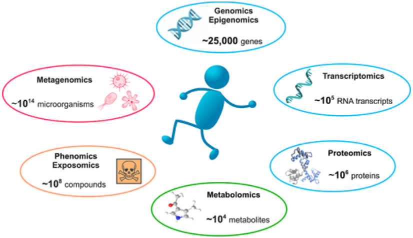
SpideR

R Package for Search, Integration and Retrieval of Big Data

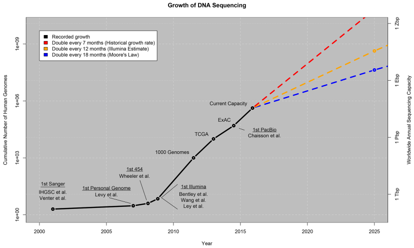
Anna M. Sozanska

Supervisors: Dr Shamith Samarajiwa, Dr Dora Bihary
MRC Cancer Unit
University of Cambridge

Biological datasets are rapidly growing in number

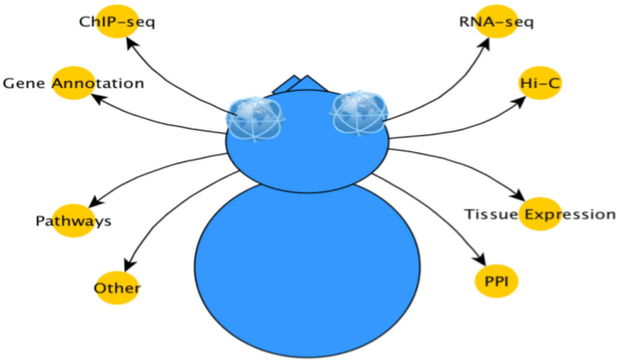


(Gligorijević et al, 2016)



(Stephens et al, 2015)

SpideR: Tool for integrated management of biological datasets

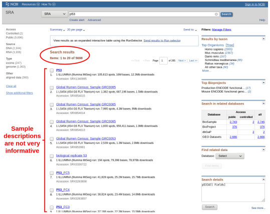


SpideR takes **minutes** to output data that it would take **months** to collect manually

Task: High-throughput bioinformatics analysis

Collect *all** ChIP-seq and RNA-seq samples for **p53** from public databases

- Identify special category samples ('inputs' for ChIP-seq)
- Integrate information from multiple databases (SRA and GEO)



NCBI Resources How To Sign in to NCBI

SRA | SRA | p53 | Search

Create alert Advanced Help

Access
Controlled (2)
Public (5,696)

Source
DNA (2,344)
RNA (3,306)

Type
exome (247)
genome (1,063)

Other
aligned data (360)

Clear all
Show additional filters

Summary 20 per page Send to:

View results as an expanded interactive table using the RunSelector. Send results to Run selector

Search results
Items: 1 to 20 of 5698

<< First < Prev Page 1 of 285 Next > Last >>

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Filters: Manage Filters

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Mus musculus (2367)
Danio rerio (167)
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Production ENCODE functional... (17)
Mouse ENCODE functional geno... (2)

Search in related databases

Database	Access		all
	public	controlled	
BioSample	2,743	2	2,745
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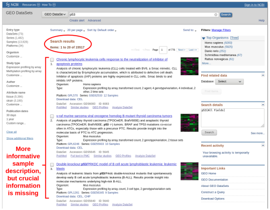
Find related data
Database: Select
Find items

Search details
p53[All Fields]
Search See more...

Sample descriptions are not very informative



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Create alert Advanced Help

Entry type
DataSets (73)
Series (1,482)
Samples (13,928)
Platforms (34)

Organism
Customize ...

Study type
Expression profiling by array
Methylation profiling by array
Customize ...

Author
Customize ...

Attribute name
tissue (5,386)
strain (3,180)
Customize ...

Publication dates
30 days
1 year
Custom range...

Clear all
Show additional filters

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Platform: GPL570 Series: GSE62533 12 Samples
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PubMed Similar studies GEO Profiles Analyze DataSet

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Filters: Manage Filters

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More...

Find related data
Database: Select
Find items

Search details
p53[All Fields]
Search See more...

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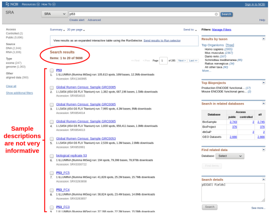

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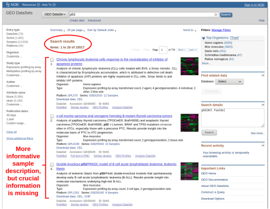

