



# IPA robustness analysis v1.4 (2020-07-09)

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July 1/3, 2020

*For feedback or questions, please email [bits@vib.be](mailto:bits@vib.be)*

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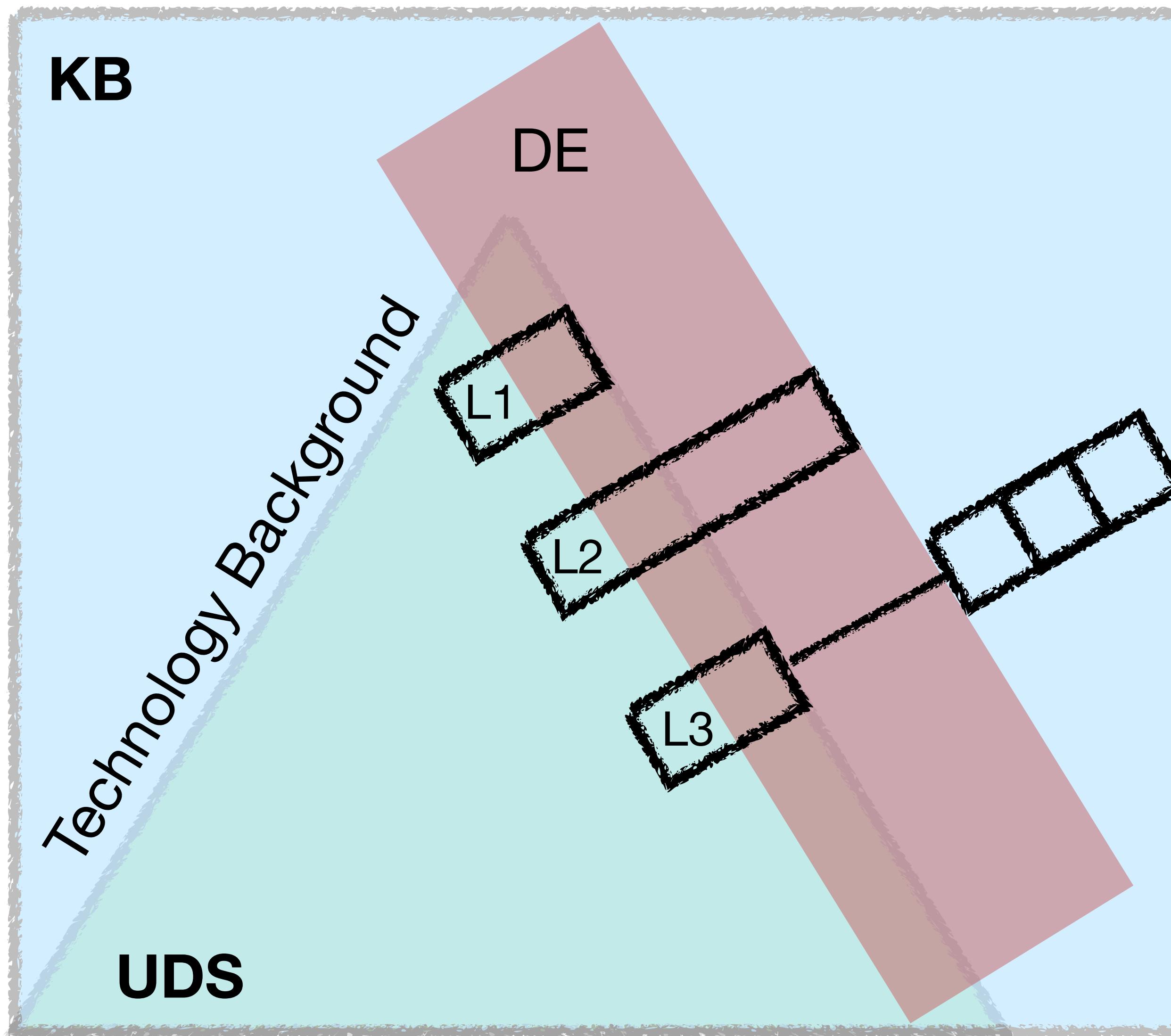


