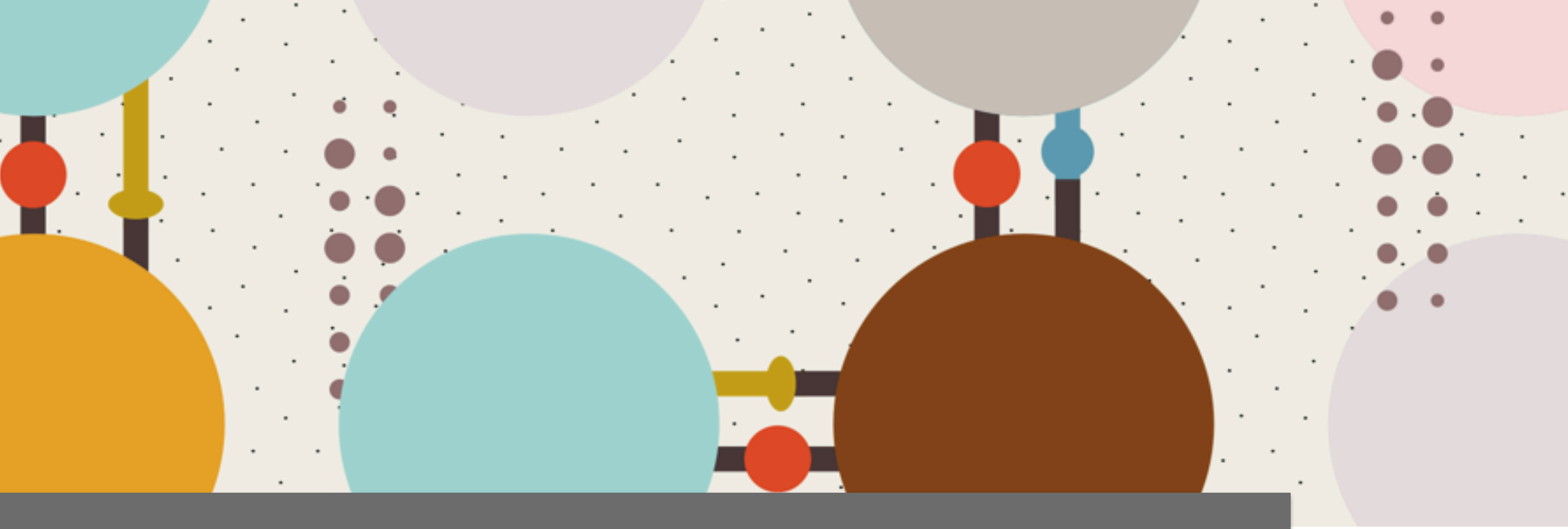


IO17 | Large Scale Bioinformatics for Immuno-Oncology

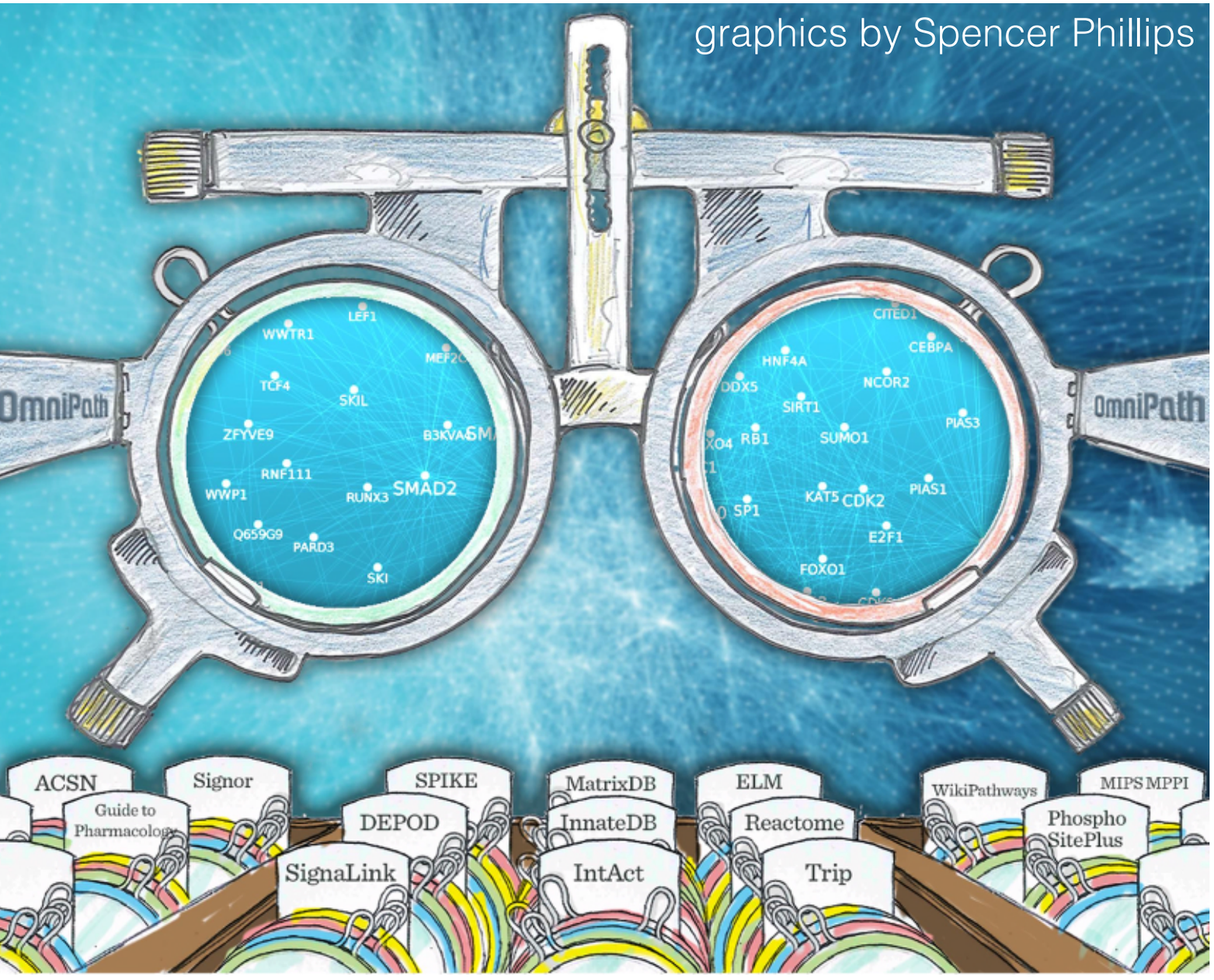
Signaling pathways with Omnipath

Francesca Finotello, Federica Eduati, and Pedro L. Fernandes

