



# The Network Data Exchange in 2017

Trey Ideker, Dexter Pratt, UCSD

aka the “Cytoscape Cloud”

NDEx is a public commons, where users store, share, and publish their networks.

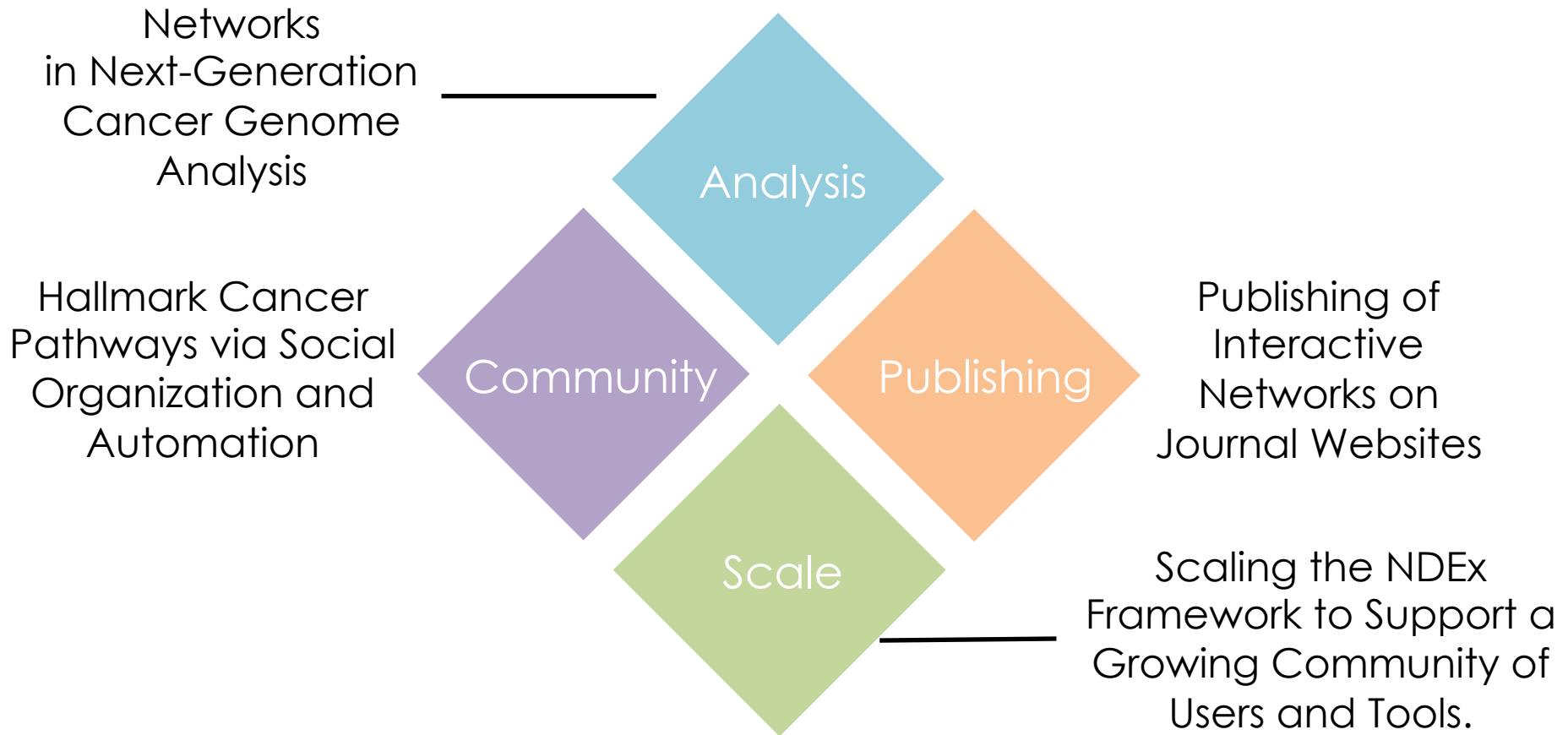
---

Scientists can search for networks and access them from the NDEx site or with their own scripts and applications.

---

NDEx networks have stable, unique identifiers and URIs, enabling reference from publications.

# NDEx Project Goals



Networks  
in Next-Generation  
Cancer Genome  
Analysis

Analysis

Hallmark Cancer  
Pathways via Social  
Organization and  
Automation

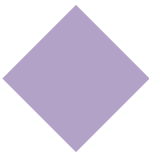
Community

Publishing

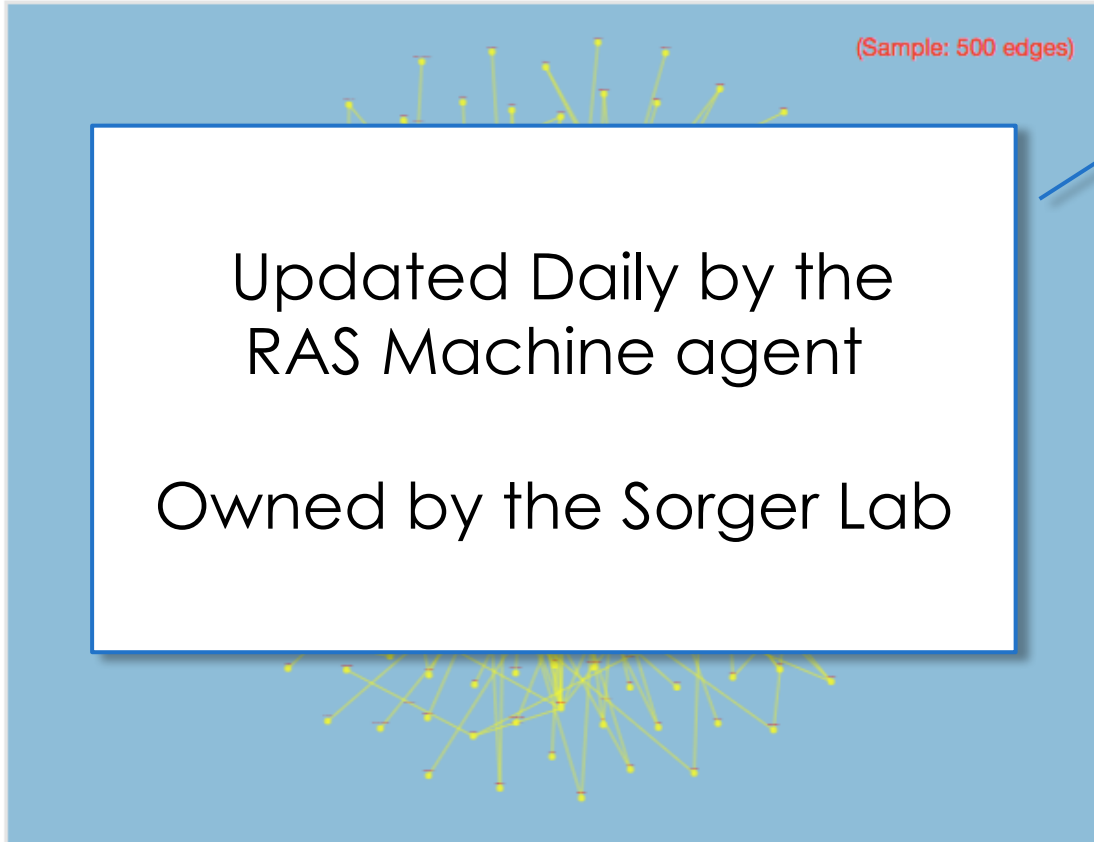
Publishing of  
Interactive  
Networks on  
Journal Websites