# IPA robustness analyses

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

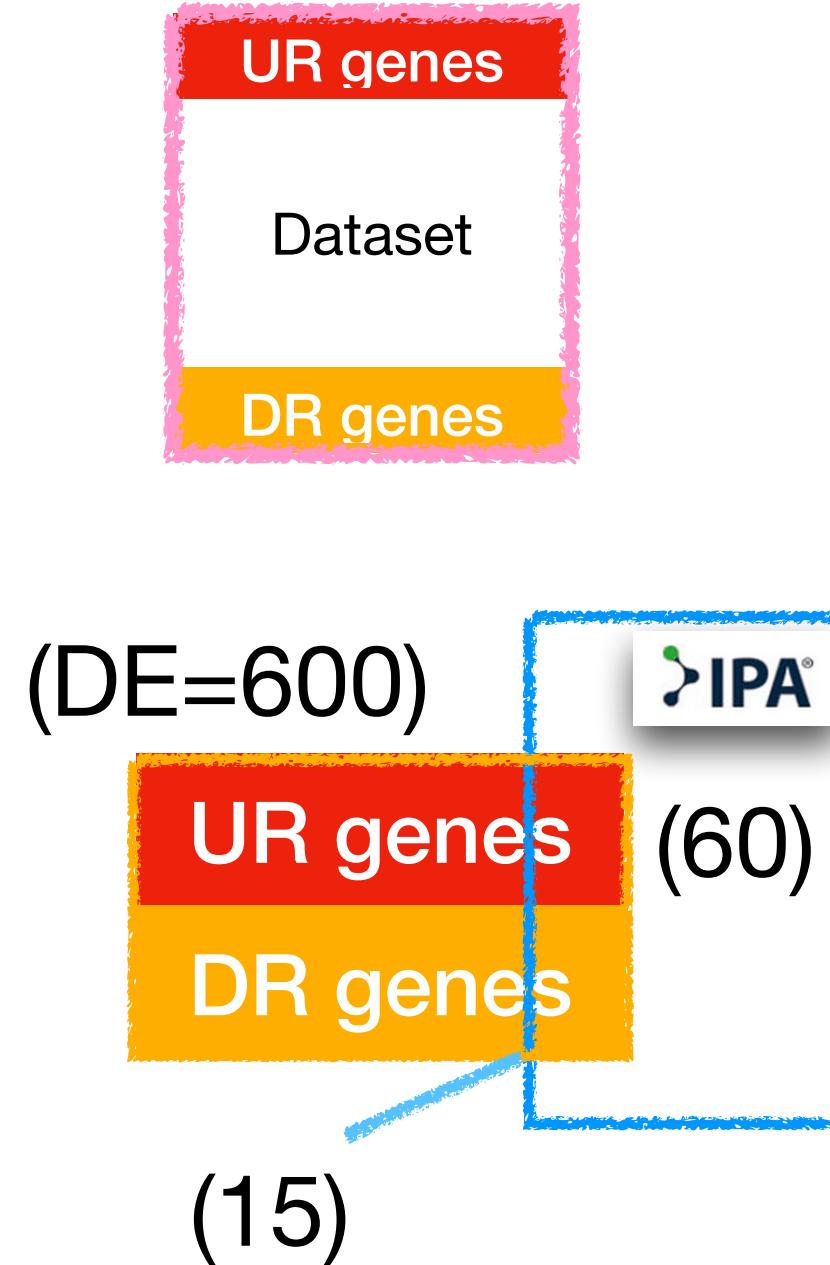
# Background effect

## Genome Background

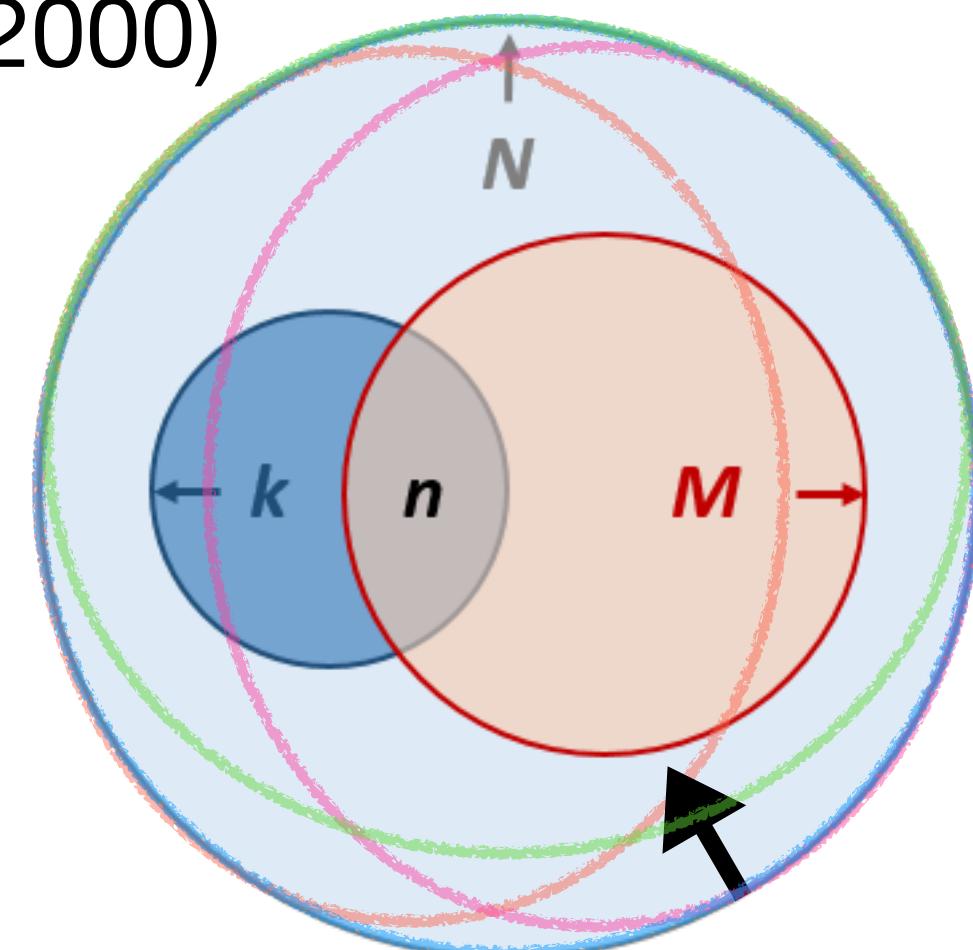


	UDS	KB	Effect
L1	50%	50%	=
L2	50%	75%	<i>underestimate</i>
L3	50%	20%	<i>overestimate</i>

# 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

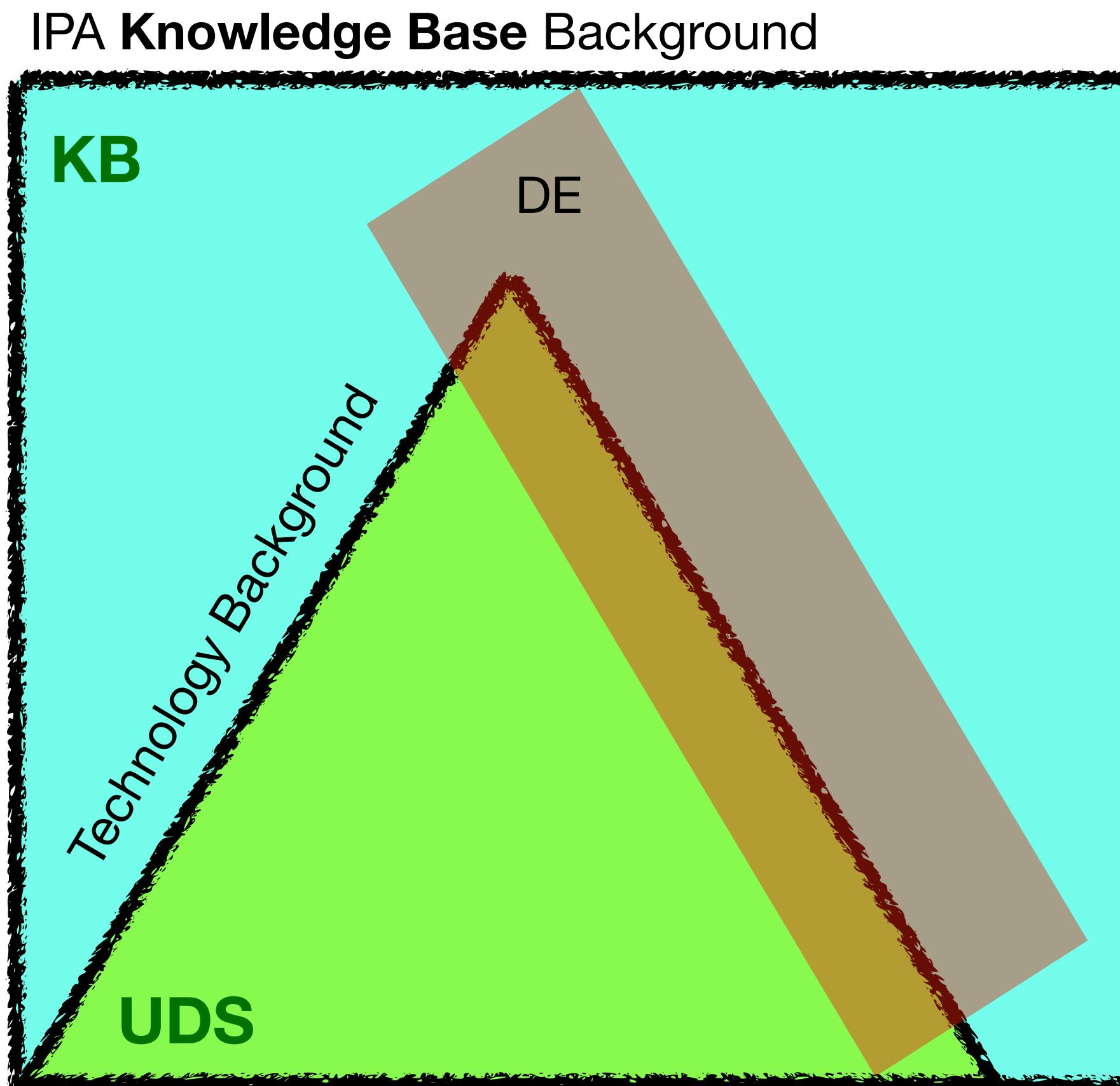
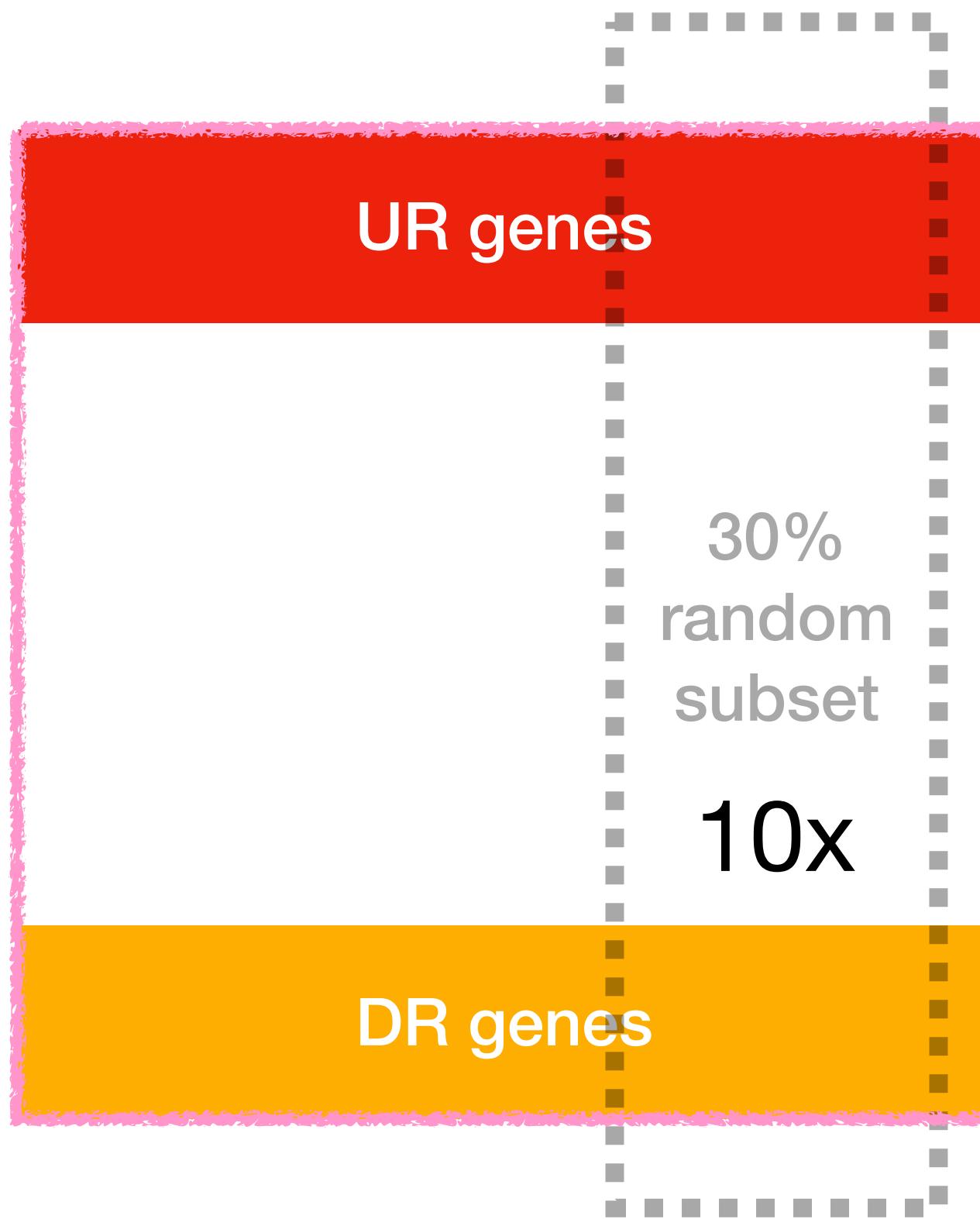
20 out of 60 from list are quantified