GTPB | The Gulbenkian Training Programme in Bioinformatics
Instituto Gulbenkian de Ciência, Oeiras, Portugal | Sept 19th-22nd, 2017

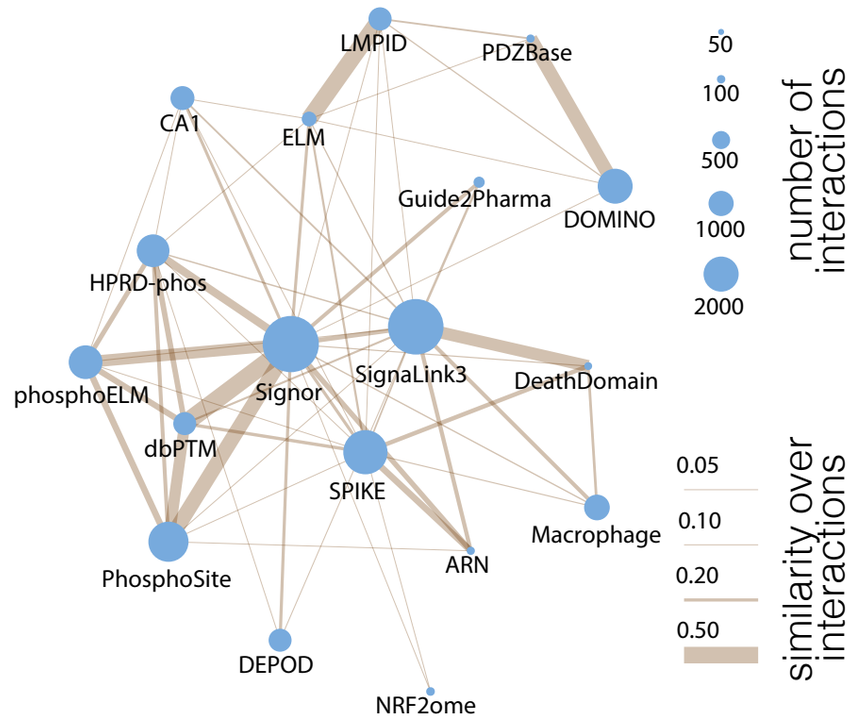
INSTITUTO GULBENKIAN DE CIÊNCIA

What is OmniPath?



