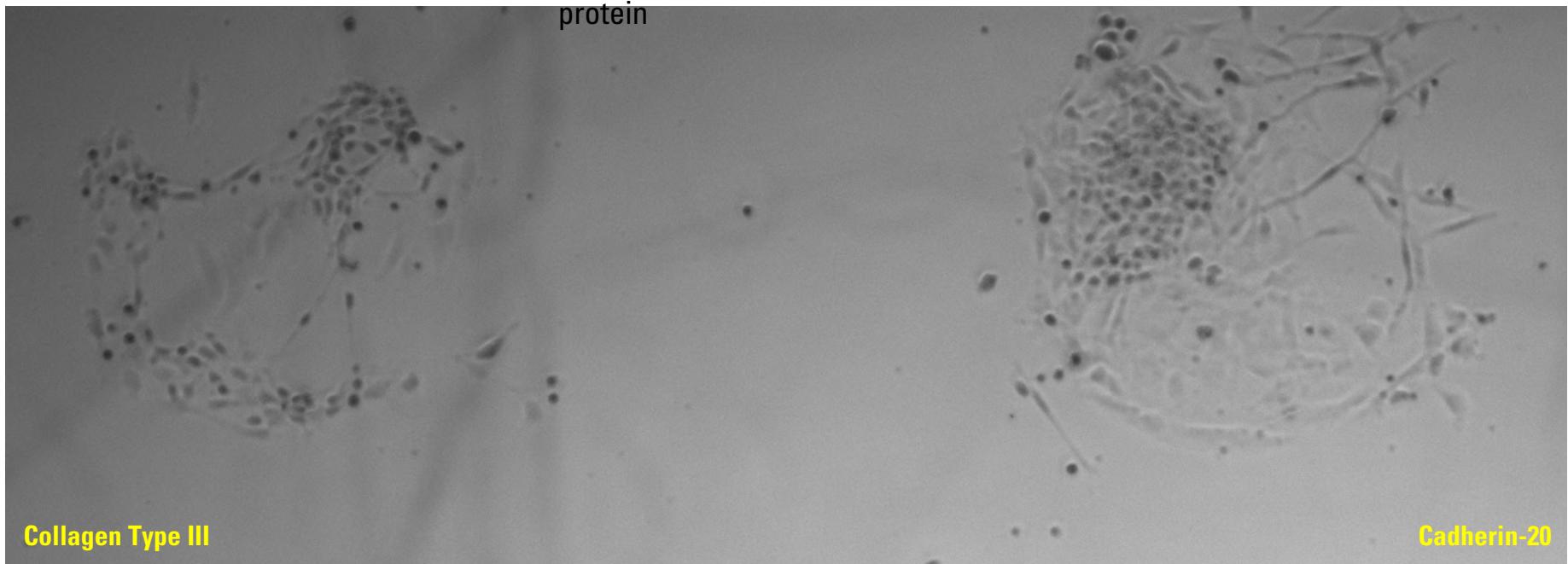
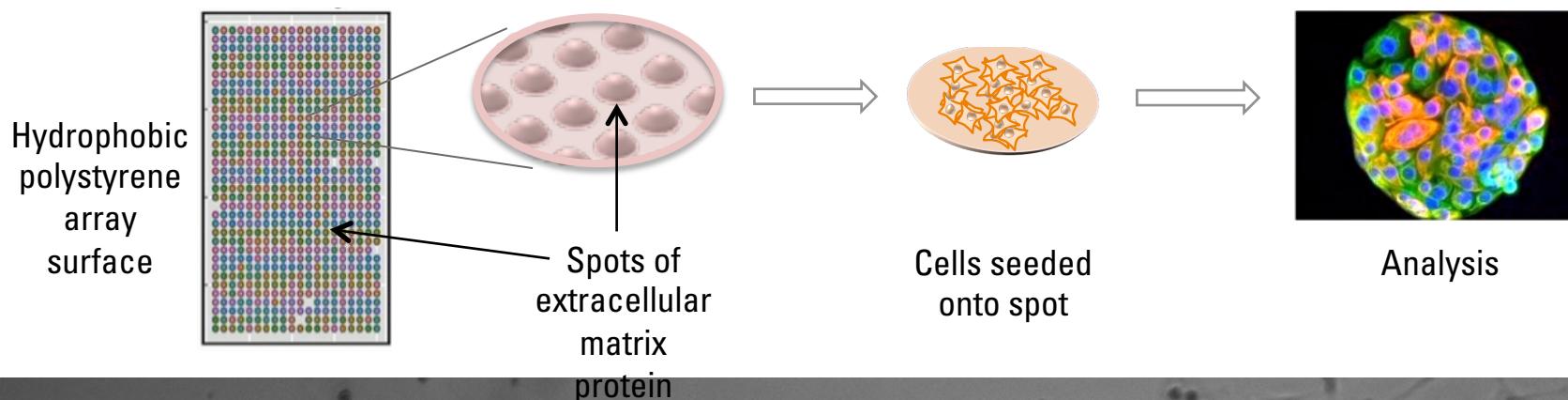
- █ Neural Progenitor Cells (NPCs)
- █ Differentiated Neurons
- █ Breast Cancer (BC) Xenograft line



N-GRID

Steve Haggarty, Isaac Kohane, Roy Perlis

Microenvironment Perturbagen (MEP) LINCS Center



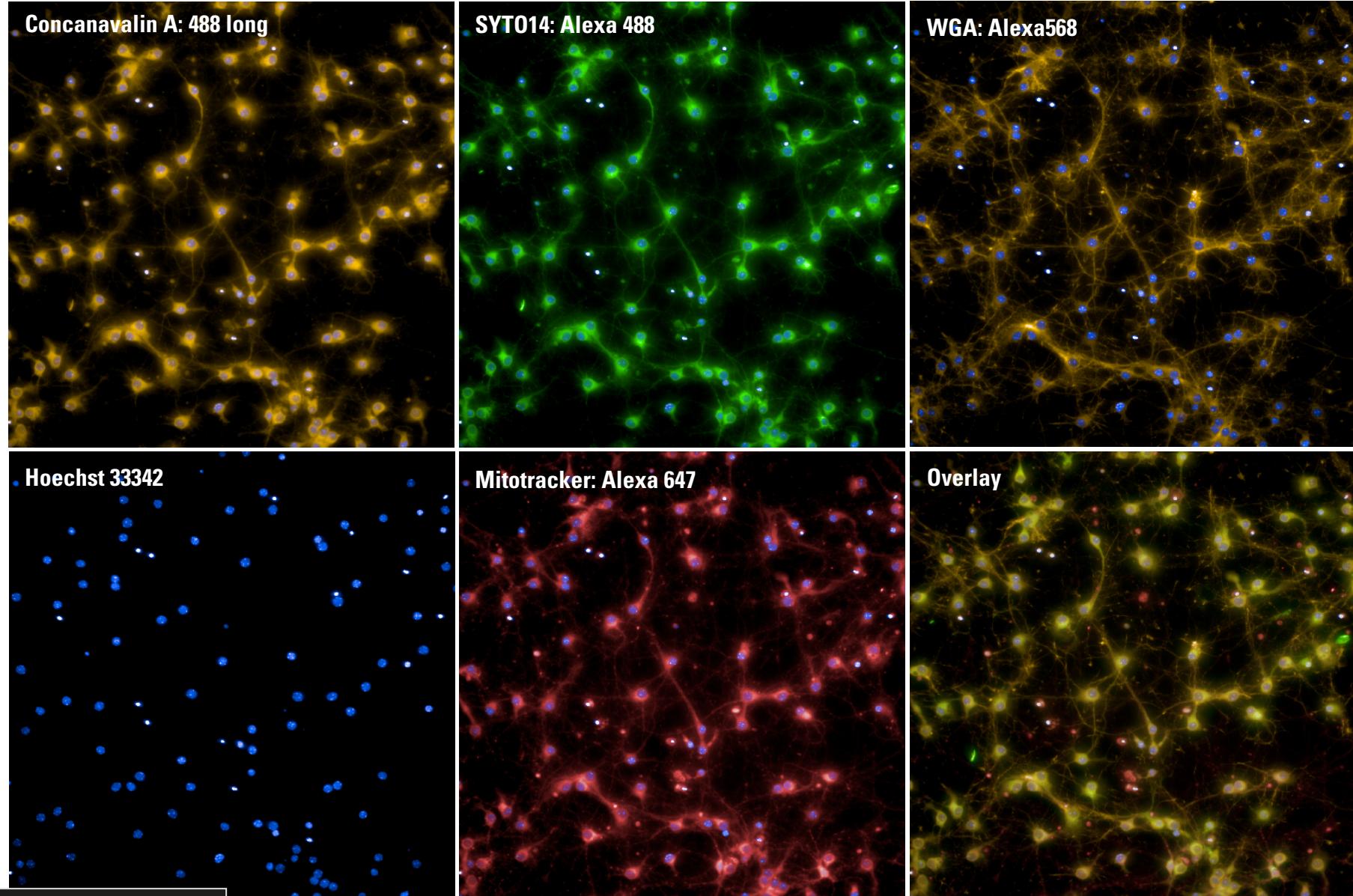
HUES8-iCAS9-13 NPCs - TWO WEEKS after GFW