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

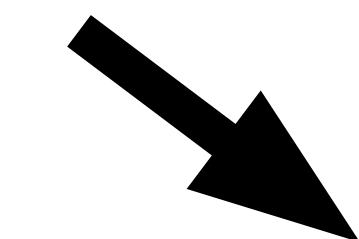
\*  $p\text{hyper}(q, m, n, k, \text{lower.tail} = \text{FALSE}, \text{log.p} = \text{FALSE})$

# Sampling x Background effect

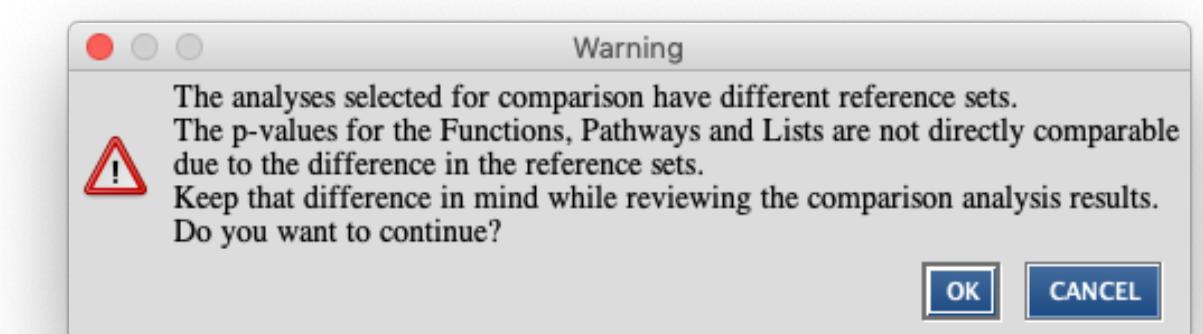


2x 10x core analysis  