Türei, Korcsmáros & Saez-Rodriguez (2016). Nat Methods, 13(12)966-967.
http://www.omnipathdb.org/

- OmniPath is a comprehensive collection of **literature curated** human **signaling pathways**
- Why Omnipath?



Türei, Korcsmáros & Saez-Rodriguez (2016)

- Available via a webservice or using pypath, a Python module for molecular networks and pathways analysis

http://omnipathdb.org/

What is OmniPath?

Structure & Mechanism

ComPPI
Gene Ontology

Subcellular localization (2)

3DCompexes
3DID
Instruct
Interactome3D

Domains and 3D structures (4)

dbPTM
ELM
HPRD
LMPID
MIMP
Phospho.ELM
PhosphoNetw.
PhosphoSite
Signor

Post-translational modifications (9)

3DComplexes
CORUM
Havugimana

Protein complexes (3)

Unified network of pathways with annotations

OmniPath & pypath

Protein-protein interaction resources (34)

Activity flow (12)
ARN+
CA1+
CancerCellMap*
DeathDomain
Guide2Pharma+
Macrophage+
NRF2ome+
PDZbase*
SignaLink3+
Signor+
SPIKE+
TRIP+

Enzyme-substrate (8)
dbPTM*
DEPOD*
DOMINO
ELM
HPRD-phos*
LMPID
phospho.ELM*
PhosphoSite*