MEP-LINCS

Joe Gray, Laura Heiser, Jim Korkola

Profiling MEMA with cell painting

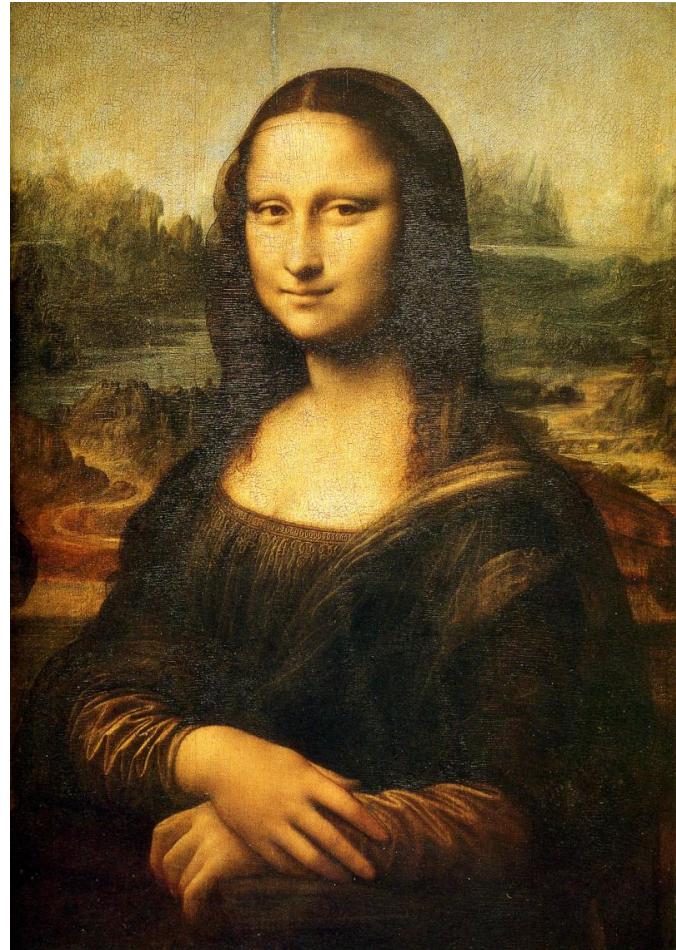


Unlocking Next-Gen MS and promoting data reuse

- What is Next-Gen mass spectrometry for proteomics?
- How will we unlock these data?
- How we will share our data and our methods with the world?

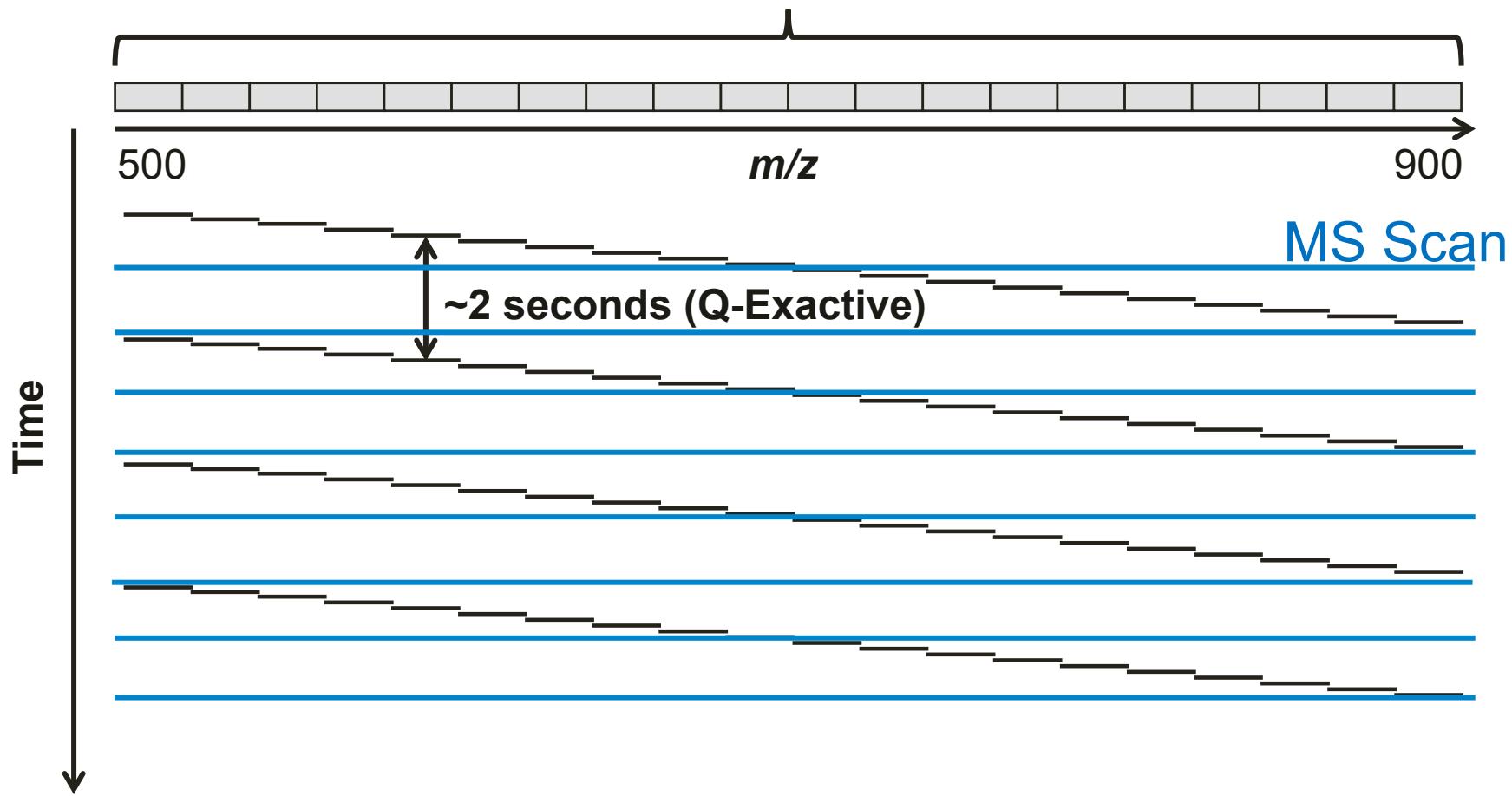
The Promise of Data Independent Acquisition MS (DIA)