different backgrounds

$|logR| > 1$  &  $adjp < 0.001$

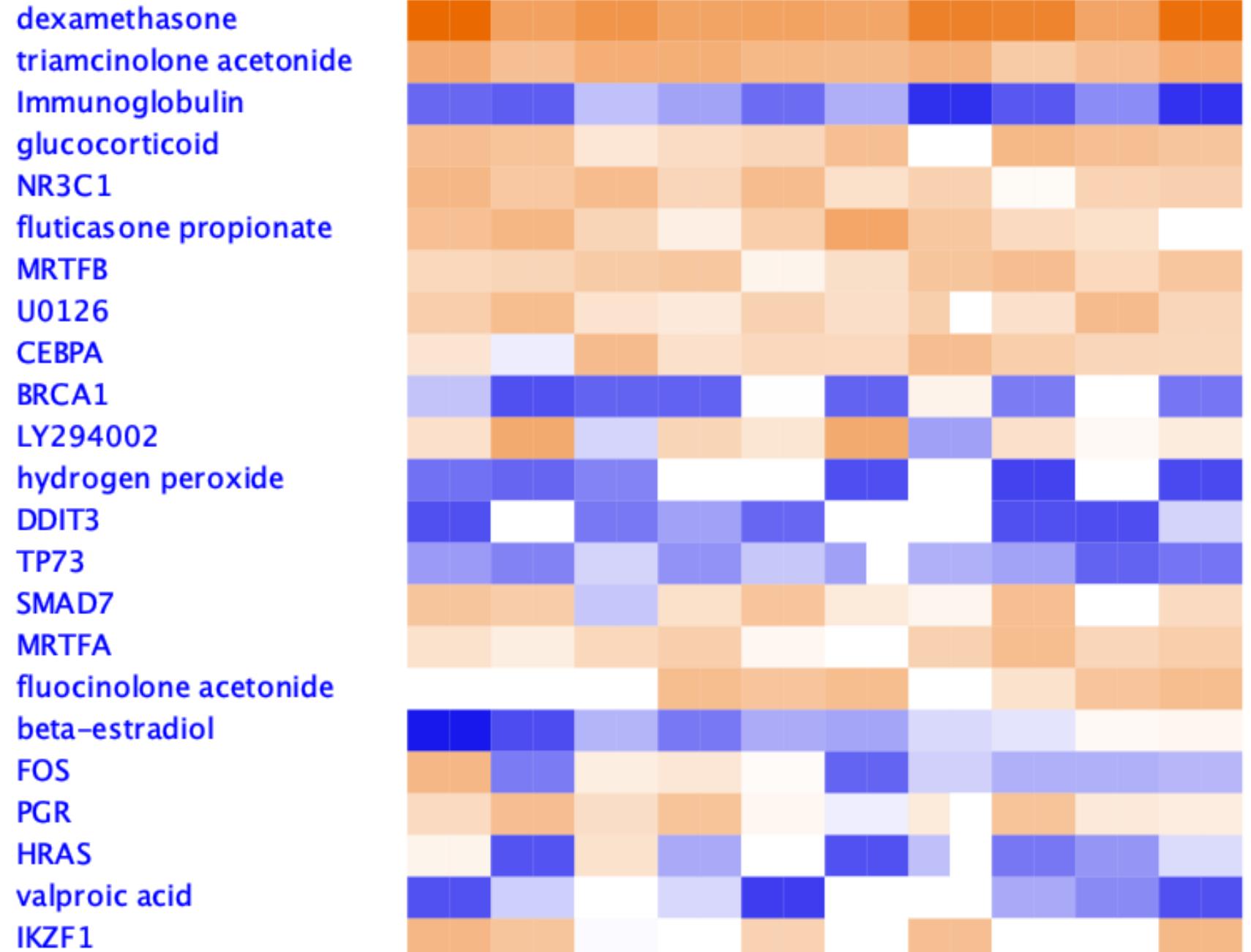


Compare

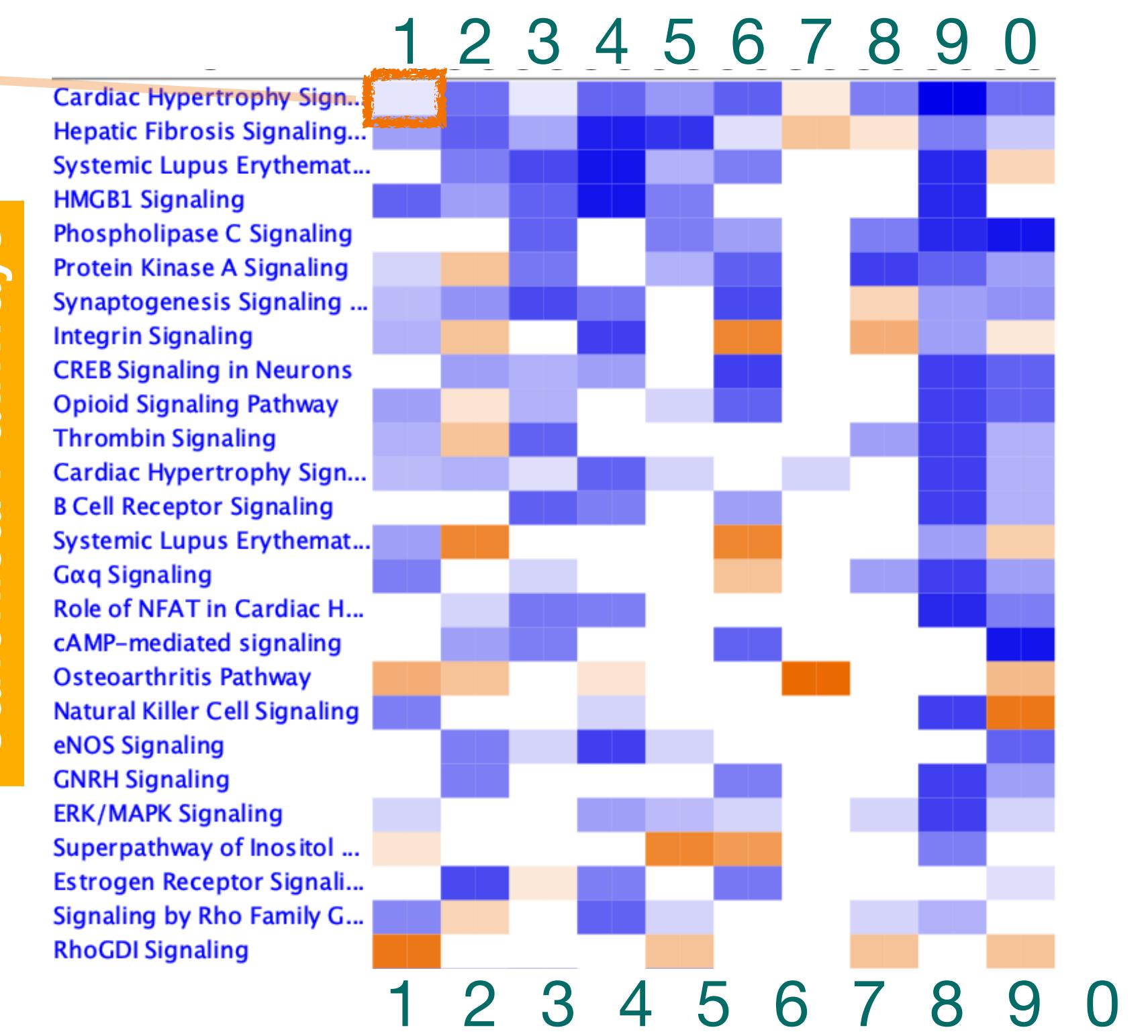


KB UDS

### Upstream regulators



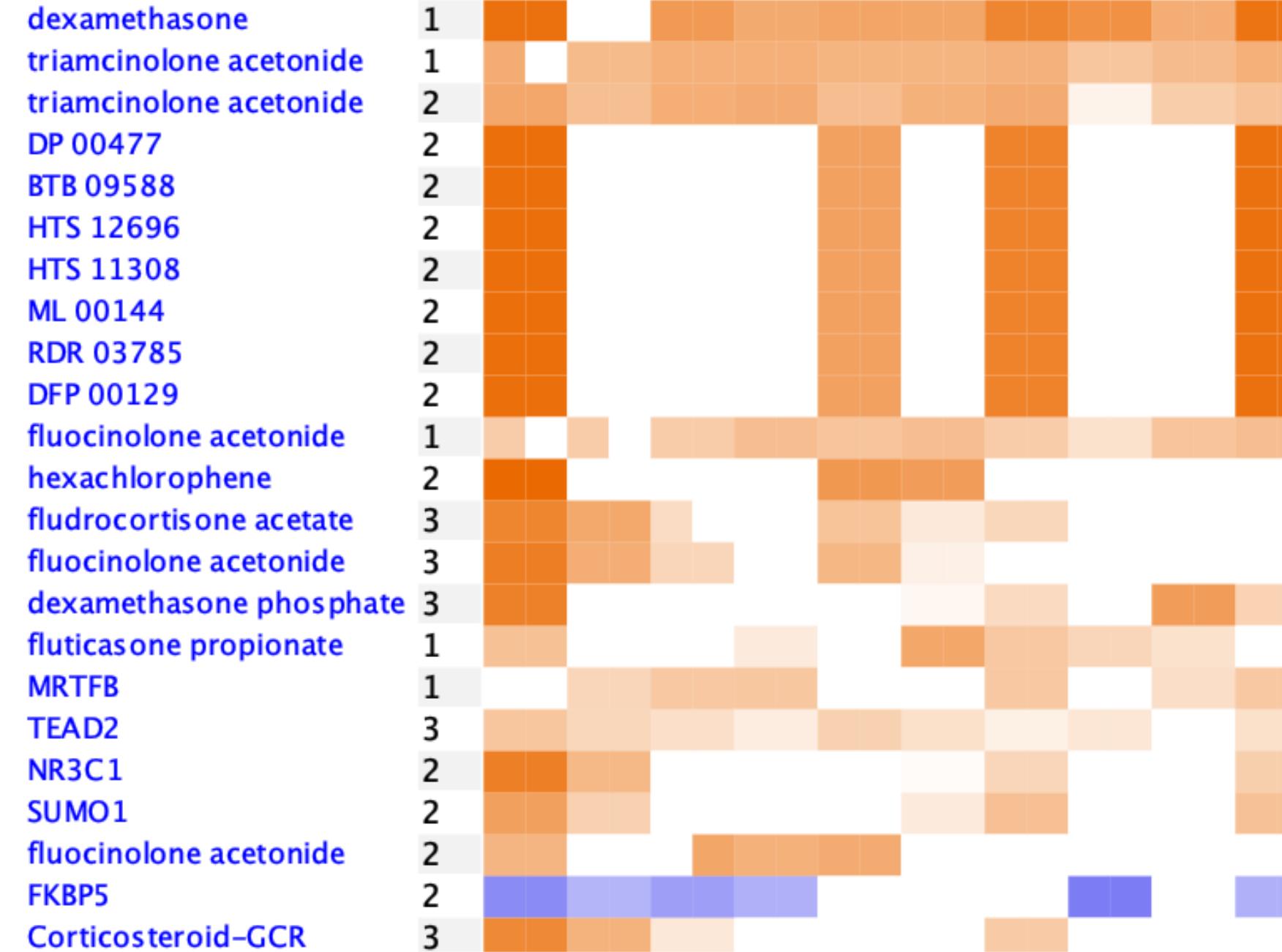
### Canonical Pathways



1 2 3 4 5 6 7 8 9 0

1 2 3 4 5 6 7 8 9 0