Scale

Scaling the NDEx  
Framework to Support a  
Growing Community of  
Users and Tools.



# Access by Users and Applications



Network Info

Nodes/Edges

Provenance

## The RAS Machine

Nodes: 819 Edges: 2685

**PUBLIC**  Read Only

Created: May 5, 2016 8:55:04 PM

Last Modified: May 31, 2017 7:10:55 AM

UUID: 50e3dff7-133e-11e6-a039-06603eb7f303

Format: Unknown

Your Privileges: None

### Description:

The RAS Machine reads new literature on RAS daily, and extracts and assembles mechanisms into a computational model using INDRA.

Version: 3.183

### Properties:

Network Terms

Depth: 1-step ↕

Run Query

[Advanced Query](#)

Download

Table View

Export

Upgrade Permission



# Access by Users and Applications



Edges Nodes

Source	Interaction	Target	Citations	INDRA
CREBBP	Acetylation	TP53	2	Acetyla
EP300	Acetylation	TP53	1	Acetyla
KAT5	Acetylation	TP53	1	Acetyla
KSR1	Acetylation	TP53	1	Acetyla
AGT	Activation	AKT	1	Activat
AKT1	Activation	AKT	1	Activat
AKT1	Activation	CREB1	1	Activat
AKT2	Activation	EZR	1	Activat
AKT	Activation	BRAF	1	Activat
AKT	Activation	BCL2	3	Activat
AKT	Activation	CNS	2	Activat

Total Items: 500

Network Info Nodes/Edges Provenance

## The RAS Machine

Nodes: 820 Edges: 2688  
PUBLIC  Read Only

Created: May 5, 2016 8:55:04 PM  
Last Modified: Jun 1, 2017 7:14:50 AM  
UUID: 50e3dff7-133e-11e6-a039-06603eb7f303  
Format: Unknown

**Description:**  
The RAS Machine reads new literature on RAS daily, and extracts and assembles mechanisms into a computational model using INDRA.

Version: 3.184

Properties:

Network Terms  Depth: 1-step  [Advanced Query](#)

# Search

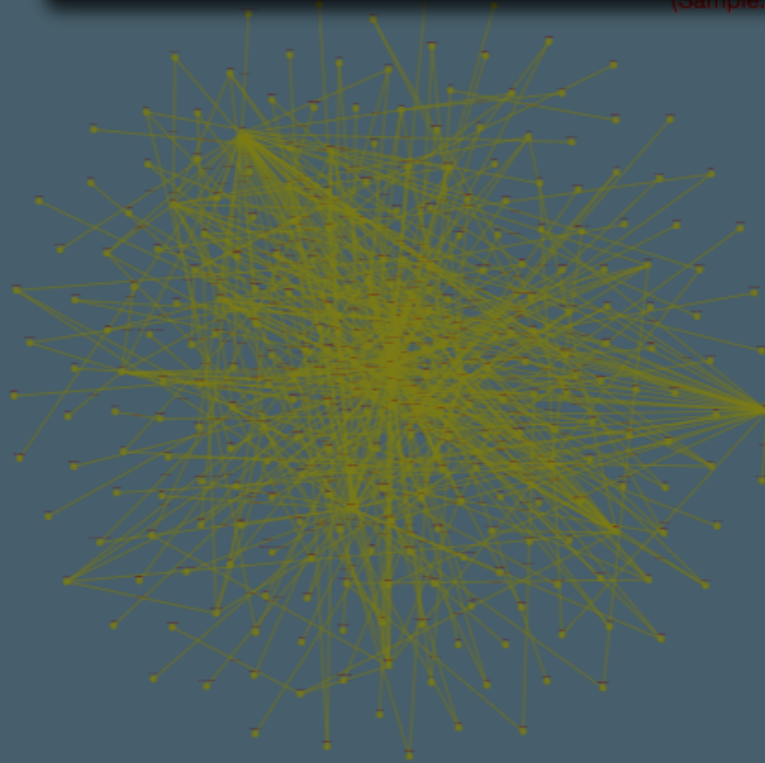


Search Examples ▾

Browse

All ▾

ras machine



## The RAS Machine

Nodes: 819 Edges: 2685

**PUBLIC**  Read Only

**Created:** May 5, 2016 8:55:04 PM

**Last Modified:** May 31, 2017 7:10:55 AM

**UUID:** 50e3dff7-133e-11e6-a039-06603eb7f303

**Format:** Unknown

**Your Privileges:** None

### Description:

The RAS Machine reads new literature on RAS daily, and extracts and assembles mechanisms into a computational model using INDRA.

**Version:** 3.183

**Properties:**

Network Terms

Depth: 1-step ▾

Run Query

[Advanced Query](#)

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Table View

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# Search



Home About Docs Report Bug Contact Us Cite NDEx Q MyAccount

Search Examples ▾ Browse All ▾ ras machine Q X

Mentioning any term in a list: "TP53 MDM2 RB1 CDK4"  
With "AND" for co-occurrence : "TP53 AND BARD1"  
By wildcard and property: "name:mel\*"  
By numeric property range: "nodeCount:[11 TO 79]"  
By UUID: "uuid:c53894ce-8e47-11e5-b435-06603eb7f303"  
Created between 1.1.16 and 4.27.16 : "creationTime:[2016-01-01T00:00:01Z TO 2016-04-27T23:59:59Z]"

[Documentation on Searching in NDEx](#)

04 PM  
7 7:10:55 AM  
UUID: c53894ce-8e47-11e5-b435-06603eb7f303  
Format: Unknown  
Your Privileges: None

# Search

Search Examples ▾

Browse

All ▾

ras machine



Networks (60)