- Acquire a “molecular image” or “digital archive” of the sample
 - Mine it over and over
 - No specific targeting or scheduling
- Direct queries (and p-values) for peptides of interest
- Better quantitation than Shotgun/DDA

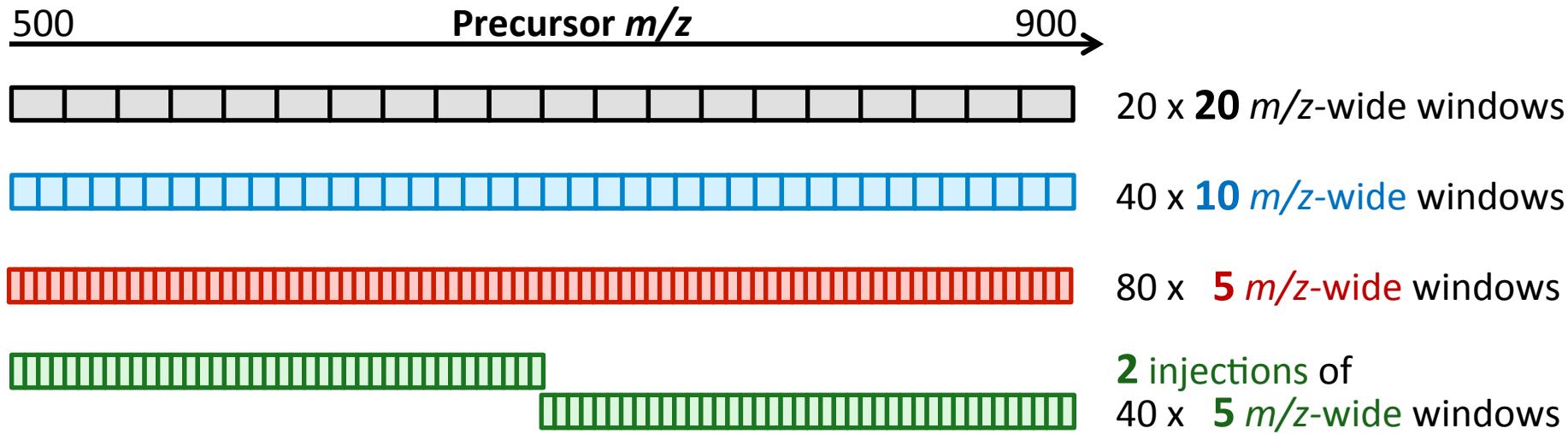


How does DIA work?

