

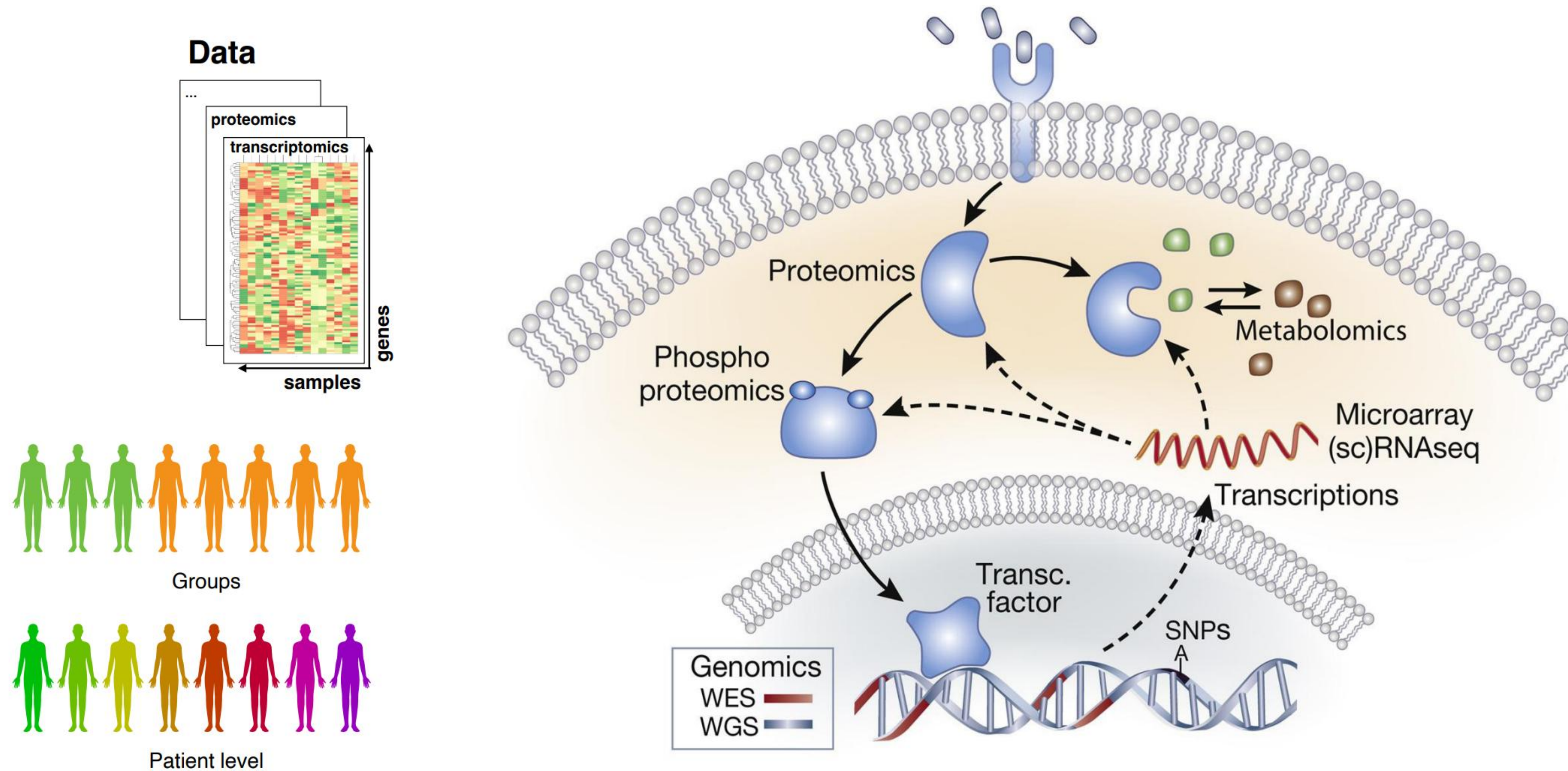
Generation of mechanistic hypotheses linking signalling and metabolism in cancer with COSMOS