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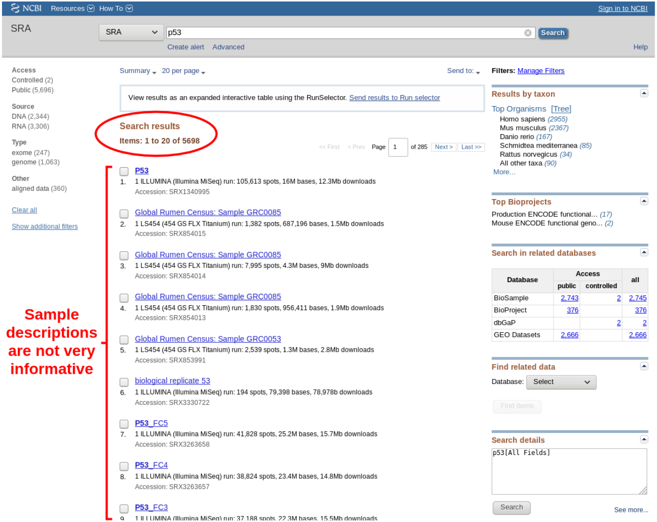

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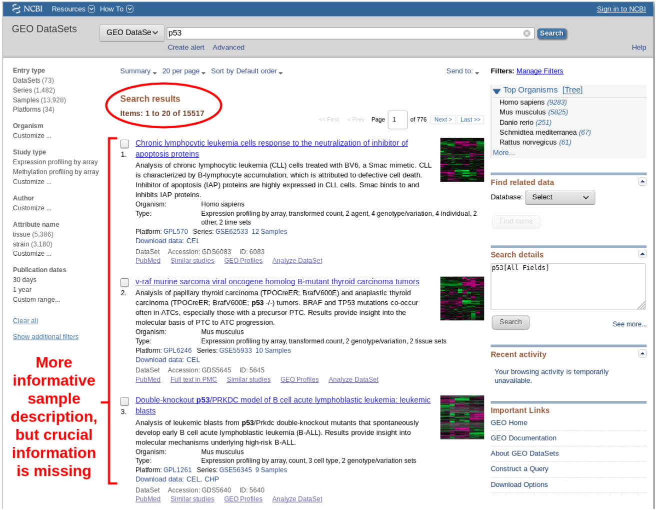

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Database: Select
Find items

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p53[All Fields]
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More informative sample description, but crucial information is missing

GEO and SRA use different accession hierarchies

SRA Name	SRA Acc.	SRA ↔ GEO	GEO Acc.	GEO Name
🟩 Project	🟥 SRP	$\Longleftrightarrow$	🟥 GSE	🟩 Series
🟩 **Sample!**	🟥 SRS		🟥	🟩
🟩 Exp.	🟥 SRX	$\Longleftrightarrow$	🟥 GSM	🟩 **Sample!**
🟩 Run	🟥 SRR		🟥	🟩

Database Accession Numbers

SRA #	SRA	SRA → GEO #	GEO	GEO #
98 028	SRP	17 300	GSE	80 782
2 974 554	SRS	396 513		
2 377 047	SRX	400 975	GSM	2 231 166
3 366 463	SRR	510 890		

Main SpideR Functions

searchForTerm

- IN:
  - library_strategy [R]
  - gene [*]
  - antibody [*]
  - cell_type [*]
  - treatment [*]
  - species [*]
  - platform
  - secondary_lib._strat.
- OUT:
  files for db & pipeline

For example:

Find human HiC data

Find ChIP-seq data
with STAT1 antibody

searchForAccession

- IN: accession list
- OUT: df or files for db & pipeline

For example:

Find runs within SRP052871

Find runs within GSE34715

Other SpideR Functions

superseriesFinder

- IN: GSM list
  List of samples of interest
- OUT: GSM list
  List of all other samples within the same superseries as the samples of interest

convertAccession

- IN: accession list
  In **one** accession format
- OUT: accession list
  In **all** accession formats

inputDetector

Labels inputs in a sample sheet

controlDetector

Labels controls in a sample sheet

dbExtractGenerator

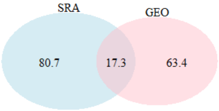
Generates db extract from df

sampleSheetGenerator

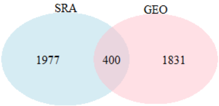
Generates sample sheet from df

SpideR uses a **custom database** to solve the non-trivial problem of SRA/GEO mapping

Projects (SRP/GSE)



Samples (SRX/GSM)



All numbers in 1000s of entries.

- No 1:1 mapping of samples
- Different accession hierarchy
- Different information in each database
- Mapping information scattered across different columns of the database

Exploring hidden sample hierarchy can help find related experiments

Task

Find related ChIP-seq and RNA-seq experiments

Case 1
Relationship easy to establish

SRP#1

- A (ChIP)
- B (RNA)
- C (RNA)

GSE#1

- A (ChIP)
- B (RNA)
- C (RNA)

Case 2
Relationship difficult to establish

SRP#1

- A (ChIP)

SRP#2

- B (RNA)
- C (RNA)

GSE#1

- A (ChIP)

GSE#2

- B (RNA)
- C (RNA)

Superseries?