Undirected PPI (8)
BioGRID
DIP
HPRD
InnateDB
IntAct
MatrixDB
MPPI
Vidal HI-III

Process description (6)
ACSN
NCI-PID
NetPath
PANTHER
Reactome
WikiPathways

Tissue patterns

Expression

GIANT
HPA
HPM
Prot.DB

Mutations

GDSC

Intervention

Compound target binding

ChEMBL
LINCS
UniChem

Function

GSEA

GO
MSigDB

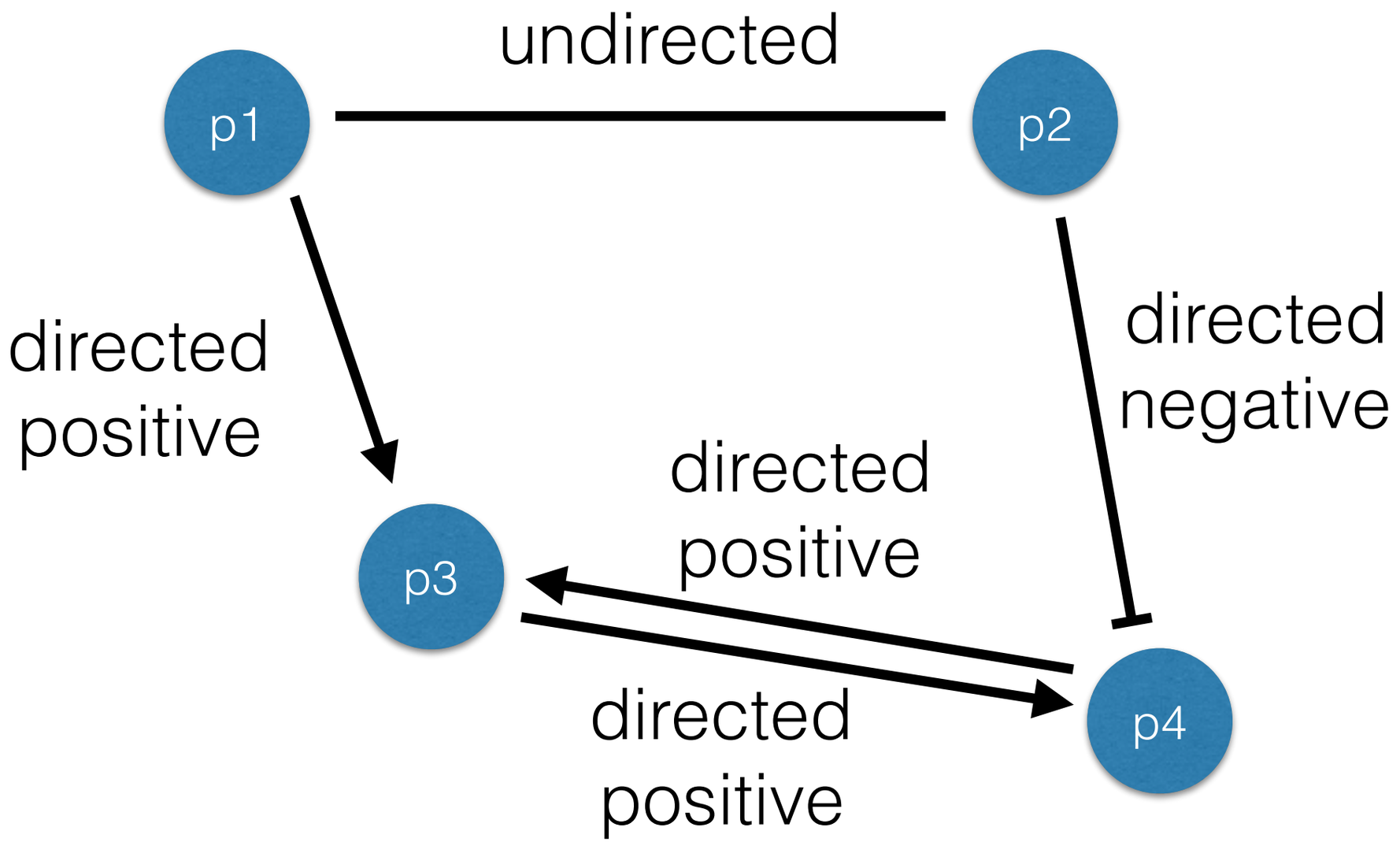
Gene Ontology

Türei, Korcsmáros & Saez-Rodriguez (2016)

Network representation

Network interpreted as a graph with:

nodes: proteins
edges: interactions



Load network as igraph

1. Load in R the functions and packages necessary for the exercise:

```
source("https://raw.githubusercontent.com/saezlab/pypath/master/r_import/r_import.r")
```

2. Import Omnipath as *igraph* using the function *omnipath_graph* and show summary:

```
op <- omnipath_graph()
summary(op)
```

```
## IGRAPH UN-- 8951 50247 --
## + attr: name (v/c), label (v/c), is_directed (e/n), is_stimulation
## | (e/n), is_inhibition (e/n), sources (e/x), references (e/x), dip_url (e/c)
```

Number of vertices and edges in the graph

Names of the attributes for vertices (v) and edges (e)

3. Import only the directed interactions

```
op <- omnipath_graph(directed = TRUE)
is.directed(op)
```

```
## [1] TRUE
```

Access nodes and edges attributes

4. Explore edges and their attributes

```
E(op)[15710]
```

```
## + 1/42503 edge (vertex names):
## [1] P01579->P15260
```

```
E(op)[15710]$sources
```

```
[[1]]
[1] "HPRD"    "Laudanna_effects" "DIP"      "Signor"    "SPIKE"              "KEGG" "SignaLink3"
[8] “BioGRID" "IntAct"           "InnateDB" "Macrophage" "Laudanna_sigflow" "Wang"
```

```
E(op)[15710]$references
```

```
[[1]]
[1] "11250200" "10986460" "11250200" "12165521" "10986460" "7673114"  "7617032"  "10860730"
[9] "10986460" "23898330" "12438563" "7617032"  "16110316" "10986460" "7673114"  "11250200"
[17] "12165521" "10986460" "7673114"
```

5. Explore vertices and their attributes

```
c(V(op)['P01579']$label, V(op)['P15260']$label)
```

```
## [1] "IFNG"   "IFNGR1"
```

Play with the network

6. Name the target node (use gene name) of the interaction represented by edge 10594

7. Check the sign (i.e. stimulation or inhibition) of the interaction represented by edge 10594

8. Extract the subgraph defined by vertices:
   "IFNG", "IFNGR1", "JAK1", "JAK2", "STAT1","EGF", “EGFR",
   "PIK3CA", "PTEN", "PIK3CA","AKT1", "NFKB1"

Hints:

- a subgraph of a graph containing only specified vertices and all edges among them can be created using the function *induced_subgraph* (see help typing ?induced_subgraph)
- *induced_subgraph* requires as input vertices IDs (i.e. their Uniprot names). Uniprot names for all vertices can be derived from their gene names as follows:

```
V(op)[label %in% c("IFNG", "IFNGR1", "JAK1",  "JAK2", "STAT1","EGF",
                   "EGFR", "PIK3CA", "PTEN", "PIK3CA", "AKT1", "NFKB1")
```

9. Find all shortest paths between AKT1 ad NFKB1 using the function *all_shortest_paths*

How to access the questions on Socrative

1. Access Socrative with student access at: https://b.socrative.com/login/student/
2. Join the IO17 room

3. Enter your name and click „done“ to start the quiz