Aurelien Dugourd
Saez-Rodriguez research group



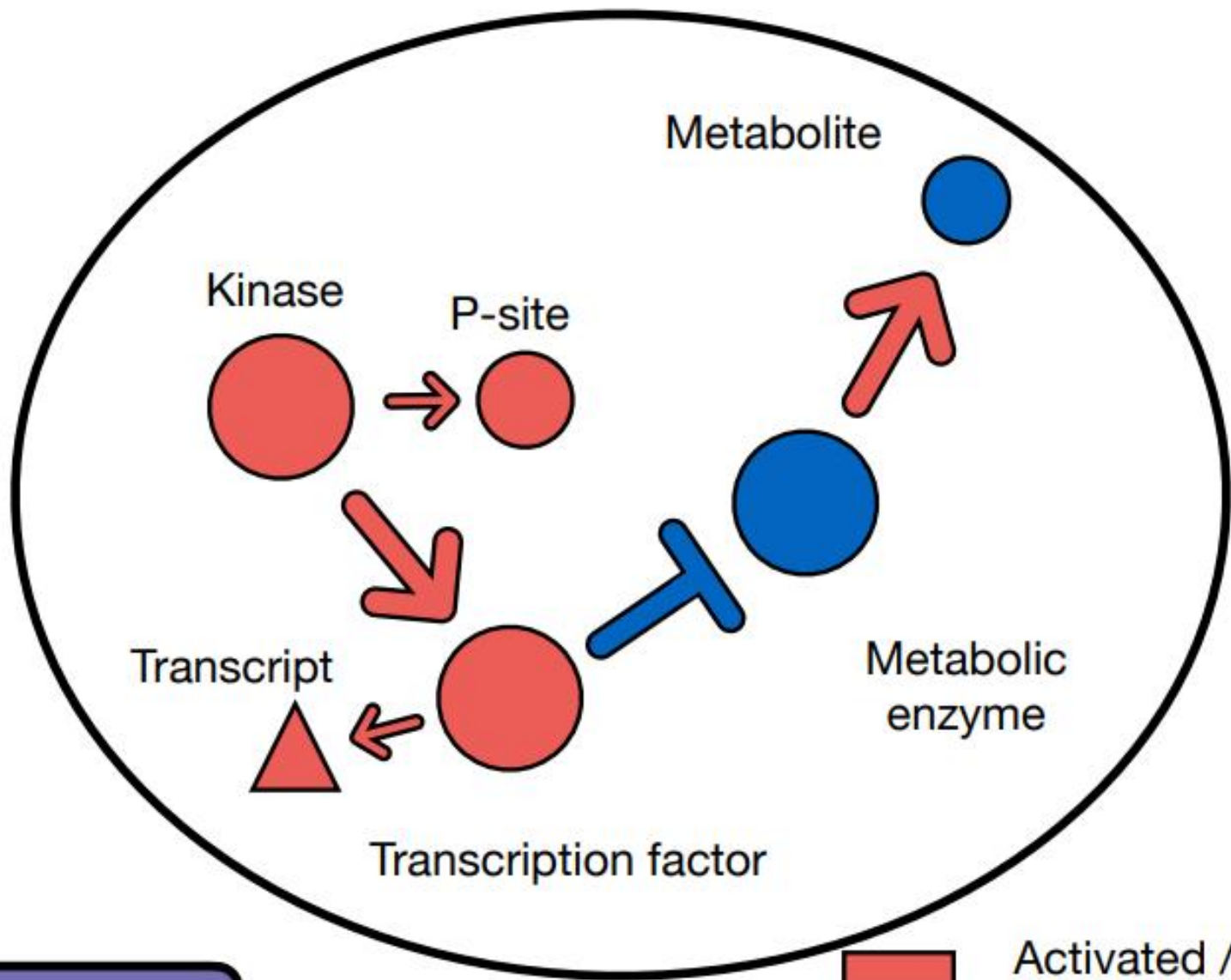
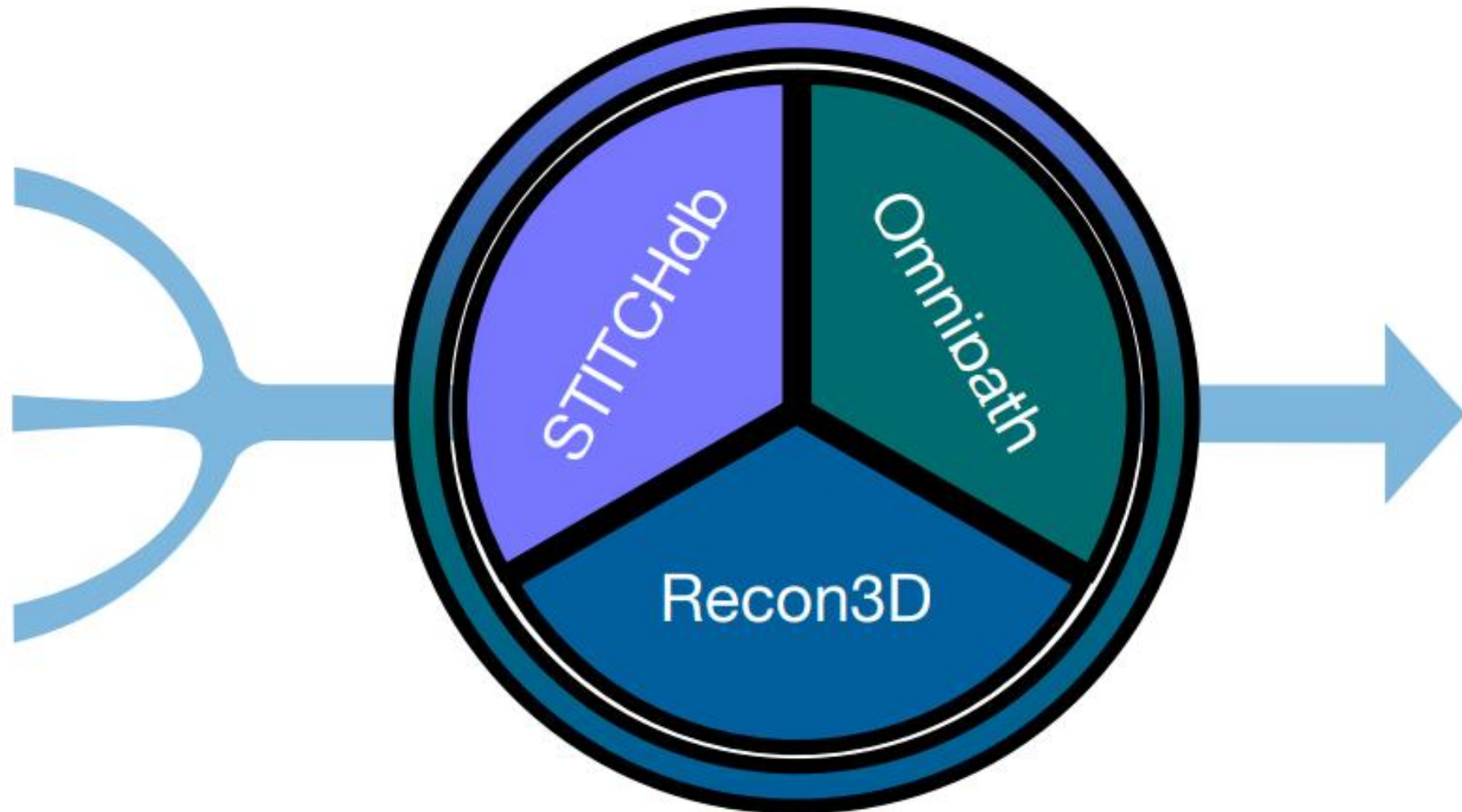
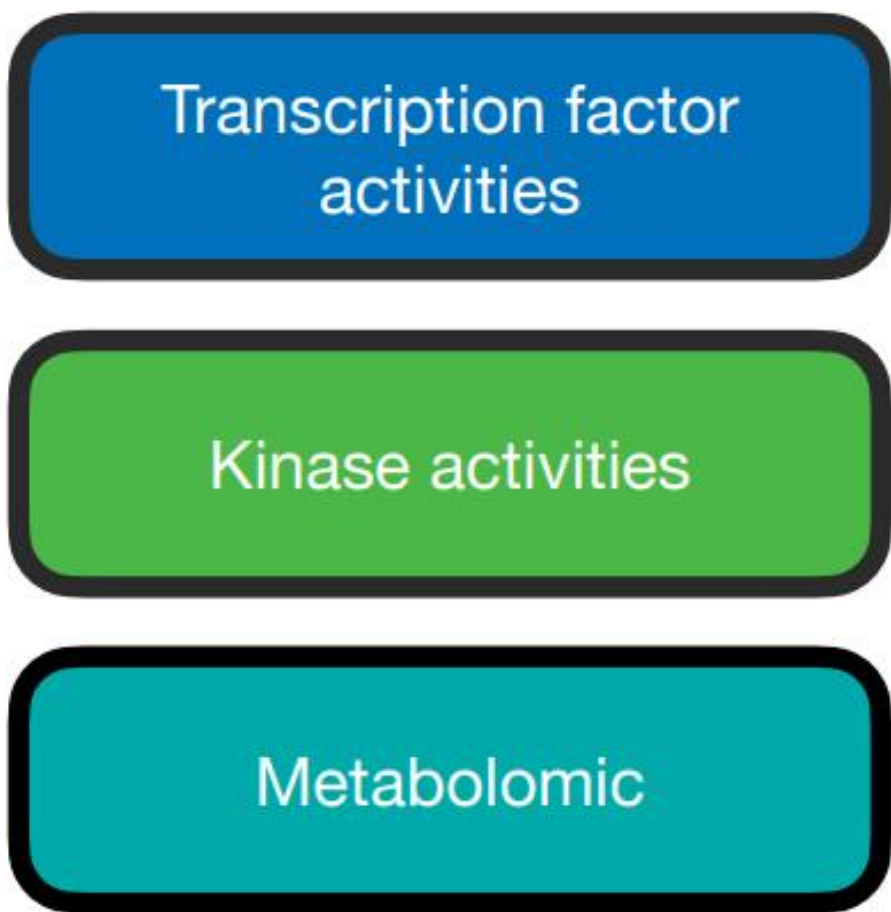


NCI60 RNA + metabolomic factor + cosmos analysis





NCI60 RNA + metabolomic factor + cosmos analysis



*Omnipath : <http://omnipathdb.org/>
**Recon3D : <https://www.vmh.life/>
***STITCH : <http://stitch.embl.de/>

Meta Causal Network contextualisation with CARNIVAL³
(signed PPI*, metabolic network**, allosteric regulations***)


Activated / Activation

Inhibited / Inhibition



Ocean metabolomic scores compared to proteomic data

Systematic generation of testable hypothesis to connect signalling and metabolism with the NCI60 datasets



NATIONAL CANCER INSTITUTE
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Last Updated: 08/11/20

NCI-60 Human Tumor Cell Lines Screen

Introduction

The **NCI-60 Human Tumor Cell Lines Screen** has served the global cancer research community for >20 years. The screen was implemented in fully operational form in 1990 and utilizes 60 different human tumor cell lines to identify and characterize novel compounds with growth inhibition or killing of tumor cell lines. It is designed to screen up to 3,000 small molecules (synthetic or purified natural products) per year for potential anticancer activity. The operation of this screen utilizes 60 different human tumor cell lines, representing leukemia, melanoma and cancers of the lung, colon, brain, ovary, breast, prostate, and kidney cancers.