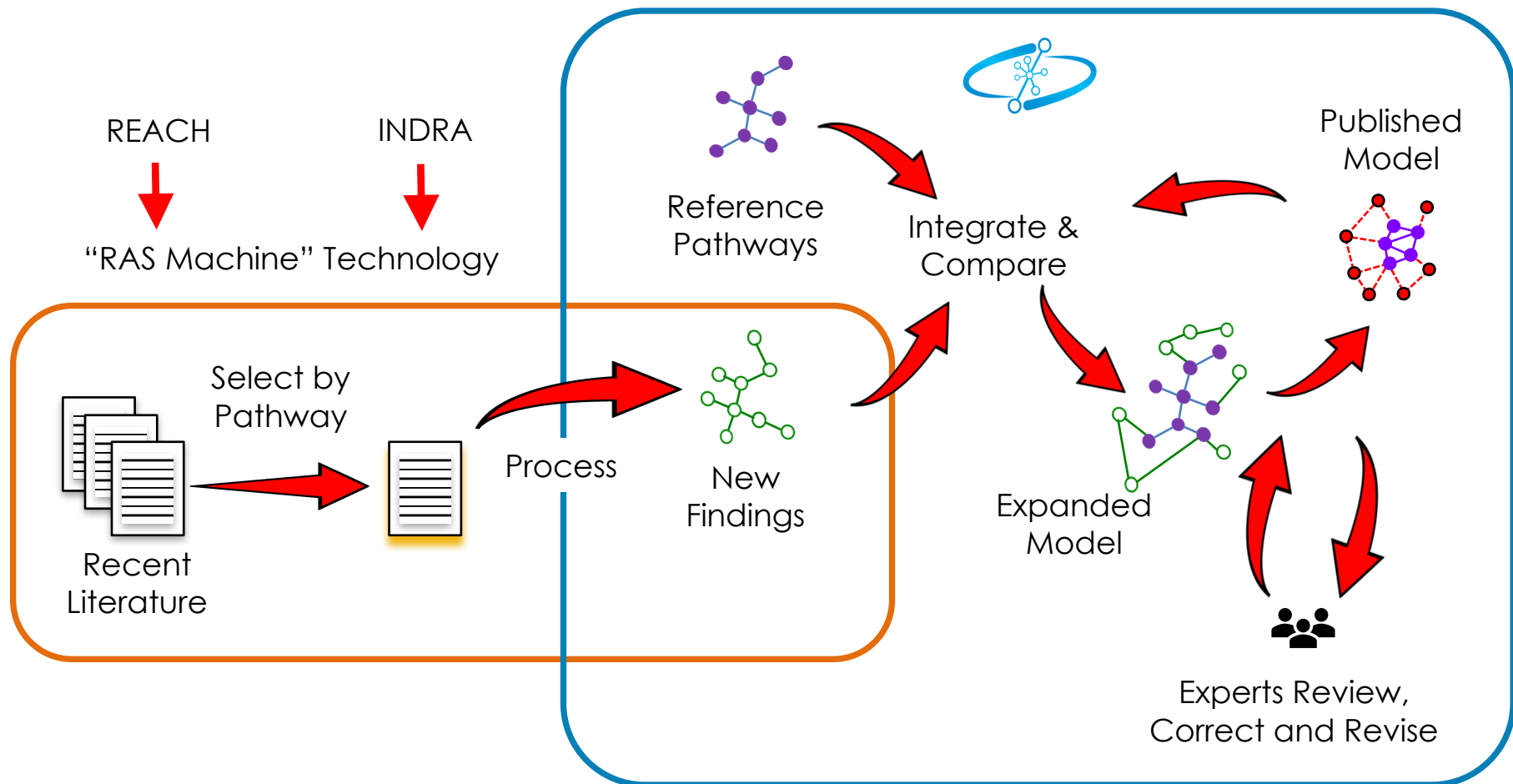
Users (1)

Groups (0)

Network Name		Format	Ref.	Disease	Tissue	Nodes	Edges	Visibility	Owner	Last Modified
<a href="#">The RAS Machine</a>						820	2688	PUBLIC	<a href="#">rasmachine</a>	6/1/17 7:14 AM
<a href="#">The Diabetes Machine</a>						396	668	PUBLIC	<a href="#">rasmachine</a>	5/31/17 8:05 AM
<a href="#">indra_assembled</a>						134	180	PUBLIC	<a href="#">bgyori</a>	4/8/16 7:36 PM
<a href="#">rasmachine</a>						232	292	PUBLIC	<a href="#">bgyori</a>	4/11/16 2:21 PM
<a href="#">Ras signaling in the CD4 TCR pathway</a>						14	24	PUBLIC	<a href="#">nci-pid</a>	12/20/16 4:59 PM
<a href="#">tcell-net-model-viz.txt</a>		XGMML				123	191	PUBLIC	<a href="#">gaten</a>	12/16/16 5:08 AM
<a href="#">insulin_secretion</a>						104	331	PUBLIC	<a href="#">bgyori</a>	4/28/16 2:16 PM
<a href="#">The Heart Machine</a>						647	1365	PUBLIC	<a href="#">rasmachine</a>	5/31/17 9:05 AM
<a href="#">EGF receptor (ErbB1) signaling pathway</a>						38	172	PUBLIC	<a href="#">nci-pid</a>	4/6/17 12:22 PM
<a href="#">RAS_227</a>						164	916	PUBLIC	<a href="#">bgyori</a>	5/5/16 1:29 PM
<a href="#">Regulation of Ras family activation</a>						35	74	PUBLIC	<a href="#">nci-pid</a>	12/20/16 4:59 PM
<a href="#">nci_pid_preview</a>						212	492	PUBLIC	<a href="#">aarongary</a>	4/7/17 3:12 PM
<a href="#">!!! NEW !!! PID MAP !!! NEW !!!</a>				Cancer		212	492	PUBLIC	<a href="#">nci-pid</a>	4/10/17 2:17 PM
<a href="#">net_of_nets_uuids.txt</a>						214	21722	PUBLIC	<a href="#">decarlin</a>	4/27/16 4:12 PM
<a href="#">BindingDB - High Affinity Compounds vs mouse targets (Commercially ava...</a>						105	134	PUBLIC	<a href="#">bindingdb</a>	5/5/16 2:04 PM