Overcoming superseries challenge can help find hidden hierarchies

Format in the database

GSE	GSM
GSE1, GSE3	A
GSE1, GSE3	B
GSE1, GSE3	C
GSE2, GSE3	**D**
GSE2, GSE3	**E**
GSE2, GSE3	**F**
GSE2, GSE3	**G**

Approach

Given a list of samples (GSMs), get all the samples that belong to the same GSEs (excluding the original samples).

Overcoming superseries challenge can help find hidden hierarchies

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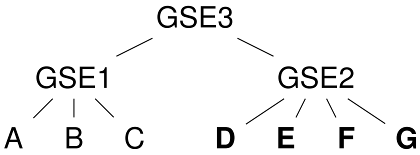

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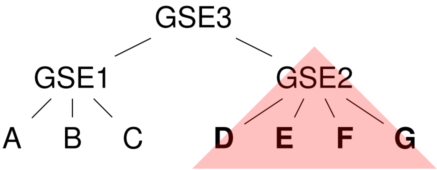

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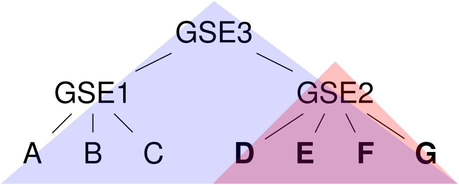
GSE2, GSE3	**F**
GSE2, GSE3	**G**



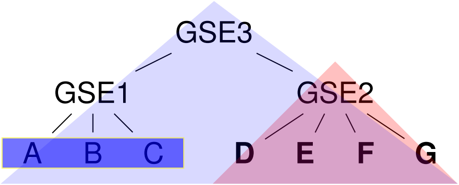
Approach

Given a list of samples (GSMs), get all the samples that belong to the same GSEs (excluding the original samples).

Overcoming superseries challenge can help find hidden hierarchies

Format in the database

GSE	GSM
GSE1, GSE3	A
GSE1, GSE3	B
GSE1, GSE3	C
GSE2, GSE3	**D**
GSE2, GSE3	**E**
GSE2, GSE3	**F**
GSE2, GSE3	**G**



Approach

Given a list of samples (GSMs), get all the samples that belong to the same GSEs (excluding the original samples).

Other SpideR Features

SpideR tackles inconsistencies in categories

For example, in sample_attribute field which contains comma-separated-categories.
E.g. tissue, source name, cell, cell_type, cell type - same/similar???

SpideR provides easily manipulable output and is easily **reproducible**

.*Rda* outputs with **data frames**
.*tab* outputs with **data frames**
.*Rda* output with the **function call** .*tab* output with function **call parameters**

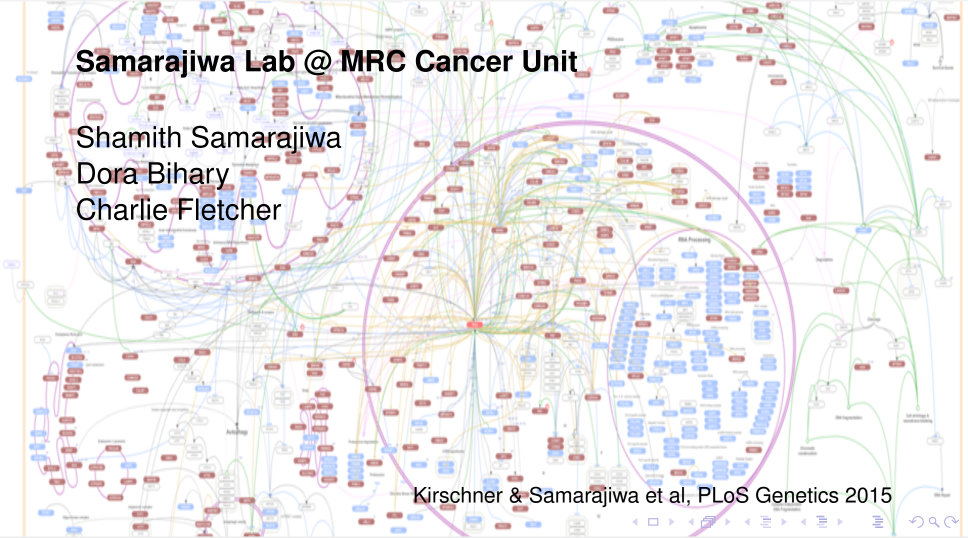
SpideR addresses most challenges with database design and integration

☑ Misleading fields in SRAdb and GEOmetadb
☑ Inconsistent attributes or categories
☑ Superseries in GEO
☑ SRA-GEO conversion
□ Erroneous or inconsistent entries

Plans for future development

- A new function for searching everywhere in the database (to get a list of all *potentially matching* samples, including those rejected by the more specific **searchForTerm** function)
- Integration of *elasticsearchr*
- Linking the search functions to gene synonyms database
- SQL(ite) database for storing samples of interest

Acknowledgements



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Kirschner & Samarajiwa et al, PLoS Genetics 2015