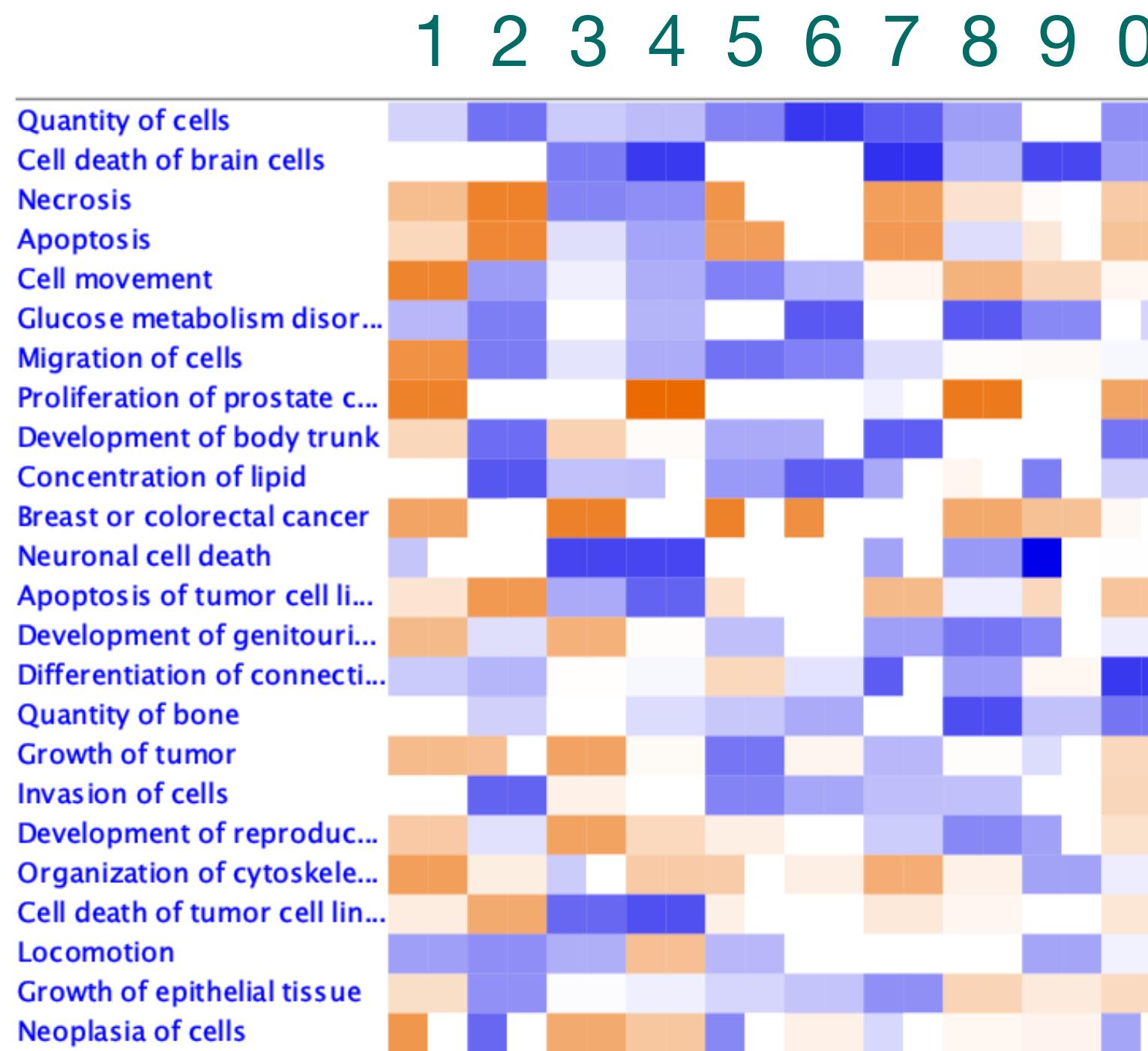
### Causal Networks



1 2 3 4 5 6 7 8 9 0

1 2 3 4 5 6 7 8 9 0

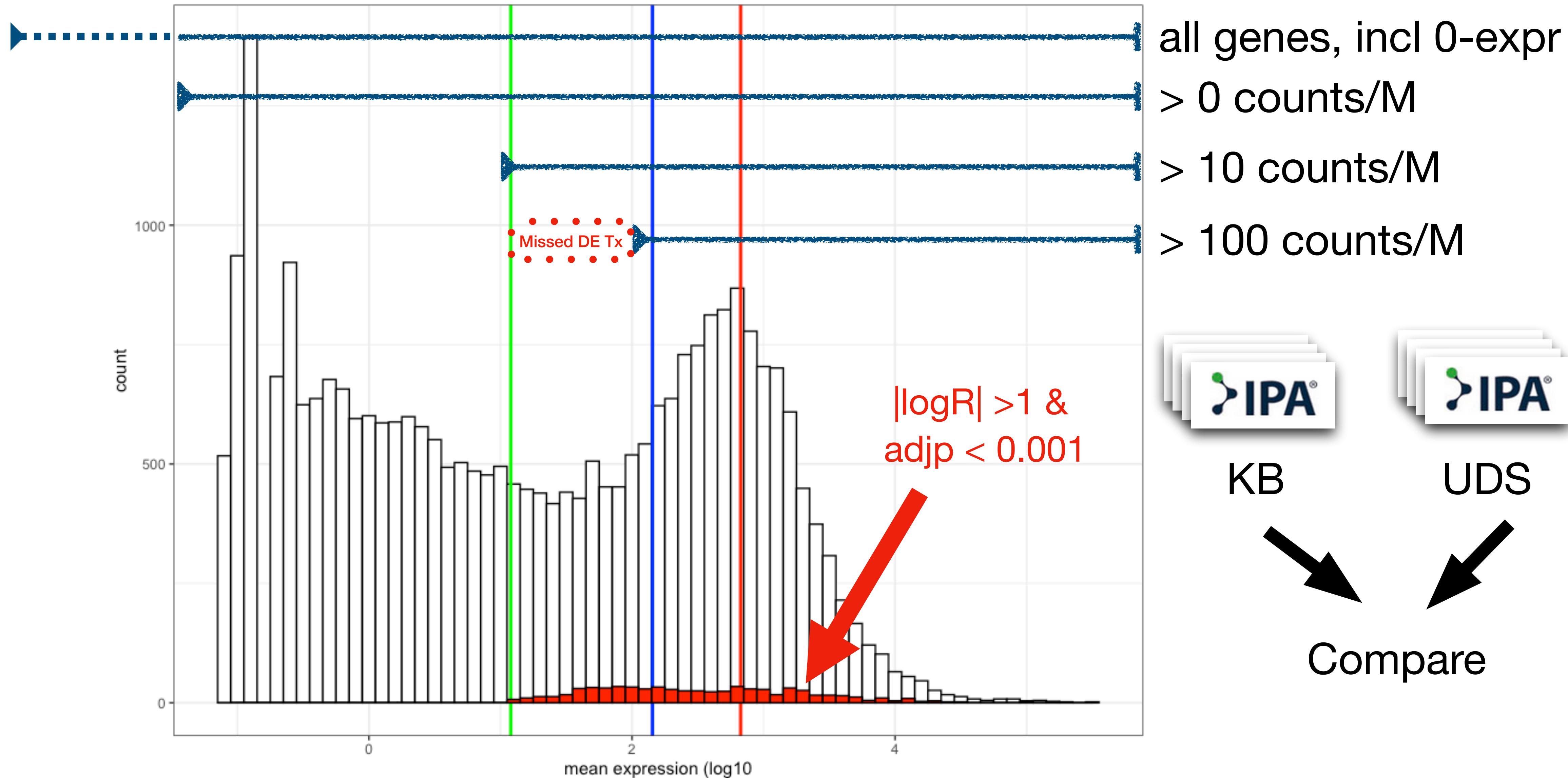
### Diseases & Functions



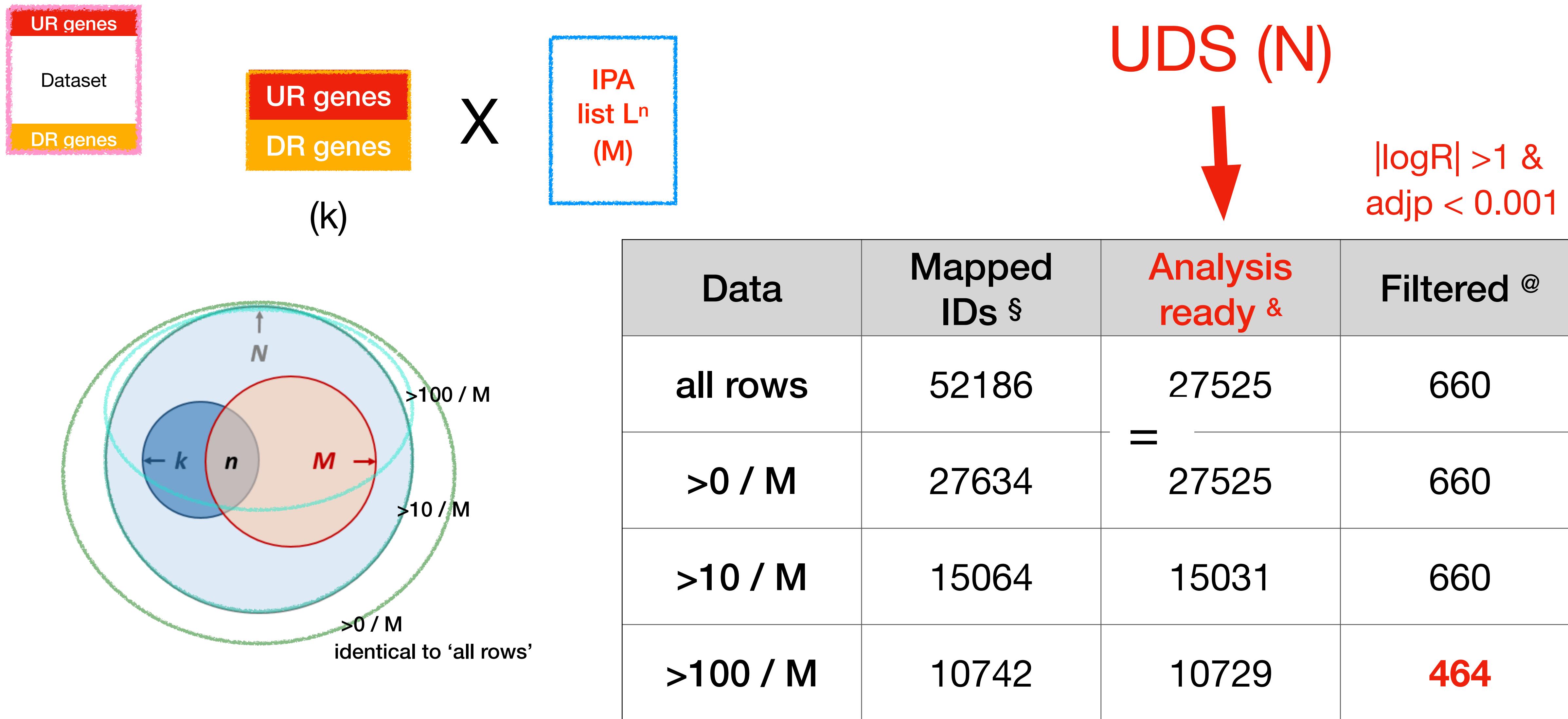
*Background effect*

!

# Background effects from low expression Tx



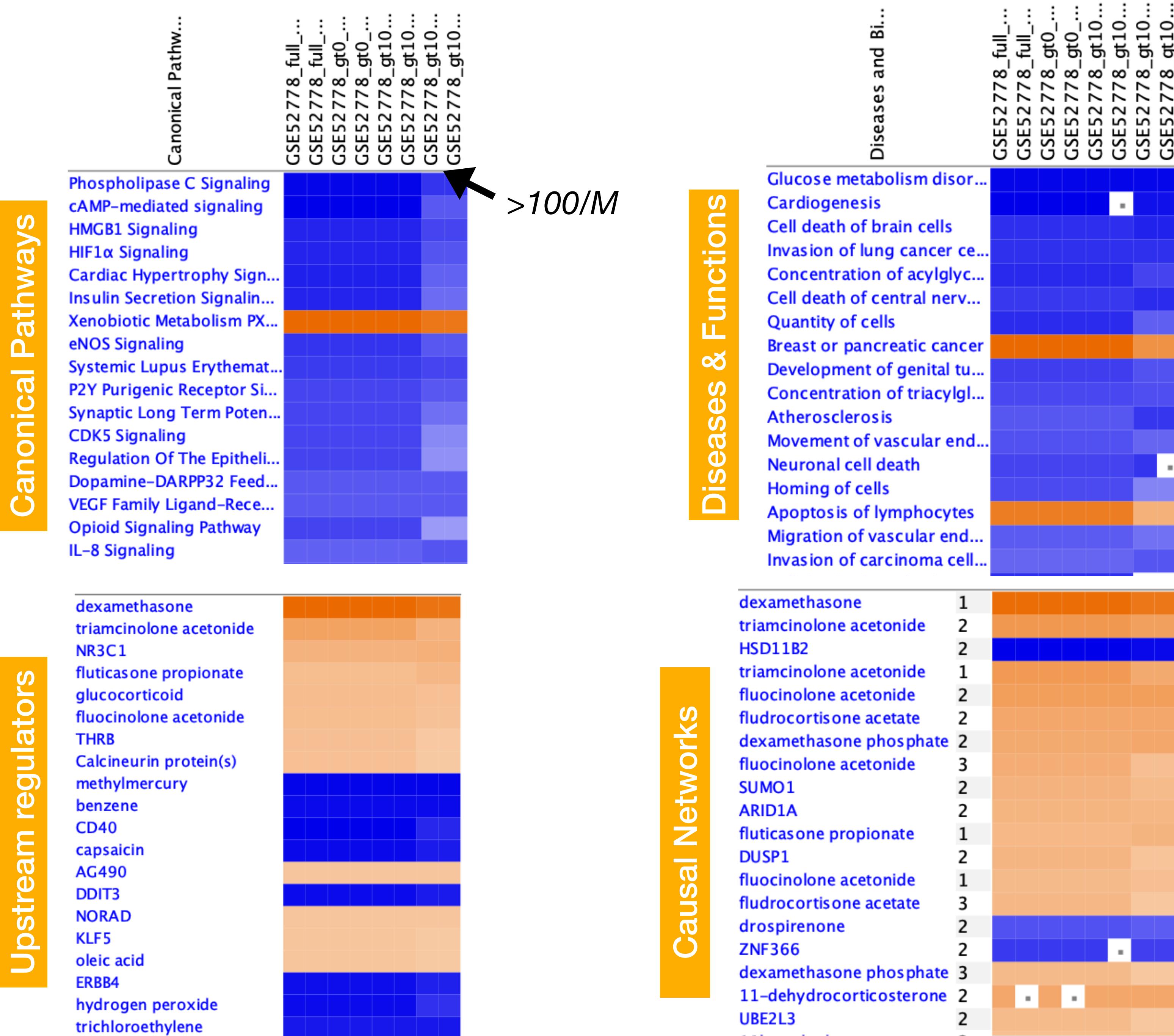