# Hallmark Pathway<sup>2</sup> Hypothesis

Social pathways to enable molecular pathways





# Review and Publish

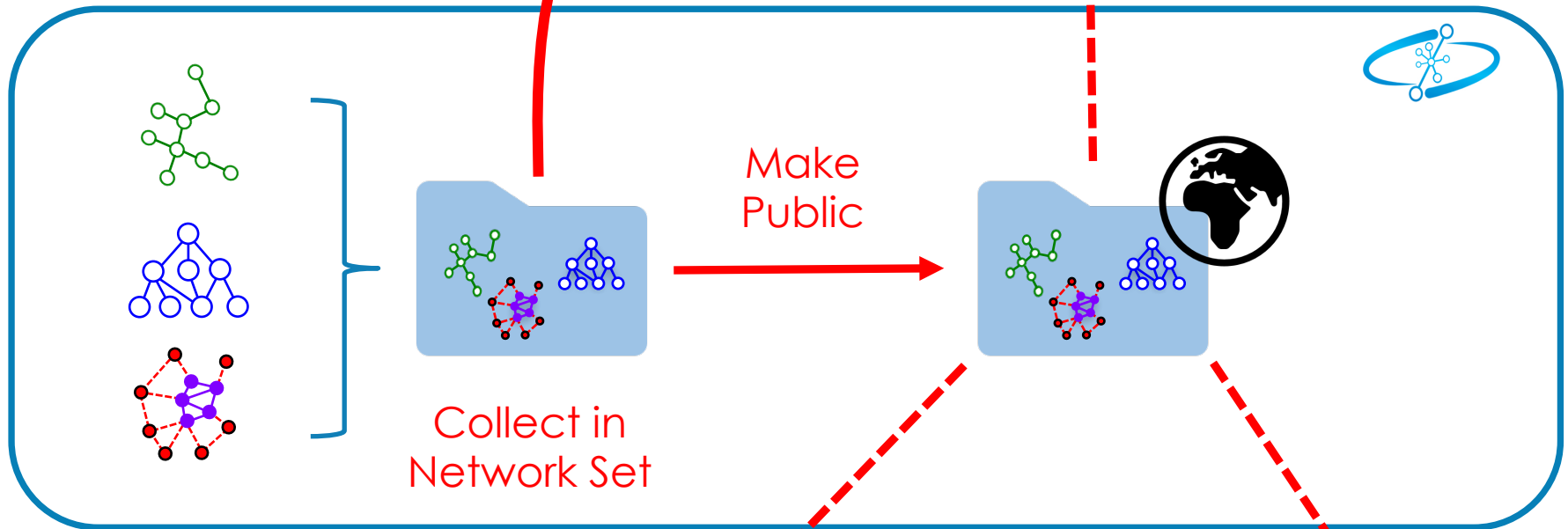
Anonymous  
Pre-Publication  
Access via a  
Shareable URL



Review



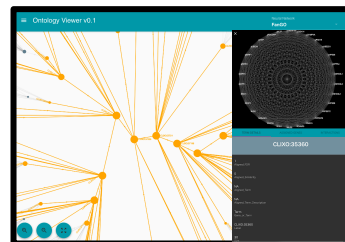
Reference  
from Article



Collect in  
Network Set

Make  
Public

Visualization



# ndexr : Access from R

- Successful Outreach and Collaboration with Bioconductor
- Special thanks to Frank Kramer<sup>1</sup>, Florian Auer<sup>1</sup>, Aleksandar Ishkin<sup>2</sup>

## NDEx R client library

Bioconductor version: Development (3.6)



This package offers an interface to NDEx servers, e.g. the public server at <http://ndexbio.org/>. It can retrieve and save networks via the API. Networks are offered as RCX object and as igraph representation.

Author: Frank Kramer <frank.kramer at med.uni-goettingen.de>, Florian Auer <florian.auer at med.uni-goettingen.de>, Alex Ishkin <aleksandr.ishkin at thomsonreuters.com>, Dexter Pratt <depratt at ucsc.edu>

Maintainer: Florian Auer <florian.auer at med.uni-goettingen.de>

Citation (from within R, enter `citation("ndexr")`):

Kramer F, Auer F, Ishkin A and Pratt D (2017). *ndexr: NDEx R client library*. R package version 0.99.14, <https://github.com/frankkramer-lab/ndexr>.

<sup>1</sup>Department of Medical Statistics, University Medical Center Göttingen, Humboldtallee 32, 37099 Göttingen, Germany.

<sup>2</sup>Discovery Science, Clarivate Analytics, 22 Thomson Pl, Boston, MA 02210, US

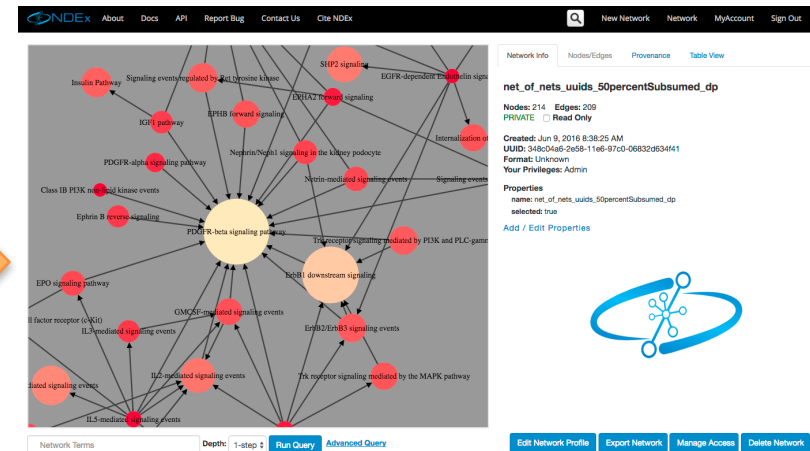
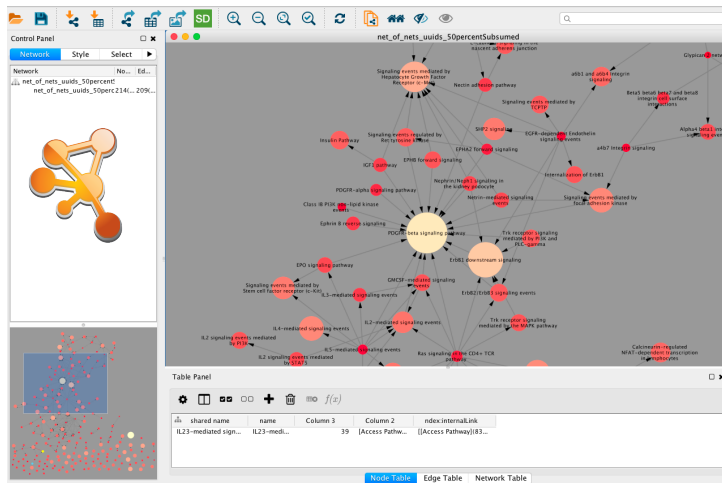
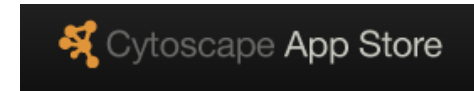