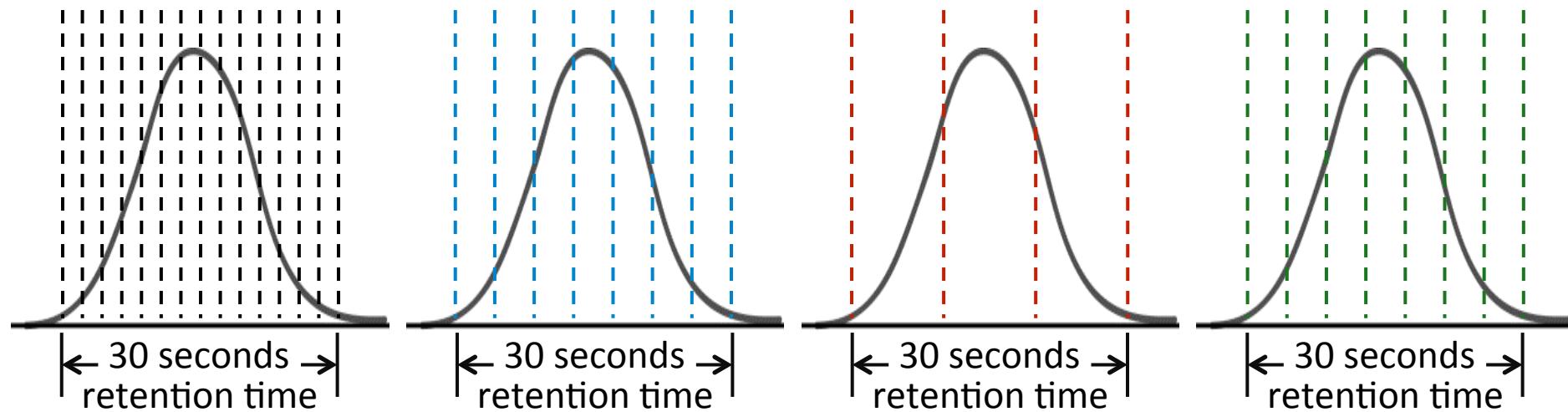
20 20 *m/z*-wide windows = 400 *m/z*



DIA is all about balance (and sacrifice) for quantification



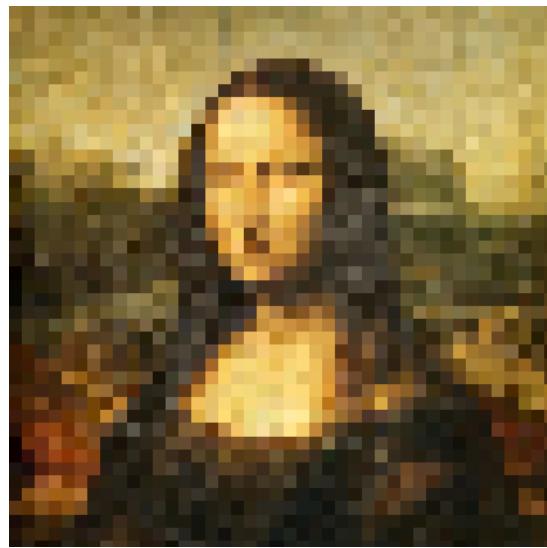
Instrument MS/MS scan speed: 10 Hz



Archive Quality



20 x **20** m/z -wide windows

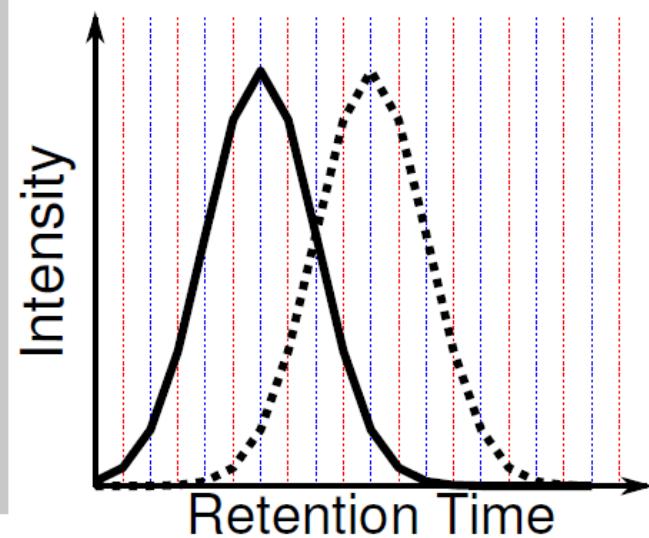
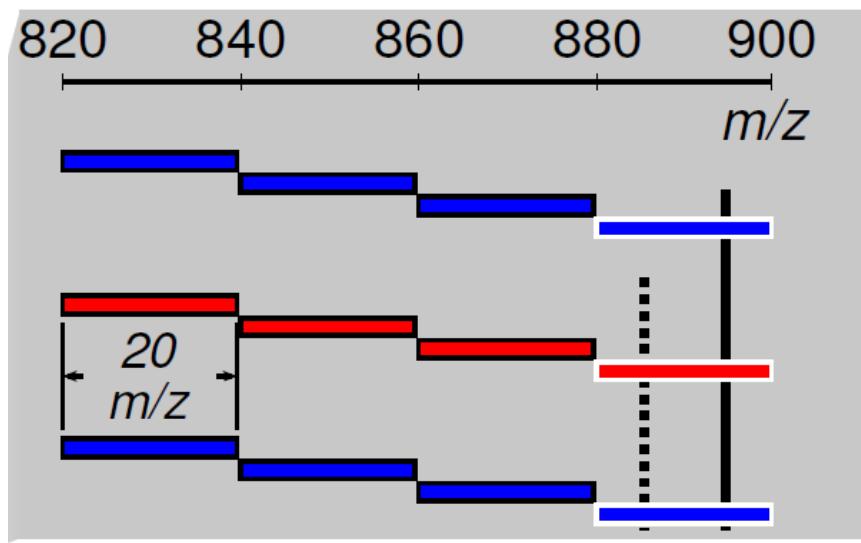


30 x **10** m/z -wide windows



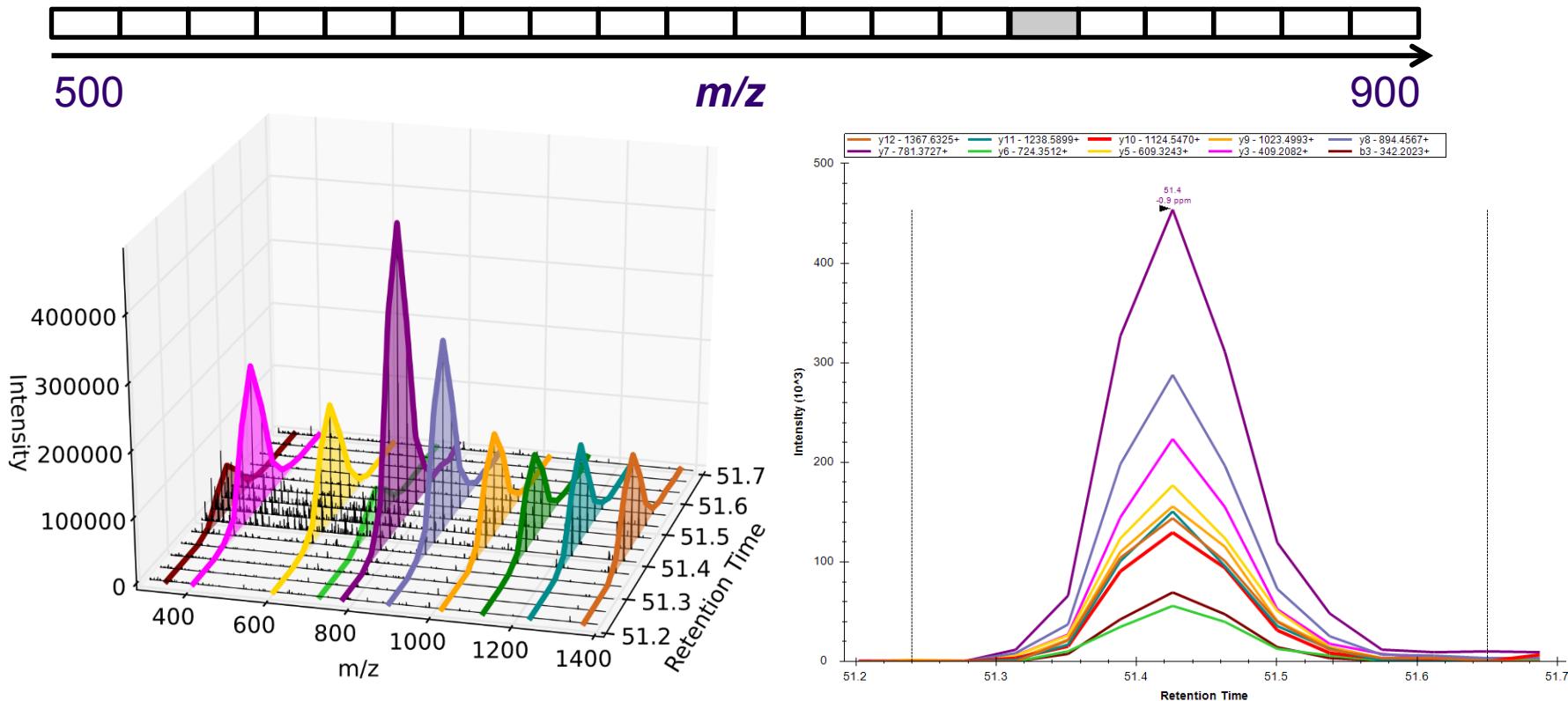
2 injections of
40 x **5** m/z -wide windows