# Effect of low-expression Tx on the UDS background size



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

§ **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

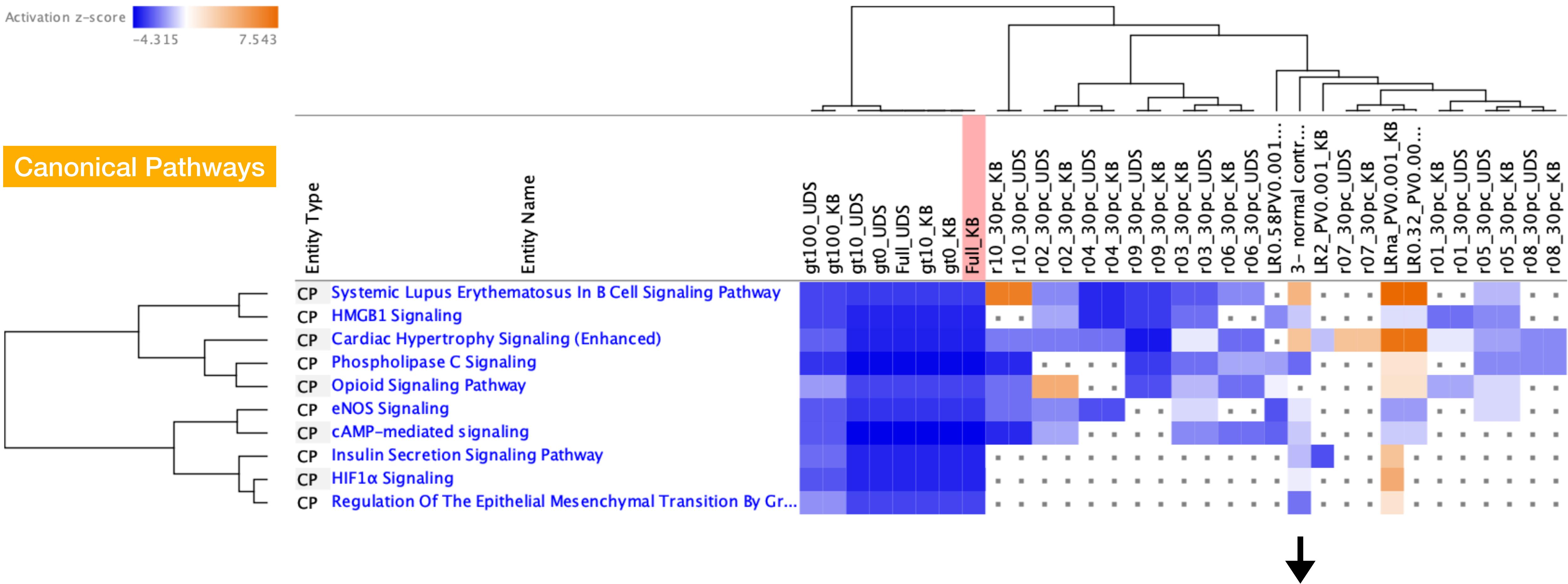
No clear  
Background  
effect  
after  
removing  
low-ex  
rows