This screen is unique in that the complexity of a 60 cell line dose response produced by a given compound results in a biological response pattern which can be utilized in pattern recognition algorithms (**COMPARE**). Using these algorithms, it is possible to assign a putative mechanism of action to a test compound, or to determine that the response pattern is unique and not similar to that of any of the standard prototype compounds included in the NCI database. In addition, following characterization of various cellular molecular targets in the 60 cell lines, it may be possible to select compounds most likely to interact with a specific molecular target.

This screen also allows prioritization of selected agents for further evaluation by NCI in collaboration with the submitter. The screening service is offered at no cost to submitters, other than shipping costs, although requests are reviewed and only those conforming to defined guidelines are selected for screening. There is a limit of 10 structure submission requests per 30 day period.

- Compound submission for NCI-60 screening
- Data Retrieval and Testing Decisions
- List of NCI-60 human tumor cell lines
- Screening methodology (One-dose and Five-dose Assay)
- Sample handling and Preparation
- Database of Screening Results
- Molecular characterization of NCI-60
- Publications

NCI-60 Human Tumor Cell Lines Screen

Main

Compound Submission

Data Retrieval and Testing Decisions

List of NCI-60 Human Tumor Cell Lines

Screening methodology (One-dose and Five-dose Assay)

Sample Handling and Preparation

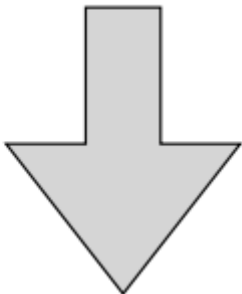
Database of Screening Results

Molecular Characterization of NCI-60

Publications

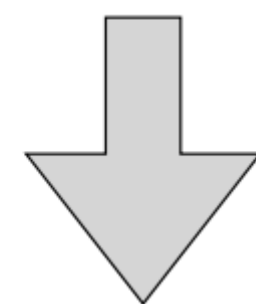


NCI60 cancer cell lines

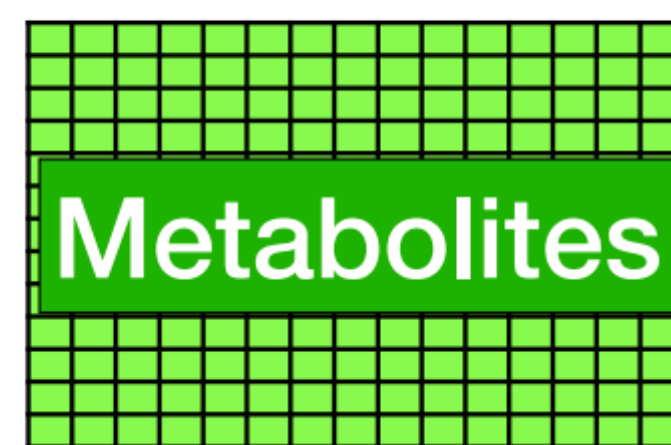




NCI60 cancer cell lines



.CSV



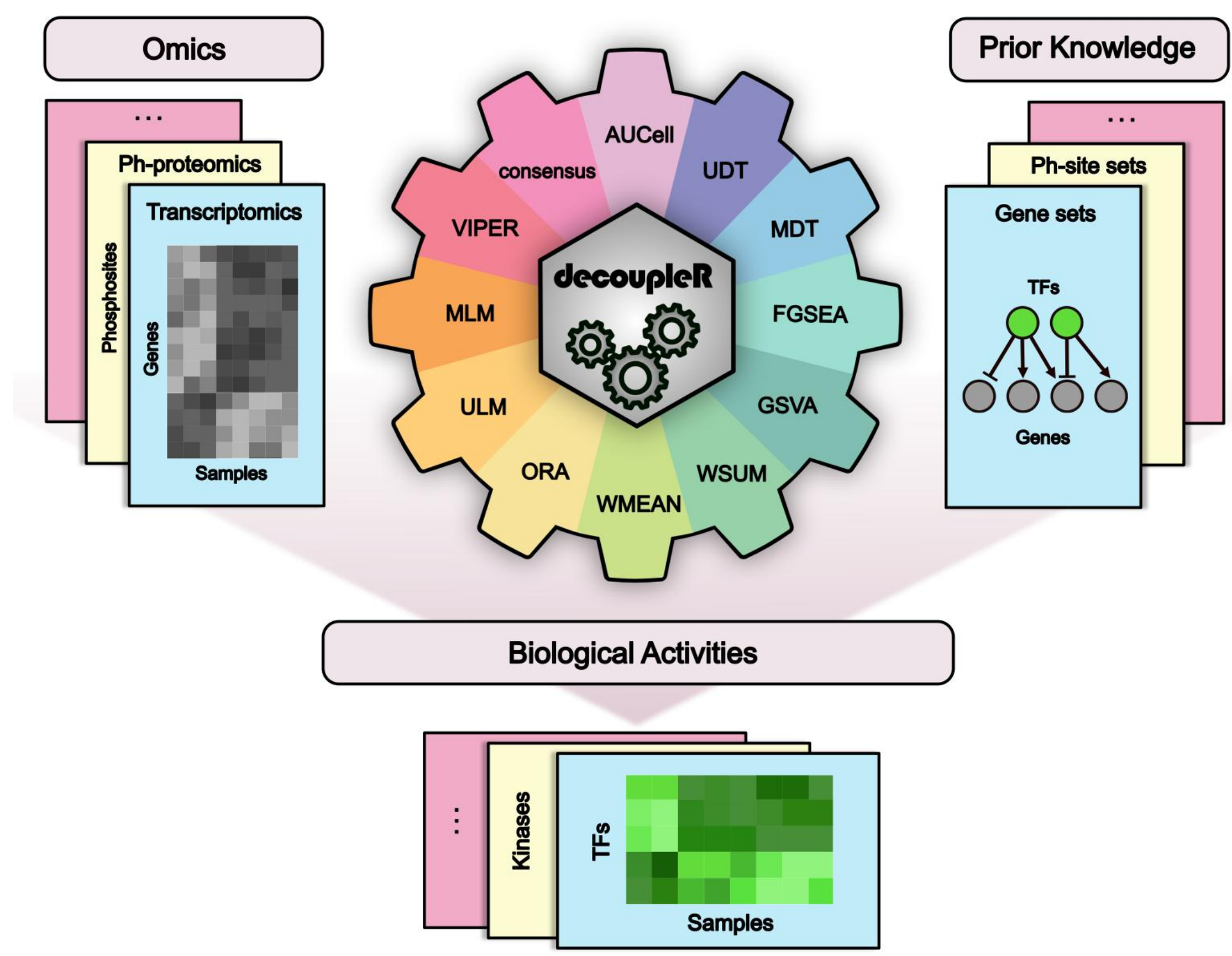
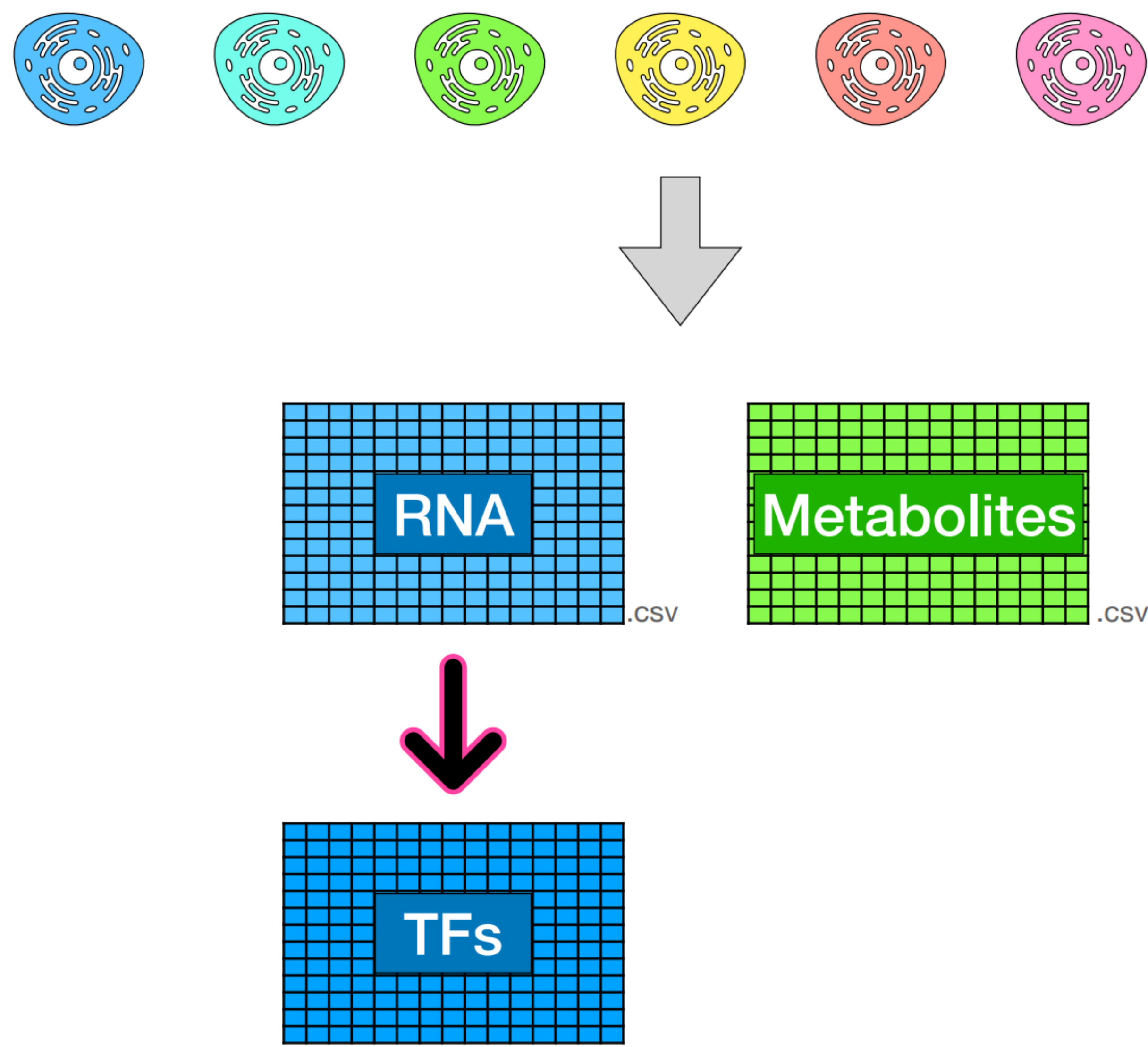
.CSV