Innovative approach to improve clarity



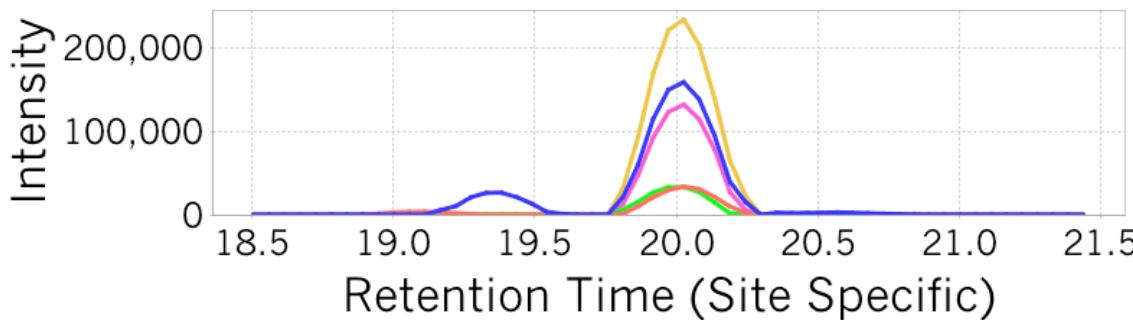
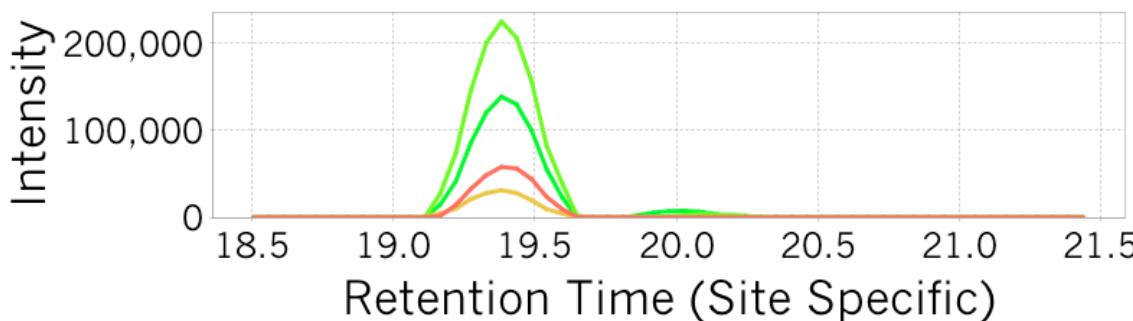
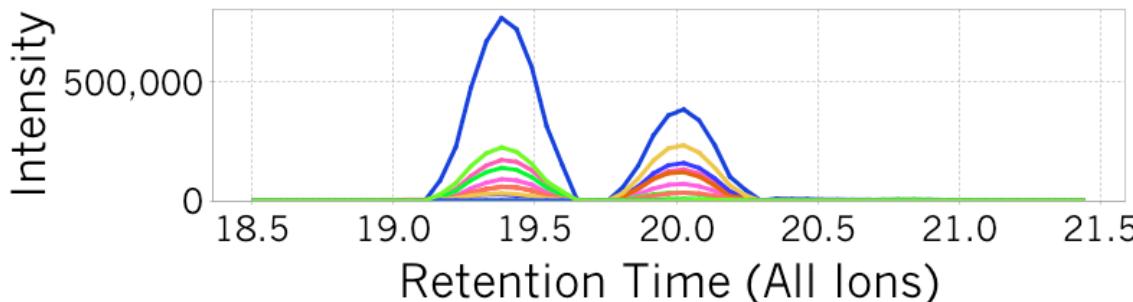
Extraction of Fragment Ions from DIA Data

VLENTFEIGSDSIFDK++ (790.4 m/z)

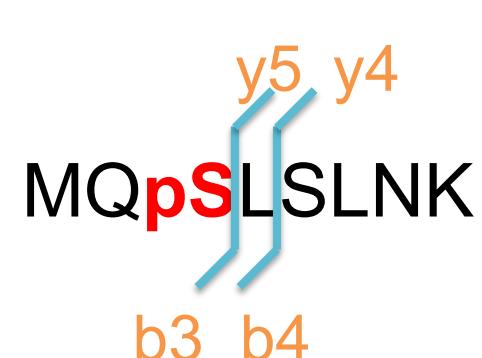


Venable et al Nat Methods 2004
Dong et al Science 2007

Localizing using site specific ions for phosphopeptides



All ions for MQSLpS_LNK
or MQpS_LS_LNK



In collaboration with Judit
Villen

DIA: Easy to collect, hard to unlock

- We want a query engine for DIA data
- We need and expect as good or better peptide detections than DDA
- We need to ensure no missing data across many runs
- Short processing times

The Idea of a Query Engine for DIA data

≡ Dunkin' Donuts  

Hours
Any time

Dunkin' Donuts
\$ · Donut Shop · 5th Ave S
Chain known for donuts & coffee
Open until 7:00 PM 

Dunkin' Donuts
4.2 ★★★★☆ (43)
\$ · Donut Shop · W Military Dr
Chain known for donuts & coffee 

Dunkin' Donuts
4.0 ★★★★☆ (6)
\$ · Donut Shop · W 11th St
Chain known for donuts & coffee
Open until 11:00 PM 

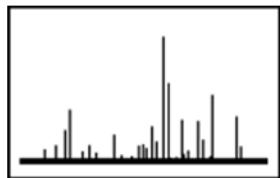
Dunkin' Donuts
3.7 ★★★★☆ (27)
\$ · Donut Shop · 15 1st Ave SW, Kahler Grand Hotel
Chain known for donuts & coffee
Open until 7:00 PM 



Peptide-Centric Analysis as a Query Engine

Spectrum-Centric Analysis

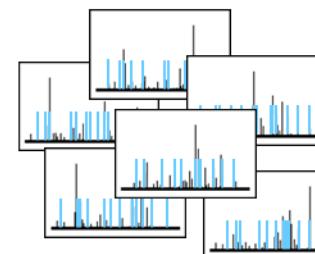
What peptide(s) best explain the data?



MS/MS spectrum



Protein sequence
database



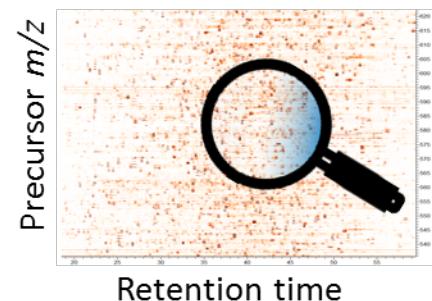
Peptide spectrum matches
(PSMs)

p-value
q-value

Peptide-Centric Analysis

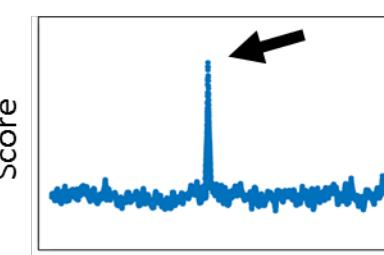
Is this peptide detected in the data?

NLPFSVENK



Peptide of interest

DIA data



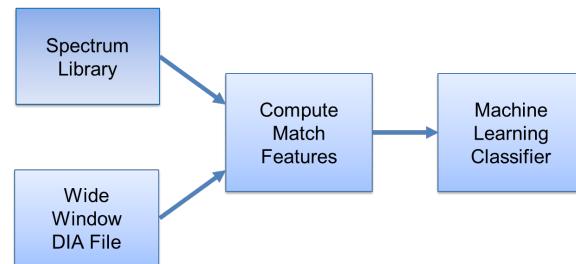
Retention time

p-value
q-value

Evidence for detection

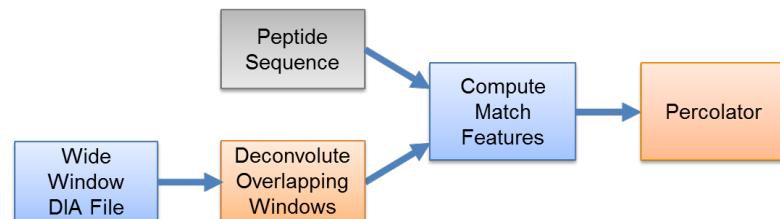
Two Innovative Tools for Peptide-Centric Analysis