# 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

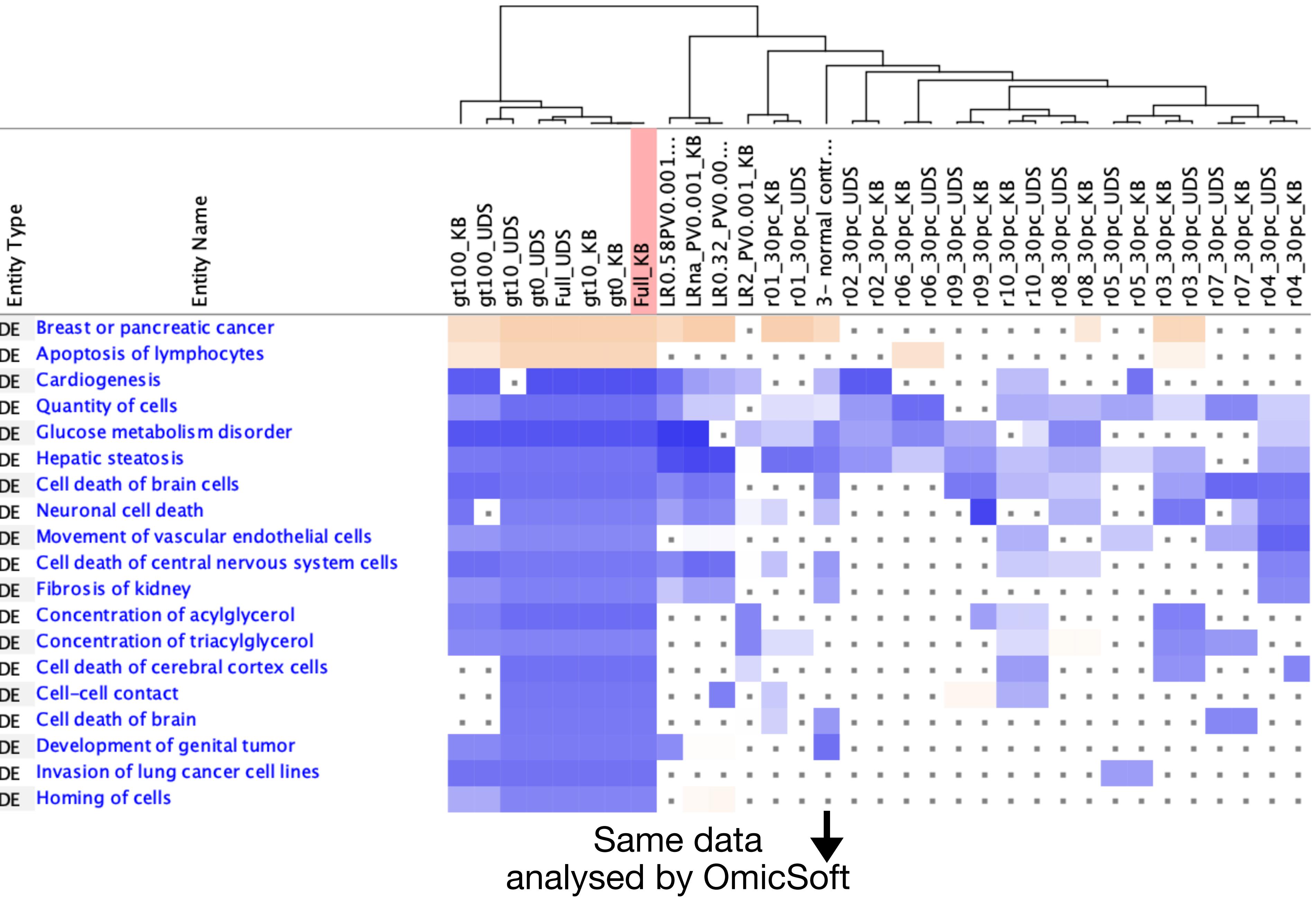
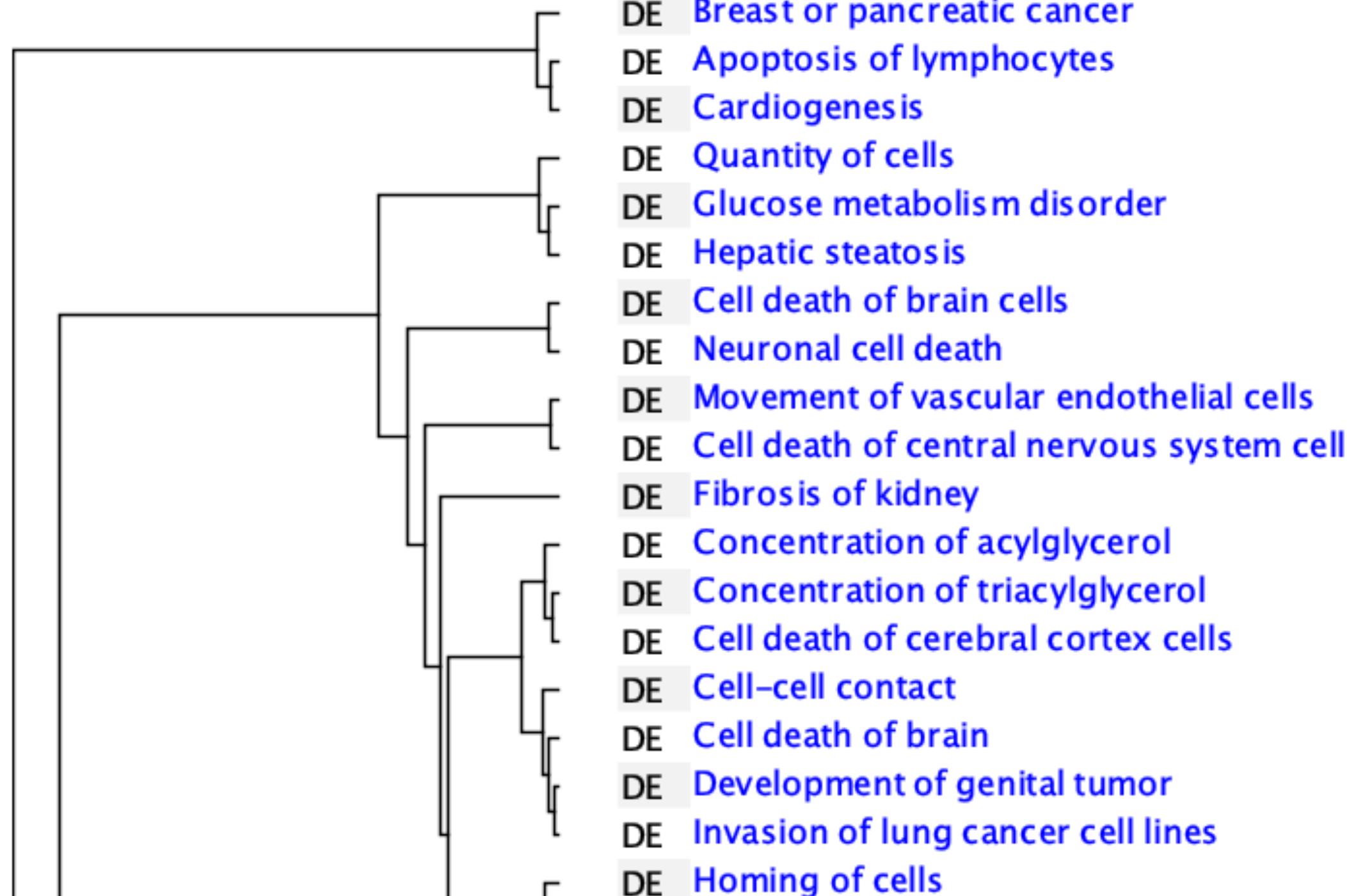