# Cytoscape and NDEx



## CyNDEx

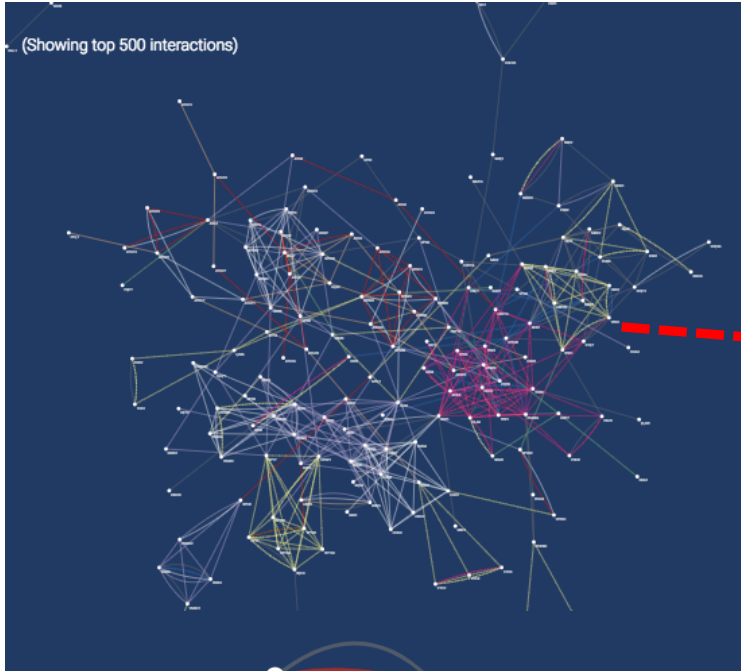
CyNDEx allows users to seamlessly transfer networks between NDEx and Cytoscape and, in certain cases, even perform network updates in NDEx.



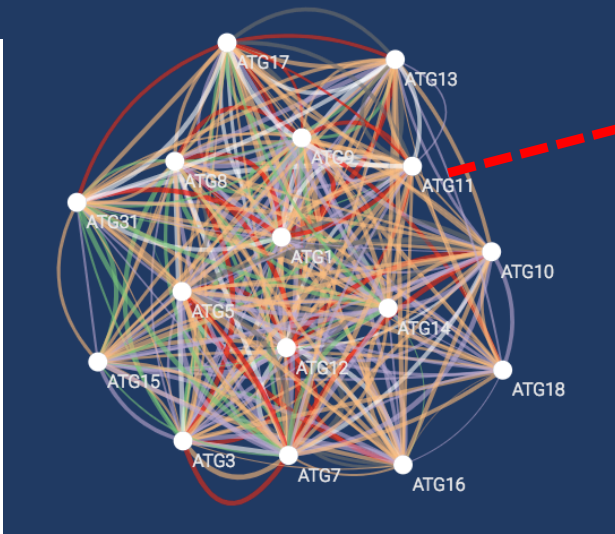
Cytoscape and NDEx communicate via the novel CX exchange format. Seamless integration with Cytoscape core in Summer 2017.

# Hierarchical Organization of a Large Network

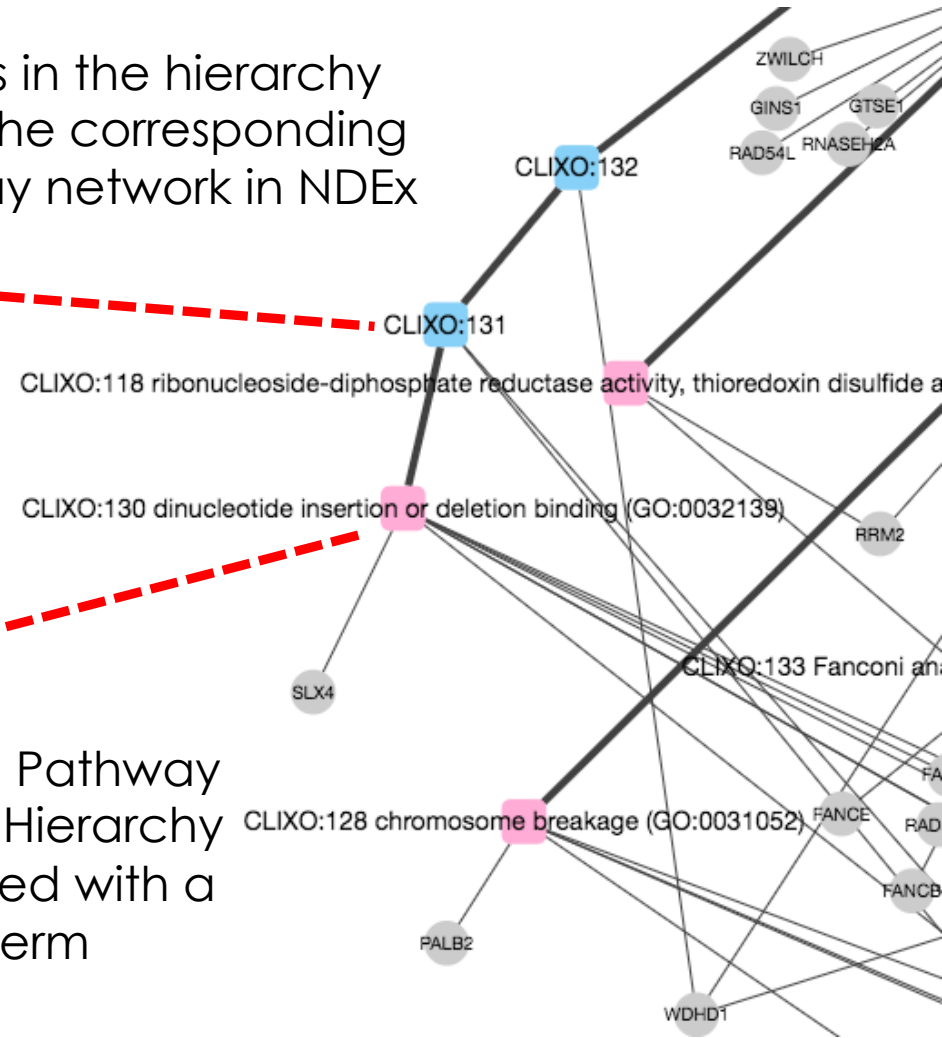
Dutkowski et al. *Nat Biotech* 2013; Kramer et al. *Mol Cell* 2017