Values are **z-transformed across cell lines** - each value represent how high or low a gene/metab is in a cell line compared to the other cell lines



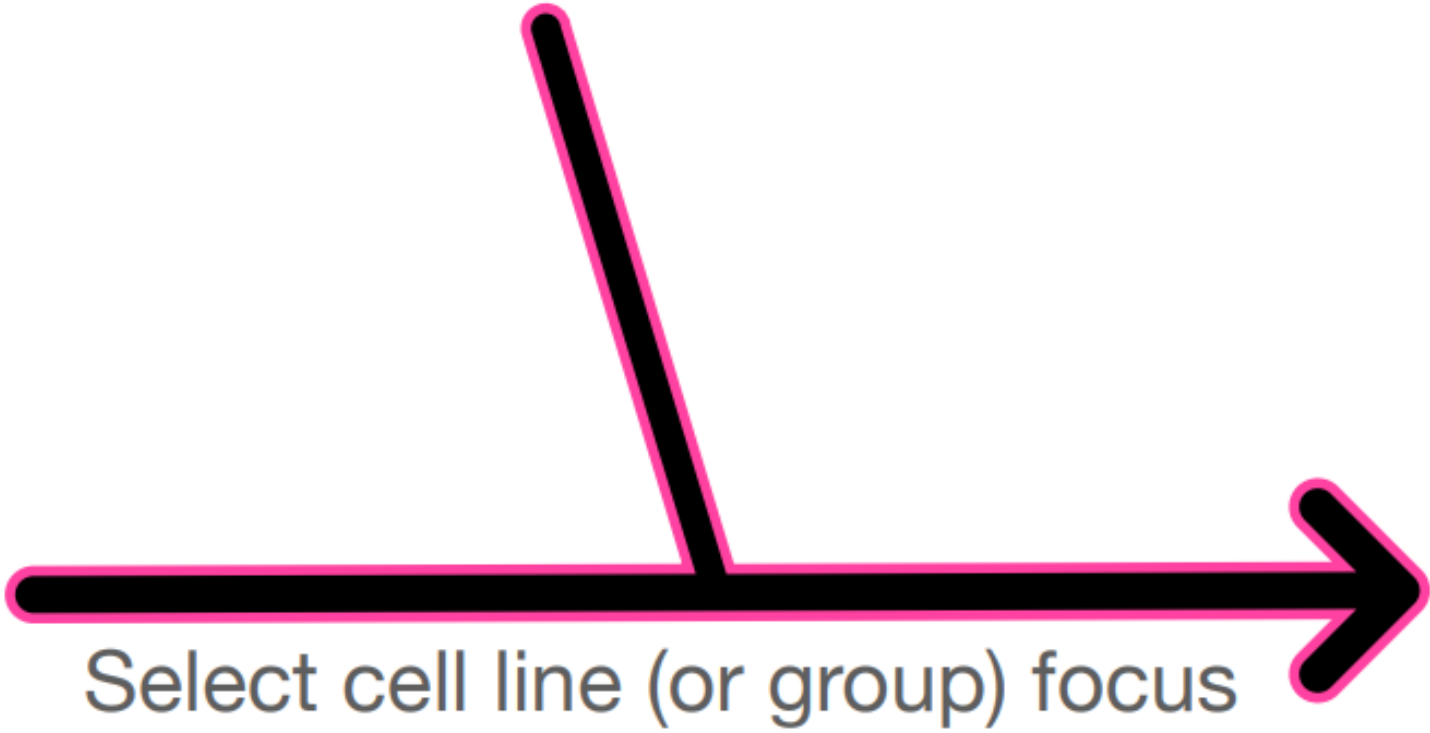
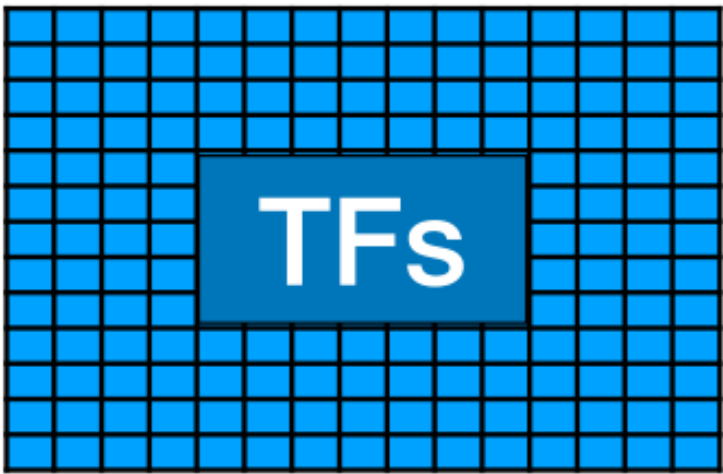
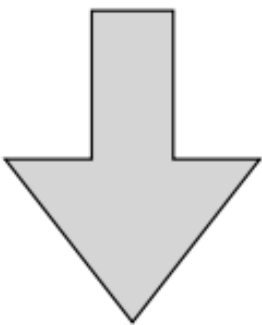
NCI60 cancer cell lines