■ Typical Workflow



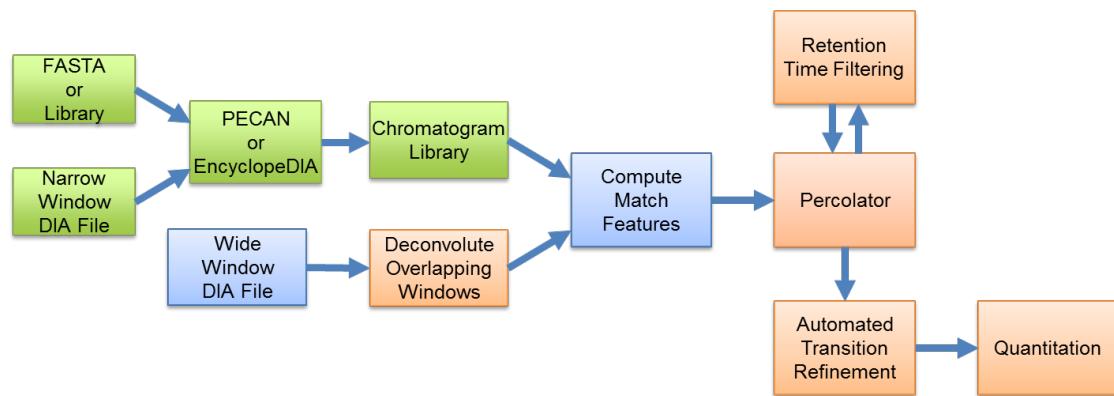
■ Tool 1: Pecan

- Uses only peptide sequences
- No spectral or retention time information

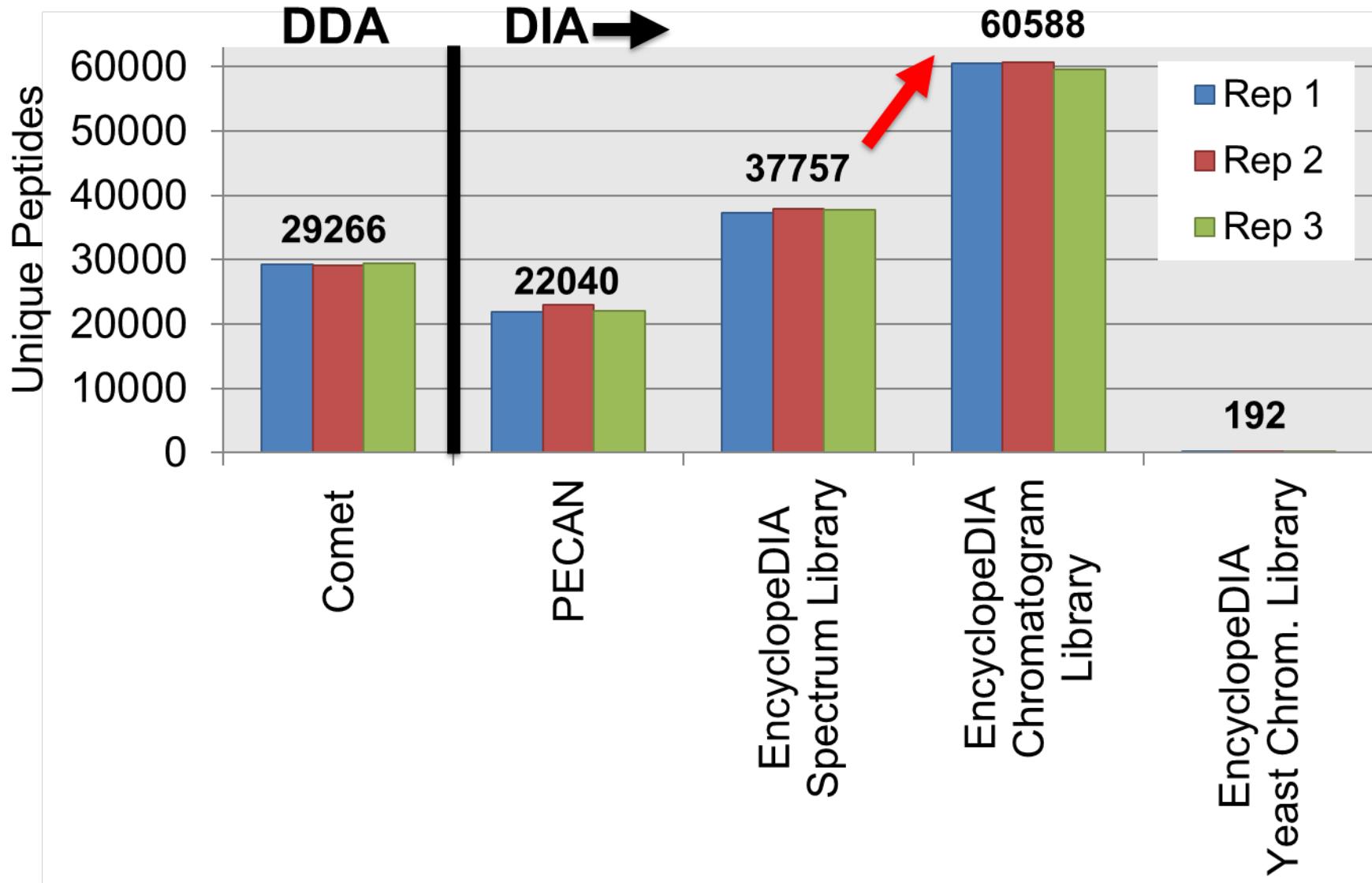


■ Tool 2: EncyclopeDIA

- Uses peptide sequences
- Spectrum or Chromatogram libraries
- Positional isomers



Pioneering methods meeting or exceeding goals



Chorus: Sharing and Dissemination of RAW Data

- The proteomics data needs to be “un-siloed”
 - A single place for all data
- Data is too large to move around.
- We need to bring algorithms to the data

Google Drive - My Drive > 2013-Slides

Name	Owner	Last modified	File size
ASMS	Michael MacCoss	9/2/14	Michael MacCoss
ASMS Short Course	Michael MacCoss	9/2/14	Michael MacCoss
Brendan	Michael MacCoss	9/2/14	Michael MacCoss
CSDL Proteomics Course	Michael MacCoss	9/2/14	Michael MacCoss
Jarrett	Michael MacCoss	9/2/14	Michael MacCoss
MSACL	Michael MacCoss	9/2/14	Michael MacCoss
120128-call with Ron Moore.pptx	Michael MacCoss	9/2/14	Michael MacCoss
120128-call with Ron Moore.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2012-IU International Isotope Symposium.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-Alen Brain Institute.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-BAIMS.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-Biogen.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-Campinas-1.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-Campinas-2.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-Celgene.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-CST.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-ISPPB-Boston.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-KHUPD.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-MacCoss-Pathology.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-MacCoss-Pathology2.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-MacCoss-Vienna.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-NIH MS Repositories.pdf	Michael MacCoss	9/2/14	Michael MacCoss
2013-NIH MS Repositories.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-Pittcon.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-Seoul National University.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-Sept-Thermo.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-Shock EAB.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-TAMIS.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-Toronto.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-USHUPO-mjm.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-YRC November.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-YRC-May.pptx	Michael MacCoss	9/2/14	Michael MacCoss
2013-YRC-May.pptx_gsides	Michael MacCoss	9/2/14	Michael MacCoss
2013-YRC-SAB-October.pptx	Michael MacCoss	9/2/14	Michael MacCoss
Big Data, Algorithms Grand Challenges.pptx	Michael MacCoss	9/2/14	Michael MacCoss
DIA focus.pptx	Michael MacCoss	9/2/14	Michael MacCoss
DIA-basics.pdf	Michael MacCoss	9/2/14	Michael MacCoss
DIA-basics.pptx	Michael MacCoss	9/2/14	Michael MacCoss
GS retreat-2013.pptx	Michael MacCoss	9/2/14	Michael MacCoss