Same data  
analysed by OmicSoft

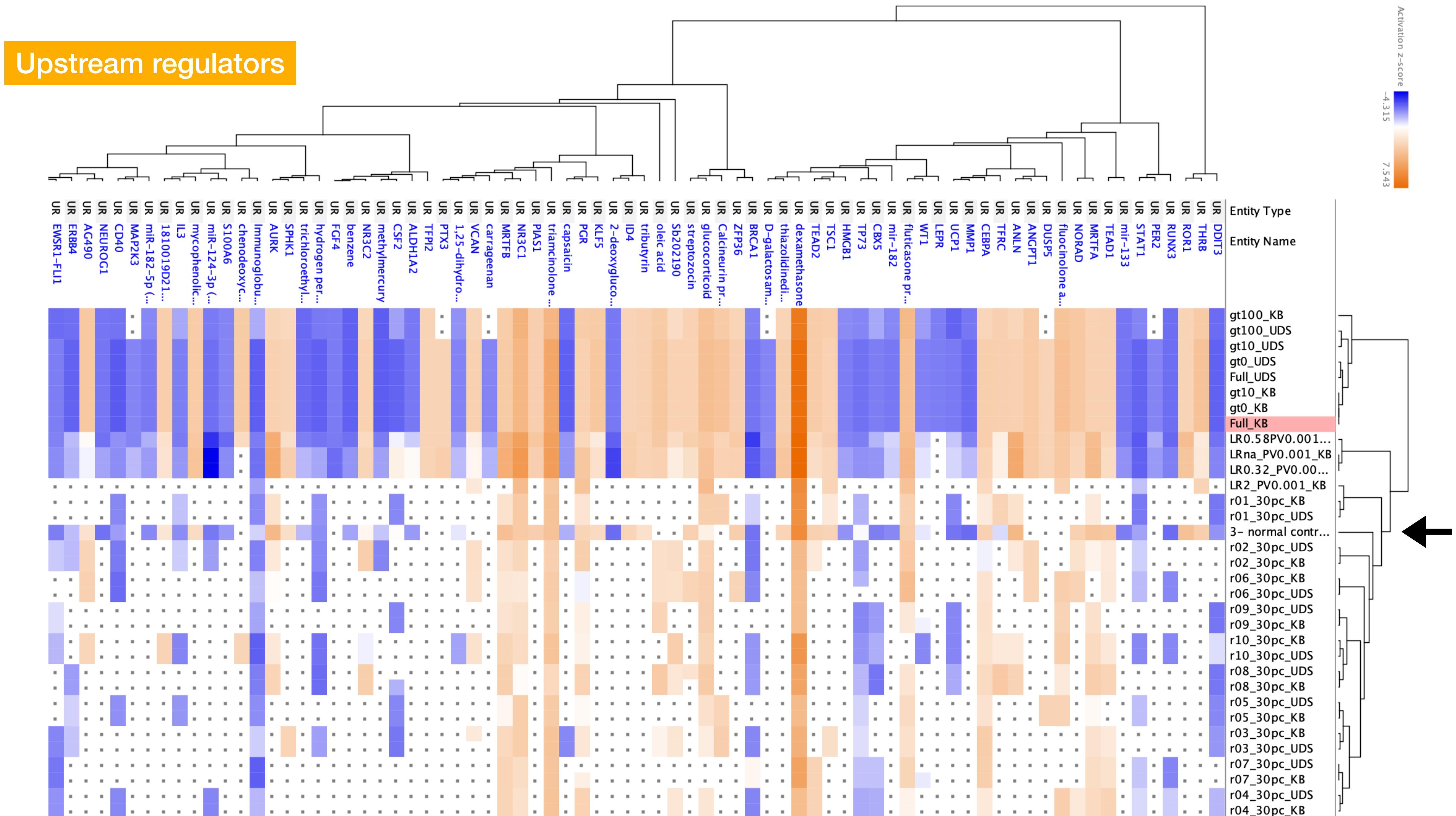
# Global robustness results: Diseases & Functions



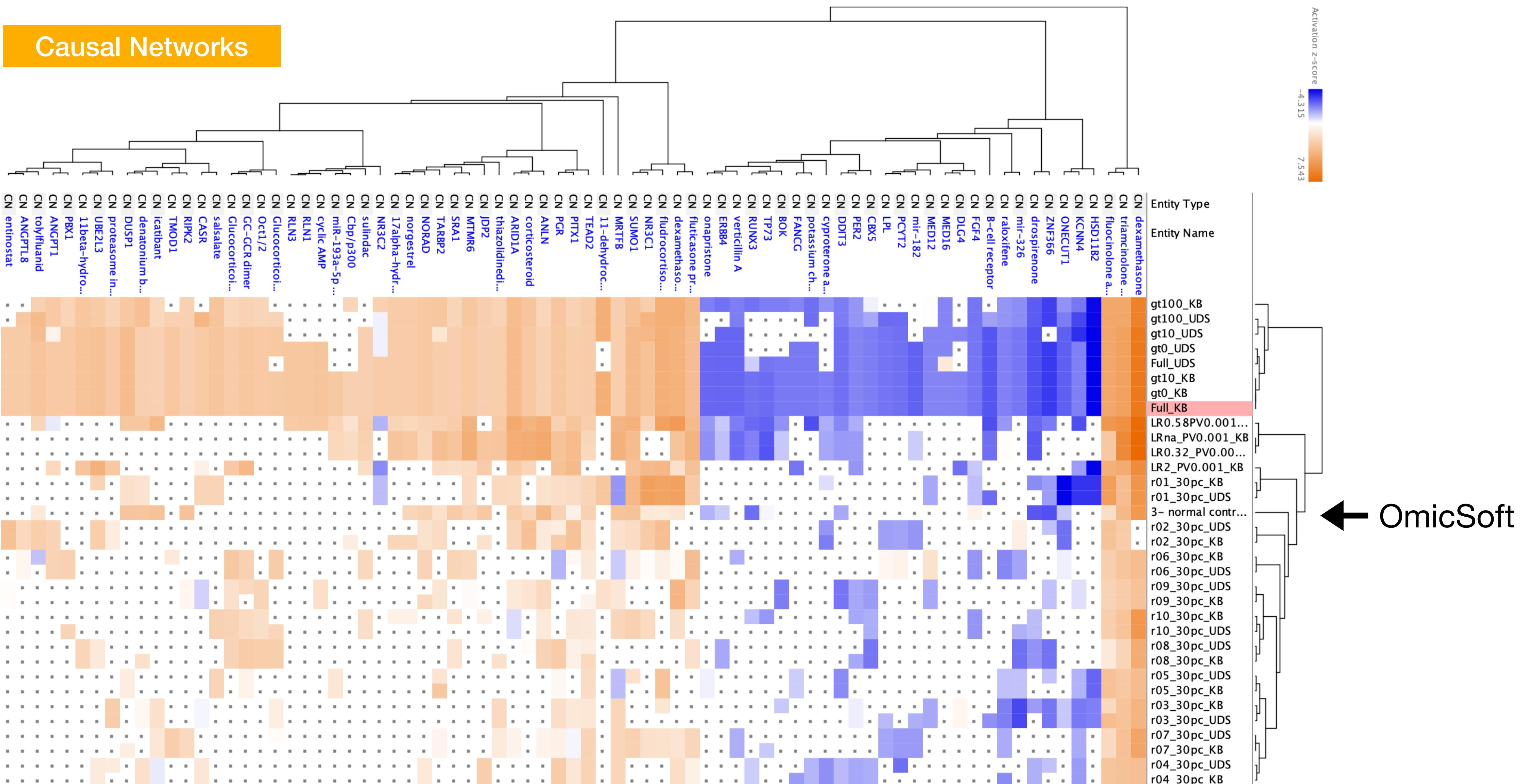
## Diseases & Functions



# Global robustness results: Upstream regulators



# Global robustness results: Causal Networks



IPA

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

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

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Software Support

Overview

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- > Tibco Spotfire
- > CLC Genomics Workbench
- > ELN
- > Genevestigator
- > GraphPad Prism
- > IPA
- > MATLAB
- > OpenRefine
- > qbase+
- > SnapGene
- > Galaxy
- > Developed@VIB
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