Badia et al. Bioinfo Advances 2022

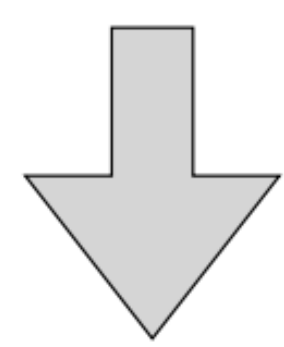


NCI60 cancer cell lines





NCI60 cancer cell lines



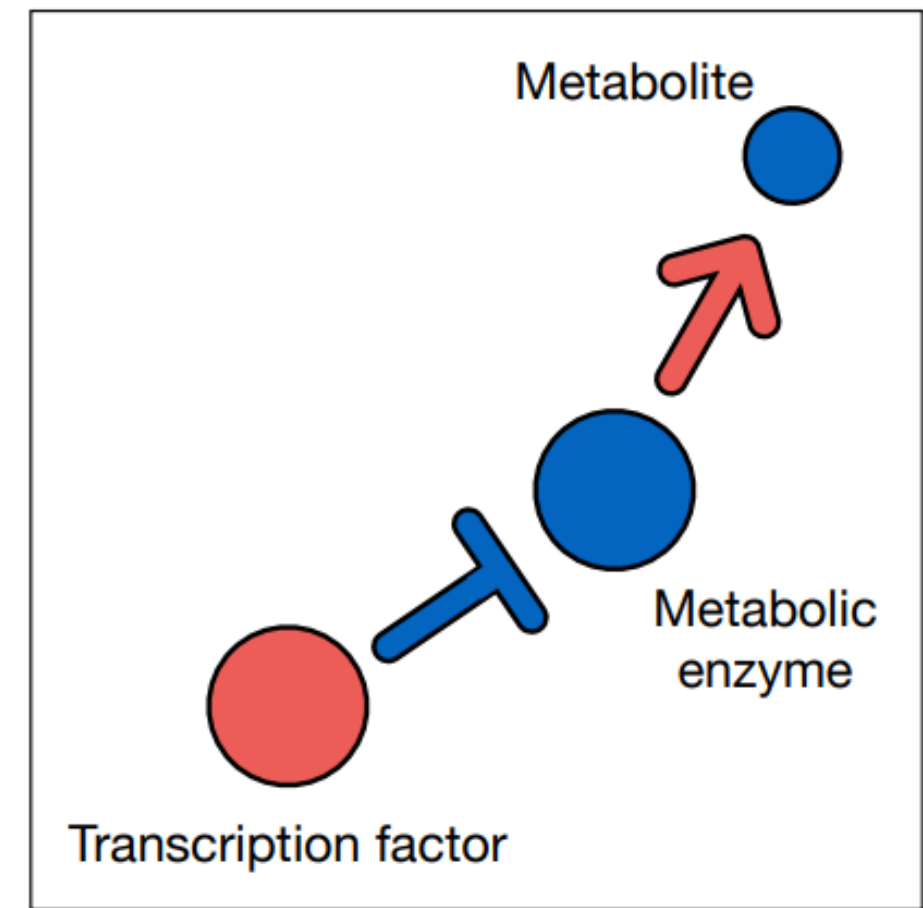
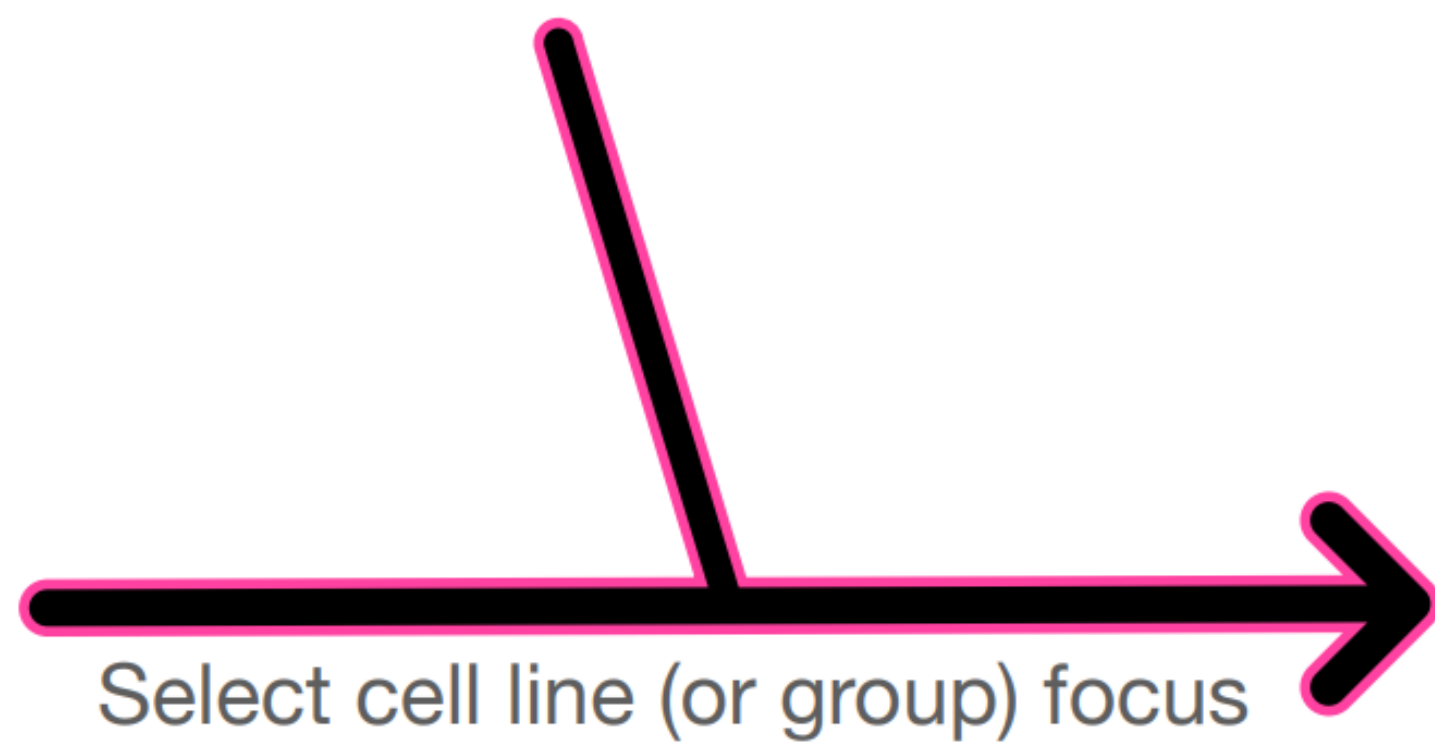
| |
|-----|
| RNA |
|-----|