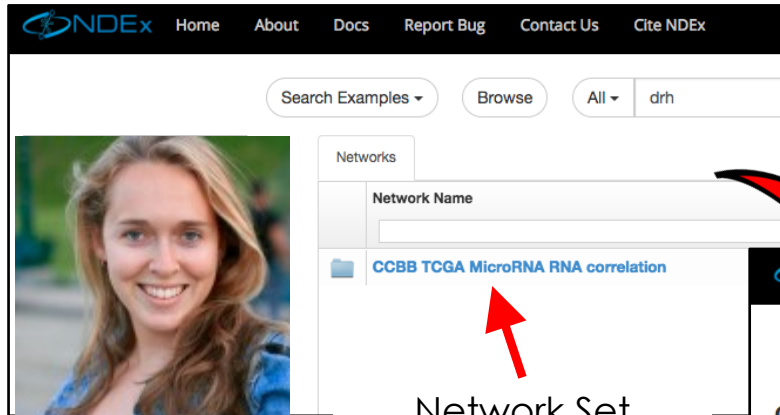
Nodes in the hierarchy link to the corresponding pathway network in NDEX



Supporting Pathway Aligned to Hierarchy Term Aligned with a GO Term



# Scaling with Network Sets



Network Set showcased on user's homepage

Network Sets are named, collections: destinations with unique IDs and URLs.

Network Sets can be published resources, such as collections reviewed by an organization.

Sets provide user-driven structure as NDEx grows to very large numbers of networks.

The screenshot shows the detailed view of the 'CCBB TCGA MicroRNA RNA correlation' network set. It includes a description: 'MicroRNA-RNA Correlation Networks based on TCGA data for ACC, BLCA, BRCA, BLBC, ESCA, HNSC MESO, OV'. Below the description is a table titled 'Networks in set CCBB TCGA MicroRNA RNA correlation' with columns for Network Name, Ref., Disease, Tissue, Nodes, and Edges. A red arrow points from the table to a network visualization showing a complex graph of nodes and edges.

Network Name	Ref.	Disease	Tissue	Nodes	Edges
TCGA Breast Invasive ...	↓	Breast Invasive Carcinoma		50	118
TCGA Bladder Urothel...	↓	Bladder Urothelial Carcinoma		74	458
TCGA Bladder Urothel...	↓	Bladder Urothelial Carcinoma		86	384
TCGA Breast Invasive ...	↓	Breast Invasive Carcinoma		81	183
TCGA Adrenocortical C...	↓	Adrenocortical Carcinoma		61	80
TCGA Adrenocortical C...	↓	Adrenocortical Carcinoma		706	7128
TCGA Adrenocortical C...	↓	Adrenocortical Carcinoma			
TCGA Bladder Urothel...	↓	Bladder Urothelial Carcinoma			
TCGA Bladder Urothel...	↓	Bladder Urothelial Carcinoma			
TCGA Adrenocortical C...	↓	Adrenocortical Carcinoma			
TCGA Adrenocortical C...	↓	Adrenocortical Carcinoma			
TCGA Bladder Urothel...	↓	Bladder Urothelial Carcinoma			

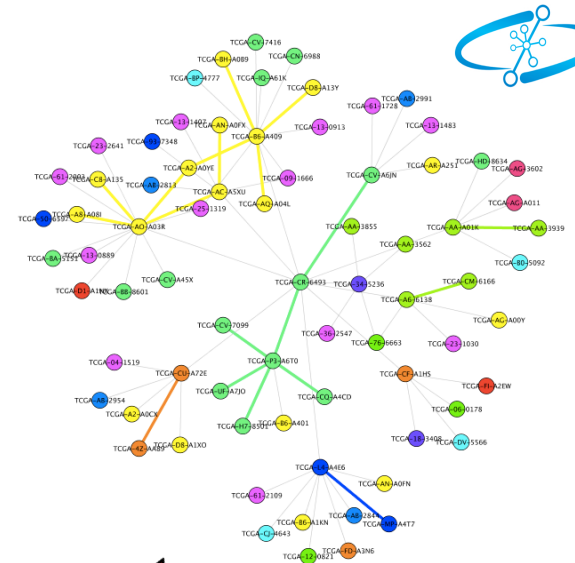
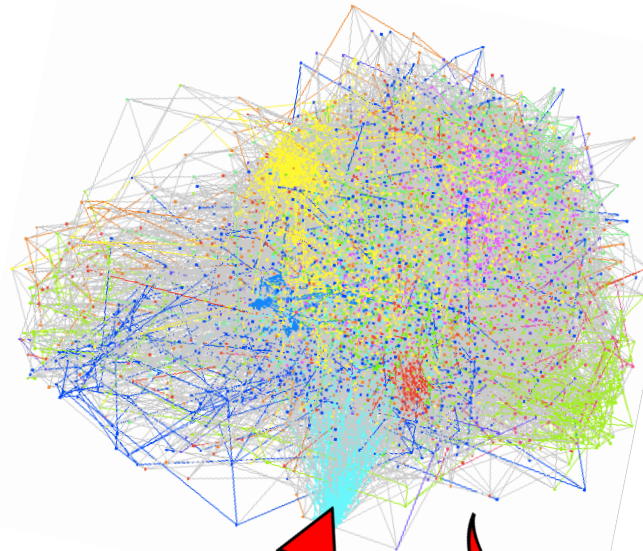
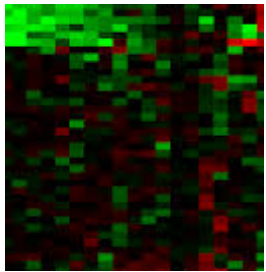
The Network Set contains 101 public networks

# Patient Similarity Networks

Very Large:  
Genome-Scale Patient Data

Large:  
Patient Similarity Network

Small:  
Patients Most Similar to Patient X



Compute Similarity  
and Filter to Create  
a Sparse Network

Query for  
Patient X

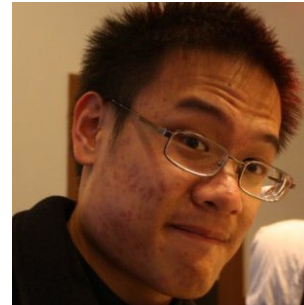
NDEx 2.0 Server Handles Networks that Span a Broad Range of Sizes

Thanks to Dan Carlin and Justin Huang for sharing excerpts from work in progress..