51 GB used (35%)
Buy more storage

Chorus - Projects

All Projects

ID	PROJECT NAME	OWNER	LABORATORY	AREA OF RESEARCH	MODIFIED
724	Comparison of bottom-up and middle...	Simone S...	Garcia Lab	Epigenetics	Dec 26, 20...
751	Cryptococcus neoformans spore prote...	Alex Hebert	Coon Lab - UW madison	Fungal Pathogen	Dec 22, 20...
747	STAT3 Interactors	Alexander...	Barry Karger Lab	Proteins identified as S...	Dec 17, 20...
745	UL97 influences global changes in phos...	David Perl...	Collaborative Proteom...	HCMV virology	Dec 15, 20...
671	IPF Proteomics	Matt Foster	Duke Proteomics Core ...	BALF Proteomics	Dec 11, 20...
679	DeBlasio_MPML_2015_PLRV_co-IP	Stacy DeB...	Cilia	Plant Virology	Nov 26, 20...
723	Proteome and secretome characterisat...	Jeroen Krij...	European Molecular Bi...	Proteomics	Nov 24, 20...
722	Detecting envelope stress by monitori...	didier vert...	de Duve Institute - Ma...	Molecular Microbiology	Nov 21, 20...
715	Detecting envelope stress by monitori...	Manuel B...	European Molecular Bi...	Bacterial cell biology	Nov 19, 20...
683	mRNA binding protein	Sophia Fo...	European Molecular Bi...	RNA-binding	Oct 30, 20...
701	SWATH™ Analysis for Characterization...	Simone S...	Garcia Lab	Epigenetics	Oct 29, 20...
670	Off-line high pH reversed-phase fractio...	Tanver B...	Novo Nordisk Foundat...	Phosphoproteomics	Oct 27, 20...
619	Azospirillum brasiliens	Greg Hurst	Organic and Biological...	microbiology	Oct 24, 20...
682	Colwellia psychrerythraea at subzero...	Brook Nunn	Nunn Lab	environmental proteo...	Oct 23, 20...
679	Skyline Tutorial Webinars	Brendan ...	MacCoss Lab	Skyline Outreach	Oct 23, 20...
663	Worm Protein Expression (PES) Study	Michael R...	MacCoss Lab	<i>C. elegans</i> developme...	Oct 7, 2014
662	Wheat Target Antigens in Celiac Diseas...	William Ve...	Western Regional Rese...	Wheat Proteomics	Oct 4, 2014
658	Yeast_Salt_Stress_MSB	Alex Hebert	Coon Lab - UW madison	yeast salt stress phospho...	Sep 30, 20...
650	Diatom response to alleopathy	Brook Nunn	Nunn Lab	Diatom proteomics	Sep 27, 20...
651	Signaling network stimulated by Beta2...	Bill Lane	Harvard Mass Spectro...	Signaling	Sep 26, 20...
639	Bacteria metaproteomics QExactive U...	Brook Nunn	UWPR (University of W...	environmental proteo...	Sep 12, 20...
638	PECAN	Ying Sonia...	MacCoss Lab	Proteomics	Sep 9, 2014
634	iCAN label-free data sets	Chengjian...	Qu's Lab	Quantitative Proteomics	Sep 9, 2014
633	Test Analyses	Michael M...	MacCoss Lab	Proteomics	Sep 3, 2014
630	Proteomics of rare cells	Alexander...	Barry Karger Lab	High sensitivity Proteo...	Sep 3, 2014

All Experiments

All Files

Search Databases

Trash

My LABS

MacCoss Lab

Files

LTQ

LTQ Orbitrap Velos

LTQ Velos Pro

LTQ-FT Ultra with lo...

MPS Orbitrap Fusion

Orbitrap Fusion

Q-Exactive

Q-Exactive HF

Quantiqa

UWPR Q Exactive

Voyager 1

Page 1 of 4

Items per page: 25 | 50 | 100 | 200

Chorus allows extensive data organization

Chorus beta News Blogs Application About Support Forum Search Nathan Yates ▾

+ Create ▾

Upload Files

Public Projects

Filter list

GLOBAL REPOSITORY	ID	PROJECT NAME	OWNER	LABORATORY	AREA OF RESEARCH	MODIFIED
All Projects	1	599 Bering Sea Sedimentary Proteins	Brook Nunn	UWPR (University of Washi...	environmental proteomics	Aug 18, 2014
• My Projects	2	438 Target Engagement Markers in Cerebrospinal Fluid - JPR ...	Nathan Yates	CHORUS Demo Lab	Proteomics	Aug 14, 2014
• Shared with Me	3	568 Arabidopsis WT and QR mutant Abscisic Acid Phosphoprote...	Benjamin Mink...		Plant Proteomics	Jul 31, 2014
• Public Projects >	4	522 NeuCode SILAC	Anna Merrill	Coon Lab - UW madison	Proteomics	Jun 30, 2014
All Experiments	5	492 Fu				
• My Experiments	6	457 St				
• Shared with Me	7	303 En				
• Public Experiments	8	366 Pr				
All Files	9	350 Al				
• My Files	10	385 Al				
• Shared with Me	11	365 H				
• Public Files	12	351 Su				
Search Databases	13	352 Heterogeneous				
Trash	14	331 Growth Factor				
MY LABS	15	349 OSU_SIP				
MY GROUPS	16	345 hippocampi his				
ADMINISTRATION TOOLS	17	325 Regulation of F				
REQUESTS	18	134 WRN proteomic				
	19	336 Disulfide bond				
	20	96 Exhaustive immu				

Public Projects > NeuCode SILAC > Filter list

ID	EXPERIMENT NAME	OWNER	LABORATORY	PROJECT	FILES
1	673 Multiplexing	Anna Merrill	Coon Lab - UW madison	NeuCode SILAC	14
2	672 NeuCode-TMT Comparison	Anna Merrill	Coon Lab - UW madison	NeuCode SILAC	24
3	671 Mixed Ratios	Anna Merrill	Coon Lab - UW madison	NeuCode SILAC	13

Public Projects > NeuCode SILAC > NeuCode-TMT Comparison > Filter list

ID	NAME	SIZE	INSTRUMENT	LABORATORY	UPLOAD DATE
1	39648 19Sep2013_4plexNeuCod...	667.91 MB	Charger	Coon Lab - UW madis...	Jun 30, 2014
2	39649 19Sep2013_4plexNeuCod...	654.67 MB	Charger	Coon Lab - UW madis...	Jun 30, 2014
3	39650 19Sep2013_4plexNeuCod...	637.12 MB	Charger	Coon Lab - UW madis...	Jun 30, 2014
4	39645 19Sep2013_4plexNeuCod...	742.07 MB	Charger	Coon Lab - UW madis...	Jun 30, 2014
5	39646 19Sep2013_4plexNeuCod...	700.27 MB	Charger	Coon Lab - UW madis...	Jun 30, 2014
6	39647 19Sep2013_4plexNeuCod...	675.21 MB	Charger	Coon Lab - UW madis...	Jun 30, 2014

Chorus to allow running pipelines in the cloud – nearly ready

537: With phosphorylation Processing Details

Create New Analysis

General Info

Analysis Name: My analysis

Workflow Type: Shotgun

Ratio: All Pairwise

Factor: Time

Using: 24

Description (optional):

Isolation Width (min 0.5): 2

Max Charge (min 1 - max 7): 7

Rt Error Max: 2

Mz Error Max: 10

Protein Search Range: Overriding the default search range to reduce execution time. However, this may affect results.