.CSV

| |
|-------------|
| Metabolites |
|-------------|

.CSV

| |
|-----|
| TFs |
|-----|

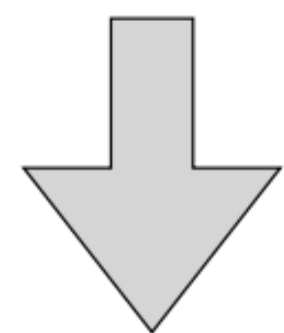


Testable hypotheses

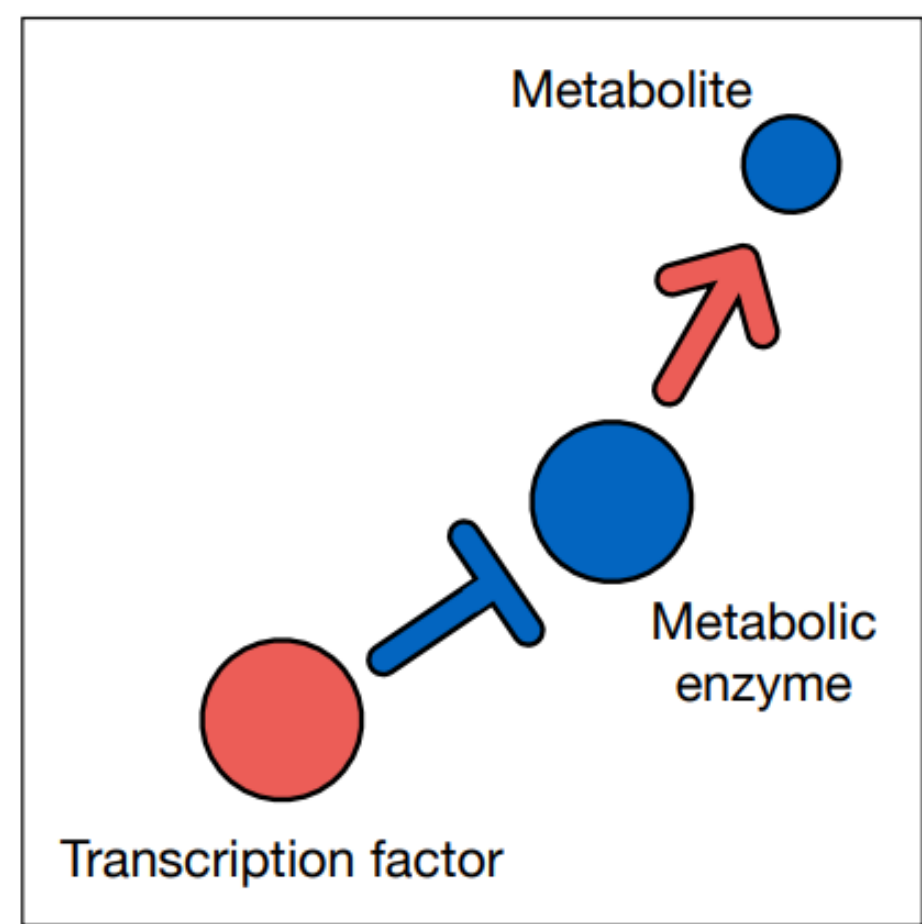




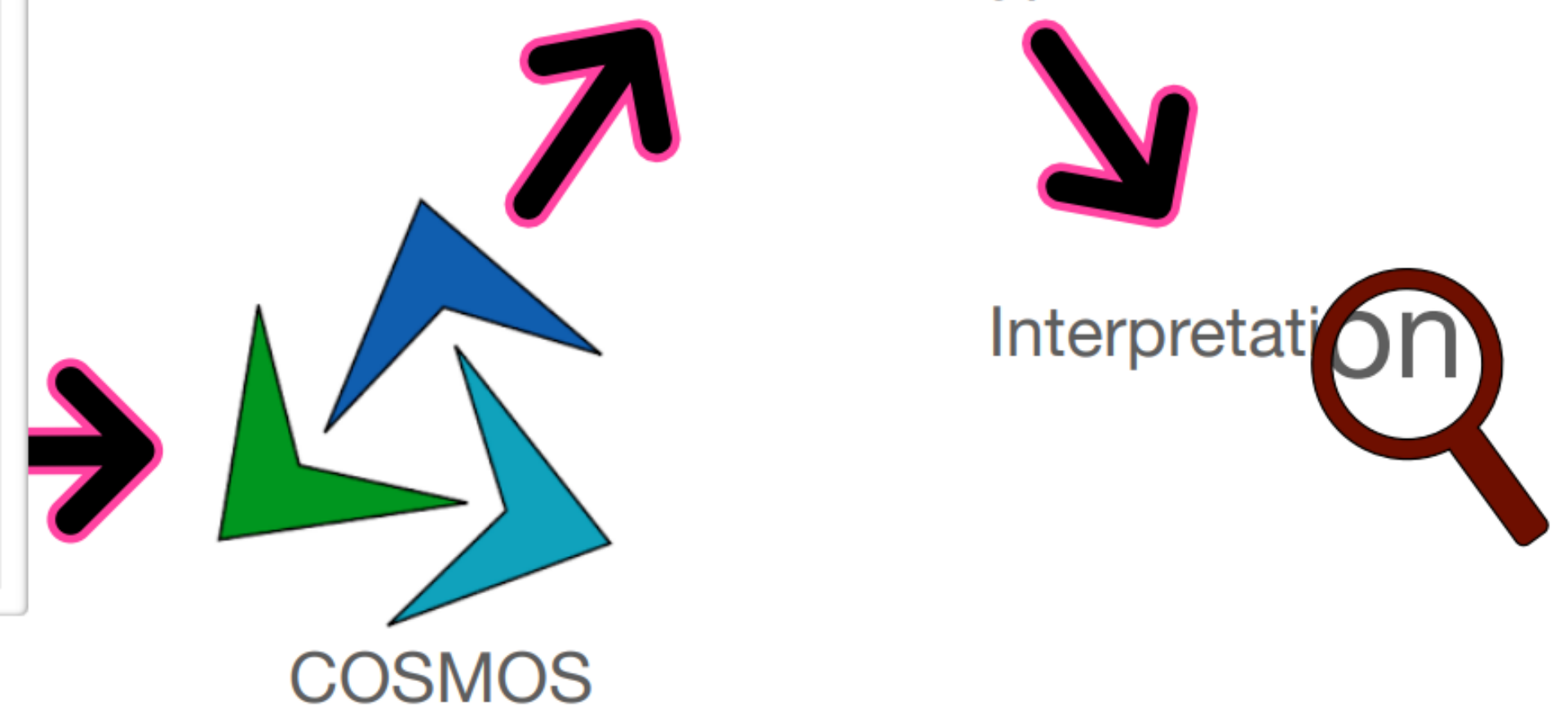
NCI60 cancer cell lines



```
1 library(cosmosR)
2 library(readr)
3 library(dplyr)
4
5 data("meta_network")
6 load("data/cosmos/cosmos_inputs.RData")
7
8 names(cosmos_inputs)
9
10 cell_line <- "786-0"
11
12 sig_input <- cosmos_inputs[[cell_line]]$TF_scores
13 metab_input <- cosmos_inputs[[cell_line]]$metabolomic
14 RNA_input <- cosmos_inputs[[cell_line]]$RNA
```

