IPA robustness analysis *v1.3 (2020-07-08)*

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For feedback or questions, please email bits@vib.be

Stephane Plaisance (stephane.plaisance@vib.be)

IPA robustness analyses

- applying different cutoffs to DE data
- data acquired with a low sensitivity technology
- data acquired with a low coverage technology
- Importance of the background

Background effect

Genome Background

DE%

	UDS	KB	Effect
L1	50%	50%	“=“
L2	50%	75%	*under-estimate*
L3	50%	20%	*over-estimate*

Simulation of a background & sampling effects

N (22000)

Part of the background is missed

k=600, n=15, M=60	
Background	Enrich test*
IPA KB	3.671516e-12
15k	9.821754e-10
10k	2.739608e-07
5k	0.001280419

only 5 out of 15 DE are quantified

k=600, n=5, M=60	
Background	Enrich test
IPA KB	0.005716096
15k	0.03180919
10k	0.1469838
5k	0.7344489

under-estimate

20 out of 60 from list are quantified

k=600, n=15, M=20	
Background	Enrich test
IPA KB	3.358551e-22
15k	1.468597e-19
10k	8.944017e-17
5k	4.627636e-12

over-estimate

** phyper(q, m, n, k, lower.tail = FALSE, log.p = FALSE)*

Sampling x Background effect

IPA **Knowledge Base** Background

2x 10x core analysis
different backgrounds

|logR| >1 & adjp < 0.001

Compare

KB
UDS
Canonical Pathways
1 2 3 4 5 6 7 8 9 0
Cardiac Hypertrophy Sign...
Hepatic Fibrosis Signaling...
Systemic Lupus Erythemat...
HMGB1 Signaling
Phospholipase C Signaling
Protein Kinase A Signaling
Synaptogenesis Signaling ...
Integrin Signaling
CREB Signaling in Neurons
Opioid Signaling Pathway
Thrombin Signaling
Cardiac Hypertrophy Sign...
B Cell Receptor Signaling
Systemic Lupus Erythemat...
Gαq Signaling
Role of NFAT in Cardiac H...
cAMP-mediated signaling
Osteoarthritis Pathway
Natural Killer Cell Signaling
eNOS Signaling
GNRH Signaling
ERK/MAPK Signaling
Superpathway of Inositol ...
Estrogen Receptor Signali...
Signaling by Rho Family G...
RhoGDI Signaling
Diseases & Functions
1 2 3 4 5 6 7 8 9 0
Quantity of cells
Cell death of brain cells
Necrosis
Apoptosis
Cell movement
Glucose metabolism disor...
Migration of cells
Proliferation of prostate c...
Development of body trunk
Concentration of lipid
Breast or colorectal cancer
Neuronal cell death
Apoptosis of tumor cell li...
Development of genitouri...
Differentiation of connecti...
Quantity of bone
Growth of tumor
Invasion of cells
Development of reproduc...
Organization of cytoskele...
Cell death of tumor cell lin...
Locomotion
Growth of epithelial tissue
Neoplasia of cells
Background effect
!
Upstream regulators
1 2 3 4 5 6 7 8 9 0
dexamethasone
triamcinolone acetonide
Immunoglobulin
glucocorticoid
NR3C1
fluticasone propionate
MRTFB
U0126
CEBPA
BRCA1
LY294002
hydrogen peroxide
DDIT3
TP73
SMAD7
MRTFA
fluocinolone acetonide
beta-estradiol
FOS
PGR
HRAS
valproic acid
IKZF1
Causal Networks
1 2 3 4 5 6 7 8 9 0
dexamethasone 1
triamcinolone acetonide 1
triamcinolone acetonide 2
DP 00477 2
BTB 09588 2
HTS 12696 2
HTS 11308 2
ML 00144 2
RDR 03785 2
DFP 00129 2
fluocinolone acetonide 1
hexachlorophene 2
fludrocortisone acetate 3
fluocinolone acetonide 3
dexamethasone phosphate 3
fluticasone propionate 1
MRTFB 1
TEAD2 3
NR3C1 2
SUMO1 2
fluocinolone acetonide 2
FKBP5 2
Corticosteroid-GCR 3

Background effects from low expression Tx

all genes, incl 0-expr

> 0 counts/M

> 10 counts/M

> 100 counts/M

Effect of low-expression Tx on the UDS background size

UDS (N)

|logR| >1 &
adjp < 0.001

Data	Mapped IDs §	Analysis ready &	Filtered @
all rows	52186	27525	660
>0 / M	27634	= 27525	660
>10 / M	15064	15031	660
>100 / M	10742	10729	**464**

§ ***Mapped IDs*** *is the list of all uploaded IDs mapping to genes*
& ***Analysis ready*** *(**N**) are IDs in IPA KB & with >0 expression values*
@ ***Filtered*** *(**k**) are Analysis ready IDs which pass the user filters*

** phyper(q, m, n, k, lower.tail = FALSE, log.p = FALSE)*

No clear Background effect after removing low-ex rows

IPA Global robustness results

- cutoff effects (LR, PV)
- sensitivity effects (top expressed genes (5k 10k 15k)
- sampling effects (30% random samples)
- background effects (removing low-expression Tx)

Global robustness results: Canonical Pathways

Same data
analysed by OmicSoft

Global robustness results: Diseases & Functions

Same data analysed by OmicSoft

Global robustness results: Upstream regulators

Upstream regulators

OmicSoft

Global robustness results: Causal Networks

Causal Networks

OmicSoft

https://www.bits.vib.be/software-overview/ingenuity-pathways-analysis

IPA

bits.vib.be/software-overview/ingenuity-pathways-analysis

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Read the archived release notes (here).

Online Tutorials

Recorded IPA webinars and tutorial videos (in particular the 3-part series covering most of IPA)

Software Support

Overview
- CLC Main Workbench
- Tibco Spotfire
- CLC Genomics Workbench
- ELN
- Genevestigator
- GraphPad Prism
- IPA
- MATLAB
- OpenRefine
- qbase+
- SnapGene
- Galaxy
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