Min Rt:

Min Mz:

Cancel

Create New Analysis

General Info

Create New Analysis

General Info

Processing

Database

Mucata new

Precursor Mass Tolerance

20

Modification Parameters (Amino Acid)

M 15.994

Static Modification Parameters (Amino Acid)

C 57.021

Mass Type Fragment

monoisotopic ma...

Cancel

Create New Analysis

General

Name: My analysis

Ratio: All pairwise

Description:

Workflow Type: Shotgun

Processing Params

Max Charge: 7

Isolation Width: 2

Search Bounds: Rt (from start - till end), Mz (from start - till end)

Comet Params

Database: Mucata new

Mass Type Parent: monoisotopic masses

Precursor Mass Tolerance: 20

Peptide Mass Units: ppm

Dynamic Modifications: 15.9949 M 0 3

Static Modifications: 57.021464 C

Mass Type Fragment: monoisotopic masses

Cancel

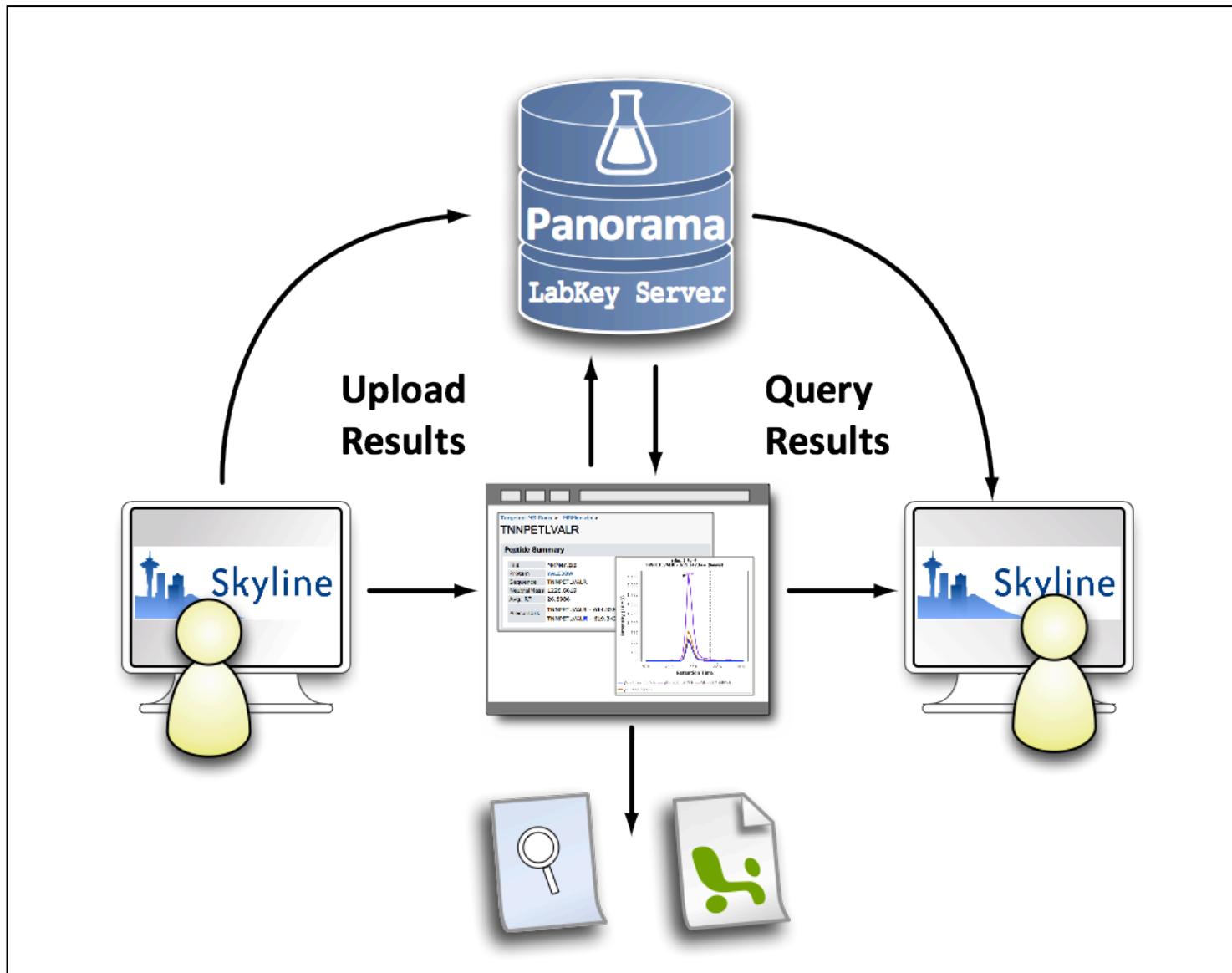
Back

Run Analysis

Database Search Engines

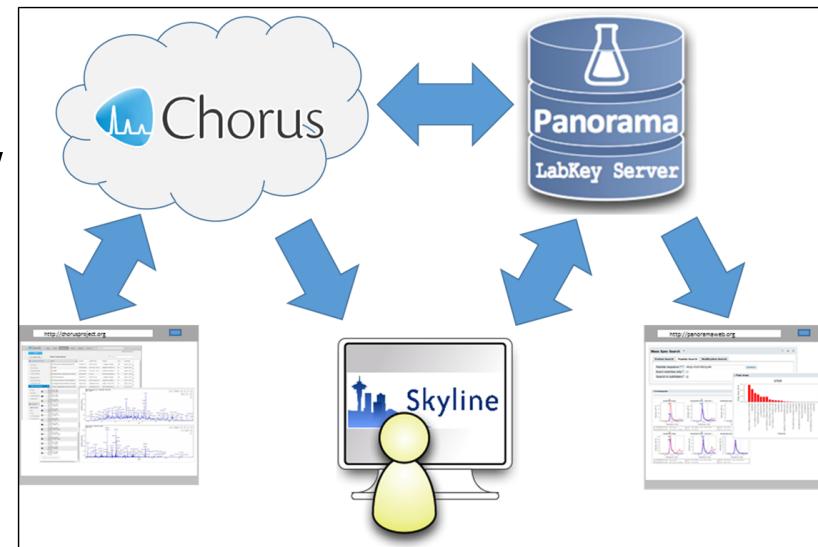
- Comet (SEQUEST) and Percolator

Sharing processed data in Panorama



Next-Gen MS summary and outlook

- Comprehensive MS (**DIA**) is already here
 - Acquisition methods will continue to improve further
- We have **promising algorithms** to monitor unprecedented numbers of analytes in LINCS P100 DIA data
- Our Chorus cloud infrastructure will help us to **share** our data and promote **reuse**.
- Chorus will also enable use to efficiently **bring compute to the data** rather than vice versa.



PCCSE Overall Summary

- Great progress has been made in the first two years in establishing our center
- Our neurobiology models are progressing nicely and we are excited to extend these further
- Next-Gen MS holds great promise for increasing the impact of our work
- We are poised to use our data “as is” for comprehensive connectivity analysis, but also as a springboard for comparison with new data to be made via:
 - Our continued efforts
 - Our outreach and collaboration efforts
 - Data made by third parties