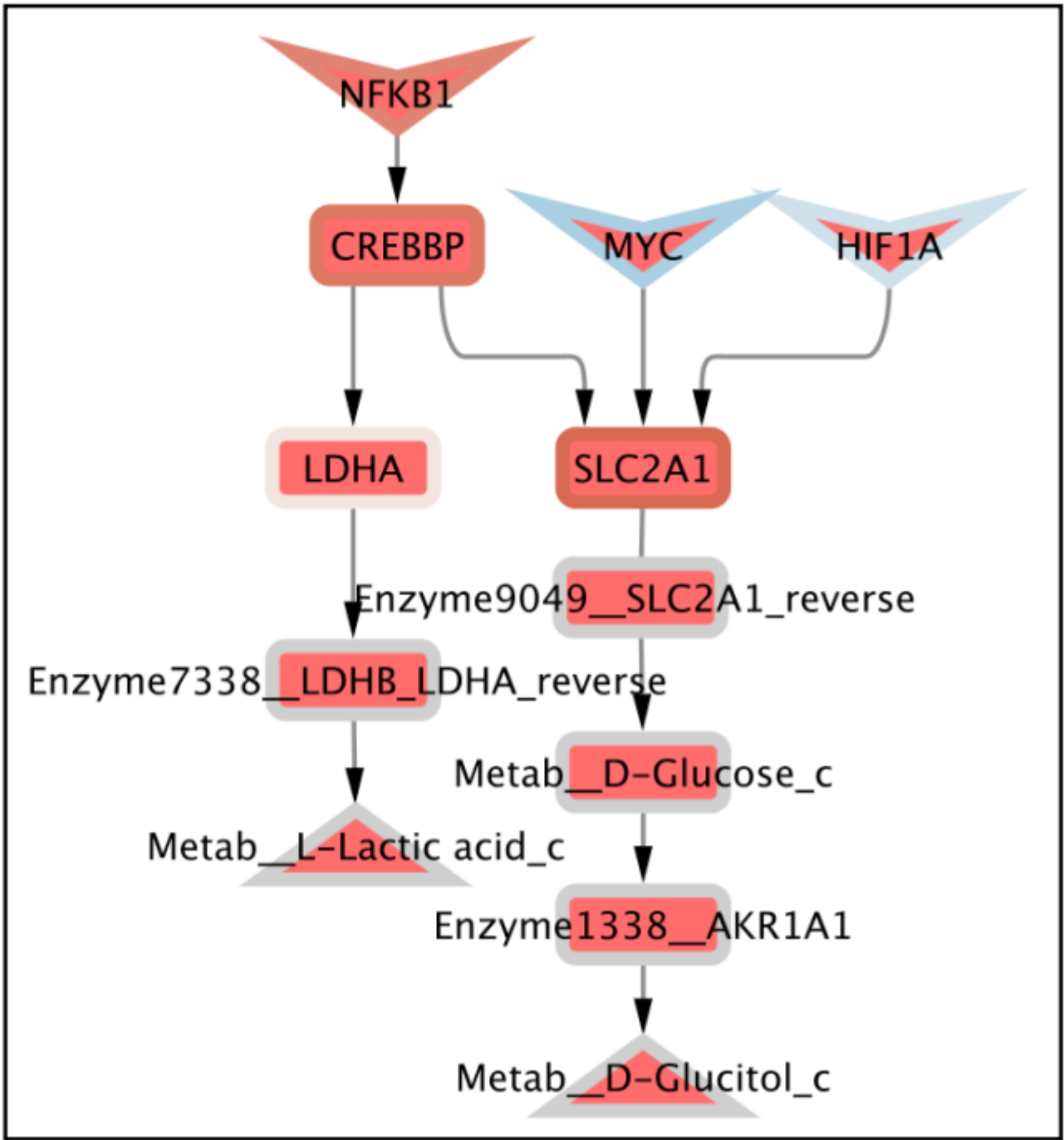
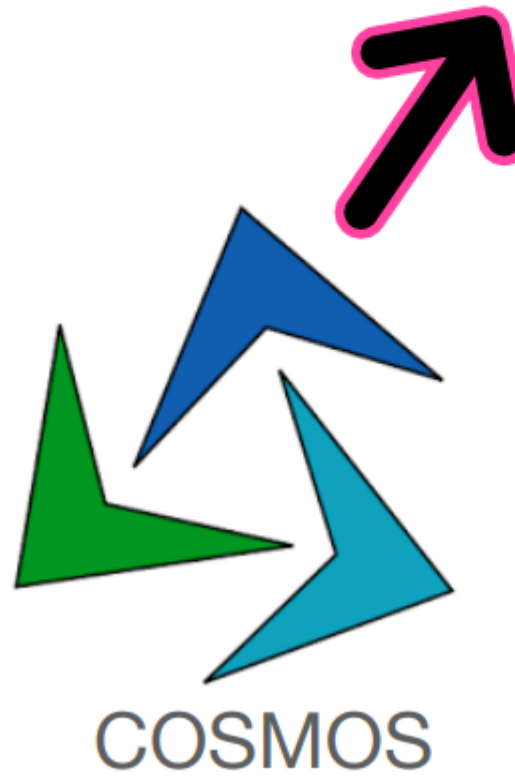
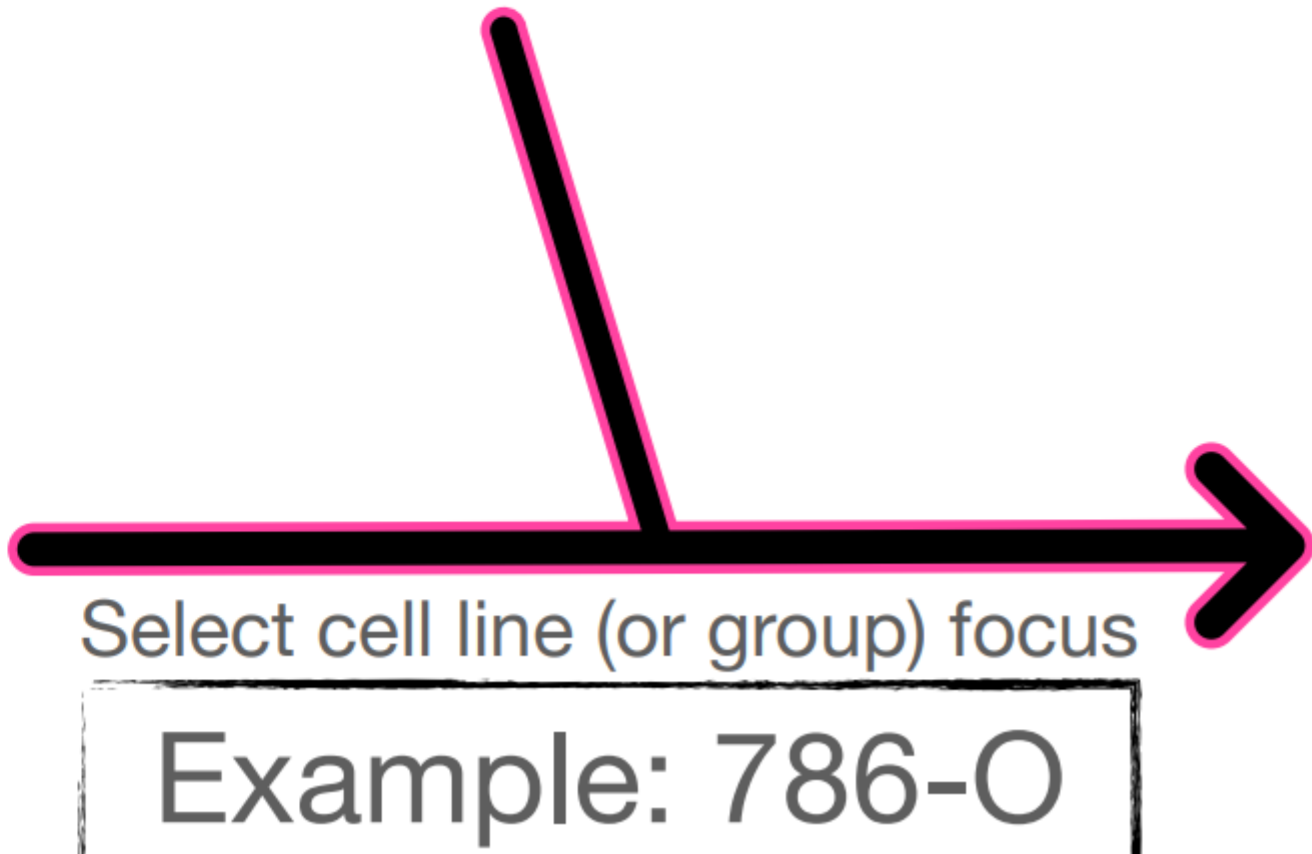
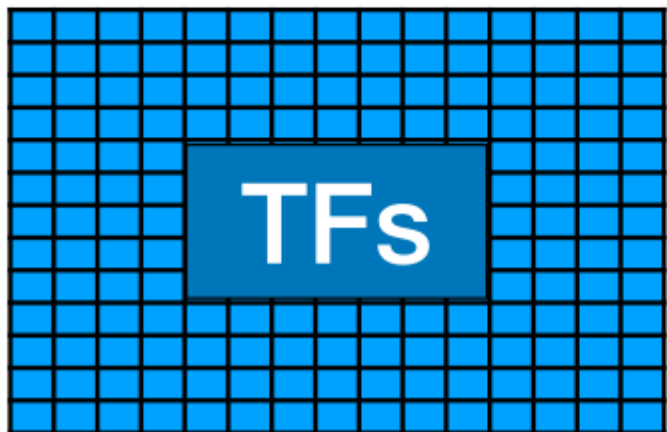
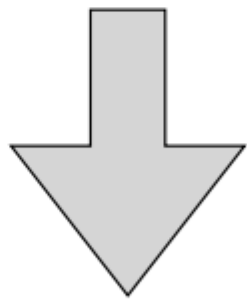