NDEx Team



Ideker Lab



CCBB



And thanks to collaborators at the Karchin and Sorger Labs



**U24 CA1884427**

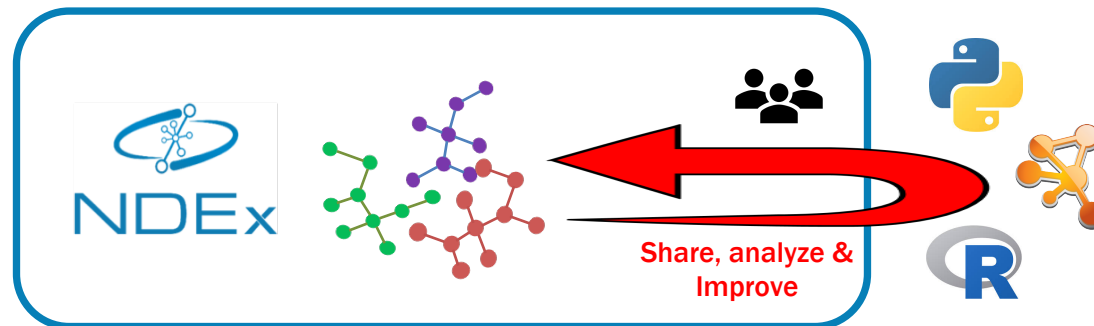


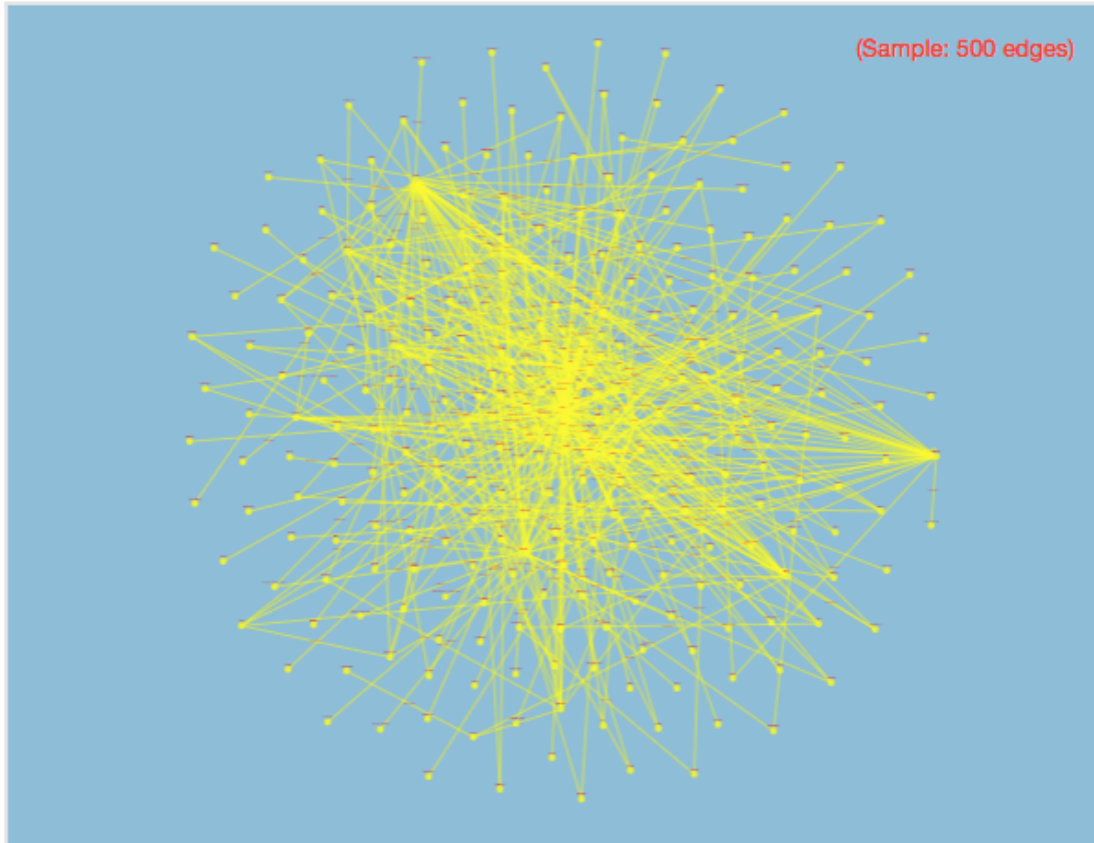
**SUPPLEMENTARY SLIDES →**



# Integration with Analysis Tools (rachel)

- Python client
- R Client
- Outreach at hackathons
  - Use-case driven feedback and prototyping
- NDEx access built into next Cytoscape release





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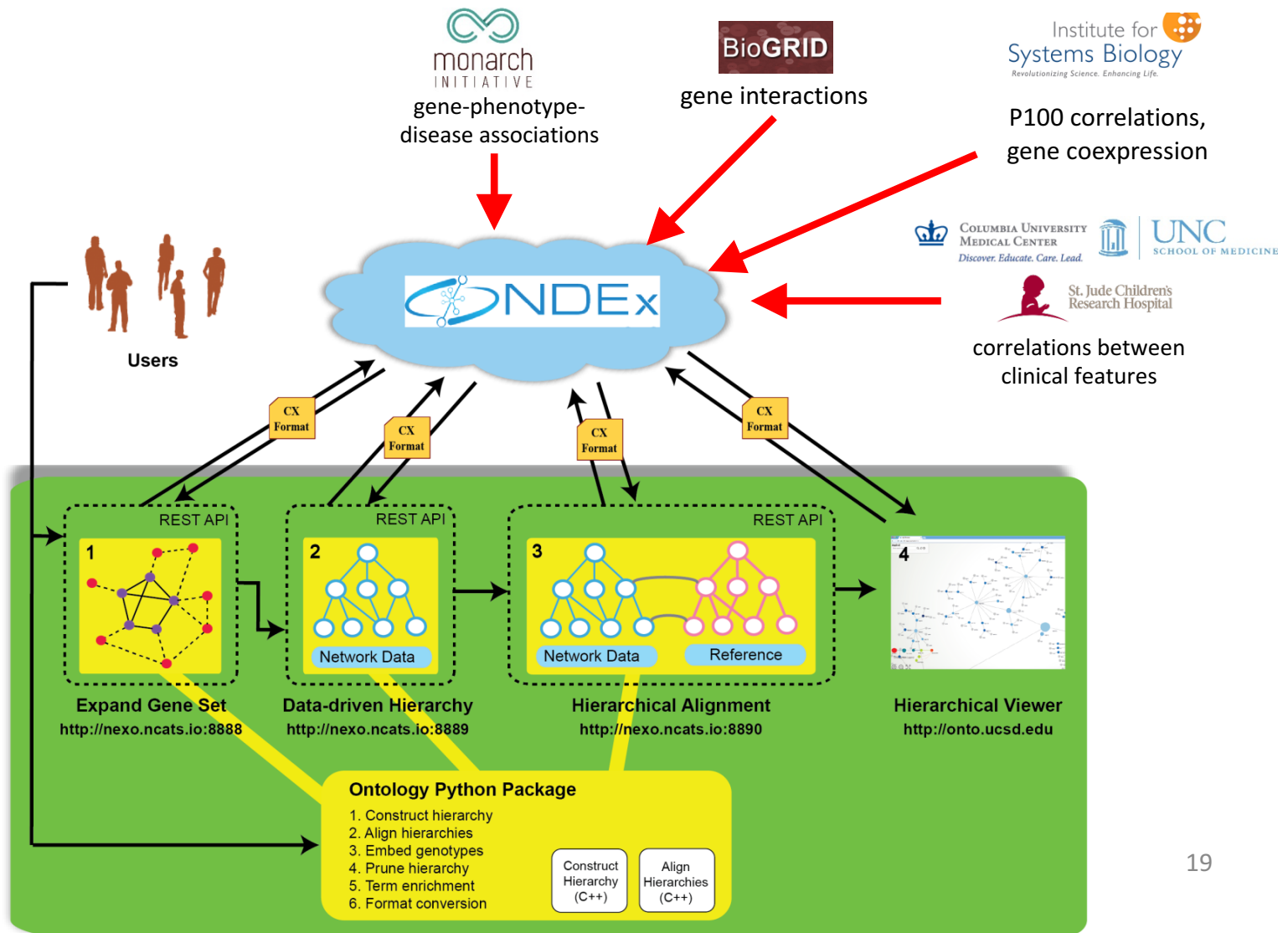
Download