Testable hypotheses





NCI60 cancer cell lines



Testable hypotheses



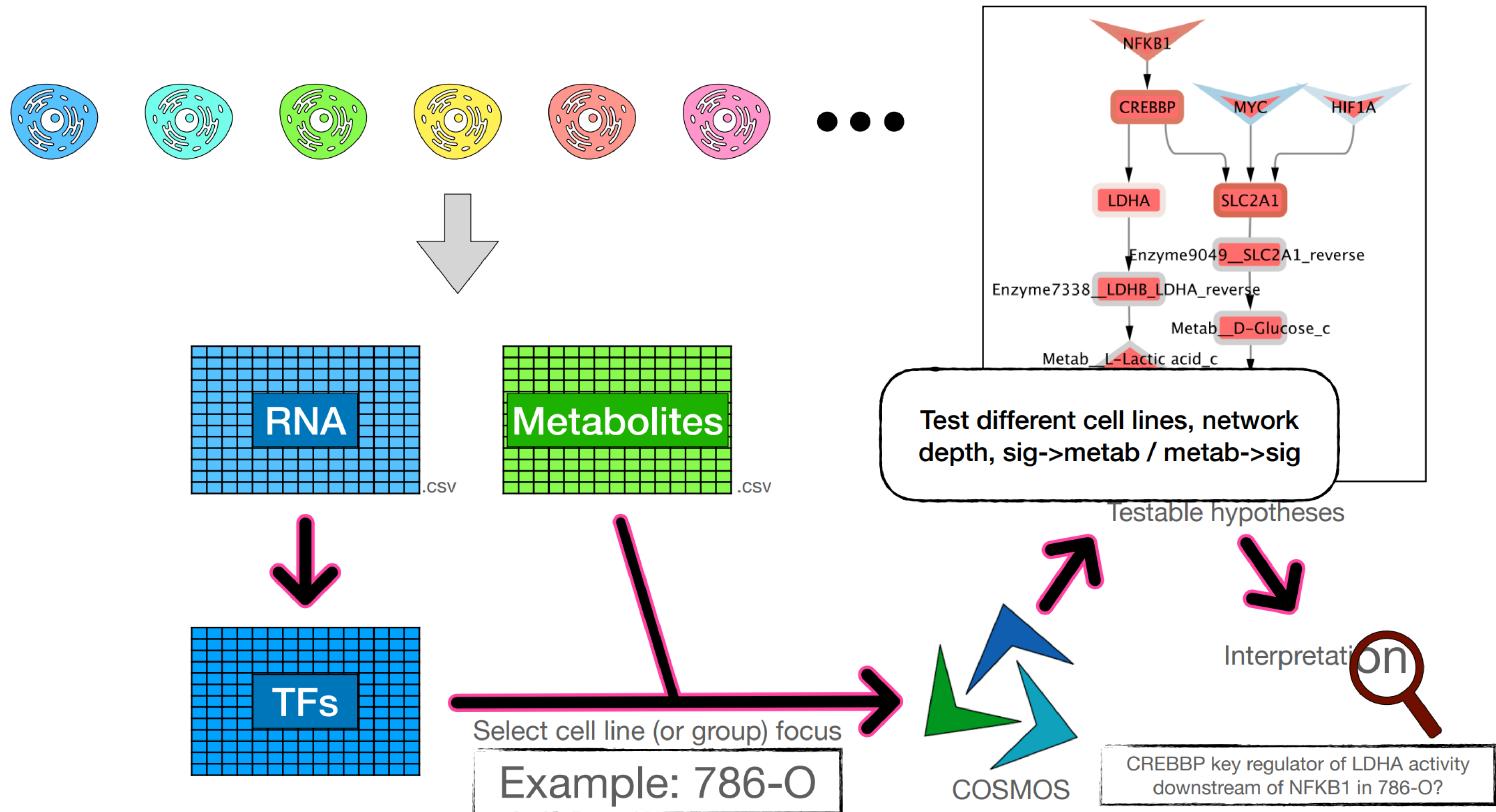
Interpretation



CREBBP key regulator of LDHA activity downstream of NFKB1 in 786-O?

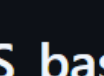



NCI60 cancer cell lines








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
 saezlab / COSMOS_basic

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<> Code

Issues 1

Pull requests


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Fork 0 ▾

Star 1 ▾

main ▾


1 Branch

0 Tags

Add file ▾

<> Code ▾

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 adugourd

Update net_compr_MOON.Rmd



44b0796 · 12 hours ago

63 Commits

| | | |
|---|--|---------------|
| EBI_practical | knitted basci script | 9 months ago |
| cbc/cbc-osx | added cbc and updated practical slides | 3 years ago |
| data | fixed stoopid mistake | 3 years ago |
| net_compr_MOON_files/figure-markdown_strict | knitted basci script | 9 months ago |
| results | M14 analysis | 10 months ago |
| scripts | knitted basci script | 9 months ago |
| support | added scripts to run without solver | 2 years ago |
| .Renviron | added translation | 2 years ago |
| .gitignore | corrected sign, added detangling | 2 years ago |
| LICENSE | Create LICENSE | 3 years ago |
| NCI60.Rproj | first commit | 3 years ago |
| README.md | made basic tuto as readme | 9 months ago |
| net_compr_MOON.Rmd | Update net_compr_MOON.Rmd | 12 hours ago |

📖 README

📄 GPL-3.0 license

Tutorial with NCI60 cohort

tutorial to use cosmosR in the context of basic downstream analysis of differential analysis or single sample.

📖 Readme

📄 GPL-3.0 license

📈 Activity

📋 Custom properties

☆ 1 star

👁 1 watching

🔗 0 forks

Report repository

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Contributors 2

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 gabora Attila Gabor



Plan for the days

Day 1 - Discussion, choice of cell line, expected results...

Day 2 - Analysis of first chosen cell line with COSMOS

Day 3 - Analysis of second chosen cell line with COSMOS - comparison to results of first cell line

Day 4 - Interpretation of results and preparation of the presentation



Expected Outcomes

- Explore NCI60 cell line omic datasets
- Interpreting TF activities estimated from RNA seq data
- Learning to use cosmos to integrate signalling and metabolic data with prior knowledge
- Generate and interpret testable hypotheses
- **Understand limits of the method and the interpretation of outputs**
- Softwares: R 4.1> - cosmosR R package