Table View

Export

Upgrade Permission

# Architecture for Reproducing the FanGO Analysis for Any Disease



**NDEx:**  
Upload data and call REST API (or run your own server instance)

**Local machine:**  
Python package



# FanGO: Fanconi Anemia Hierarchy

## Hierarchical Pathway Models Managed in NDEx

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Network Info Nodes/Edges Provenance

**20 known FA genes**

**Data-derived gene similarity network**

CLIXO:141

CLIXO:140

CLIXO:139

CLIXO:138

CLIXO:137

CLIXO:136 double-strand break repair via synthesis-dependent strand invasion (GO:0042148)

CLIXO:135

CLIXO:134

CLIXO:133

CLIXO:132

CLIXO:131

CLIXO:130 dinucleotide insertion or deletion binding (GO:0032139)

CLIXO:129 DNA recombinase assembly (GO:0040730)

CLIXO:128

CLIXO:127 Rad51B-Rad51C-Rad51D-XRCC2 complex (GO:0033063)

CLIXO:126

CLIXO:125 DNA unwinding involved in chromosome breakage (GO:0031052)

CLIXO:124 DNA replication factor C complex (GO:0005663)

CLIXO:123 BRCA1-BARD1 complex (GO:0031436)

CLIXO:122 Rad51C-XRCC3 complex (GO:0033065)

CLIXO:121 nucleotide excision repair involved in interstrand cross-link repair (GO:1901255)

CLIXO:119 rbonucleoside-diphosphate reductase activity, thionin disulfide as acceptor (GO:0004748)

CLIXO:118

CLIXO:117

CLIXO:116

CLIXO:115

CLIXO:114

CLIXO:113

CLIXO:112

CLIXO:111

CLIXO:110

CLIXO:109

CLIXO:108

CLIXO:107

CLIXO:106

CLIXO:105

CLIXO:104

CLIXO:103

CLIXO:102

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CLIXO:8

CLIXO:7

CLIXO:6

CLIXO:5

CLIXO:4

CLIXO:3

CLIXO:2

CLIXO:1

CLIXO Term (match in GO)

CLIXO Term (no match in GO)

Gene

Interpreting gene ontologies from pairwise similarity data. Bioinformatics. 2014 Jun 15;30(12):i34-42. doi: 10.1093/bioinformatics/btu282. Dutkowski J, Kramer M, Surma MA, Balakrishnan R, Cherry JM, Krogan NJ, Ideker T. A gene ontology inferred from molecular networks. Nat Biotechnol. 2013 Jan;31(1):38-45.

Thanks to Mike Yu for sharing excerpts from work in progress..

# Automation

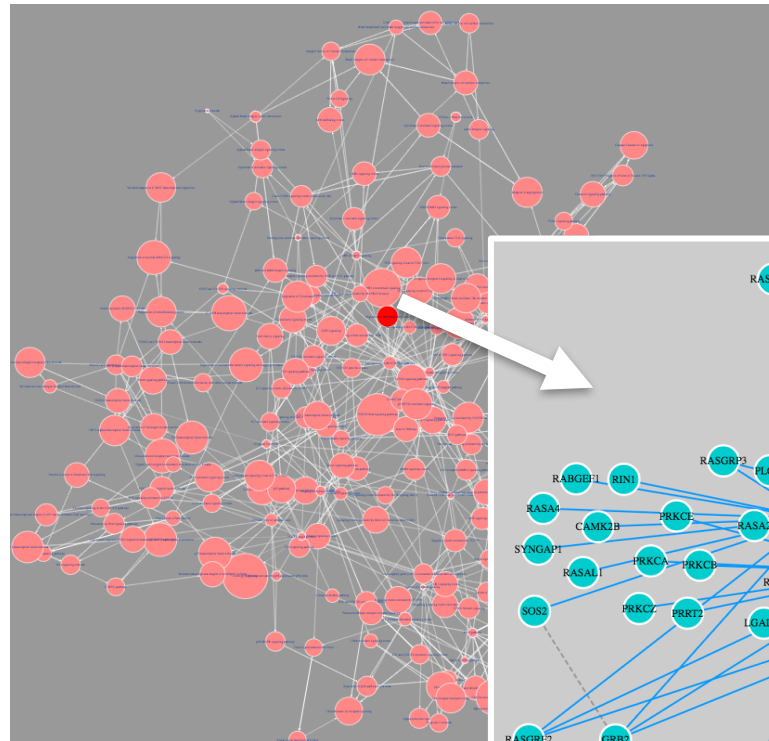
Python Utilities:

Apply Style  
Templates Created  
in Cytoscape

Apply a Layout to  
All Networks in a Set

Next:

Automated Update from Tabular Data  
Sources and Literature Mining



Updated  
NCI PID  
Pathways

