

# Multi-omics analysis of metabolic genes perturbations in *Saccharomyces cerevisiae*

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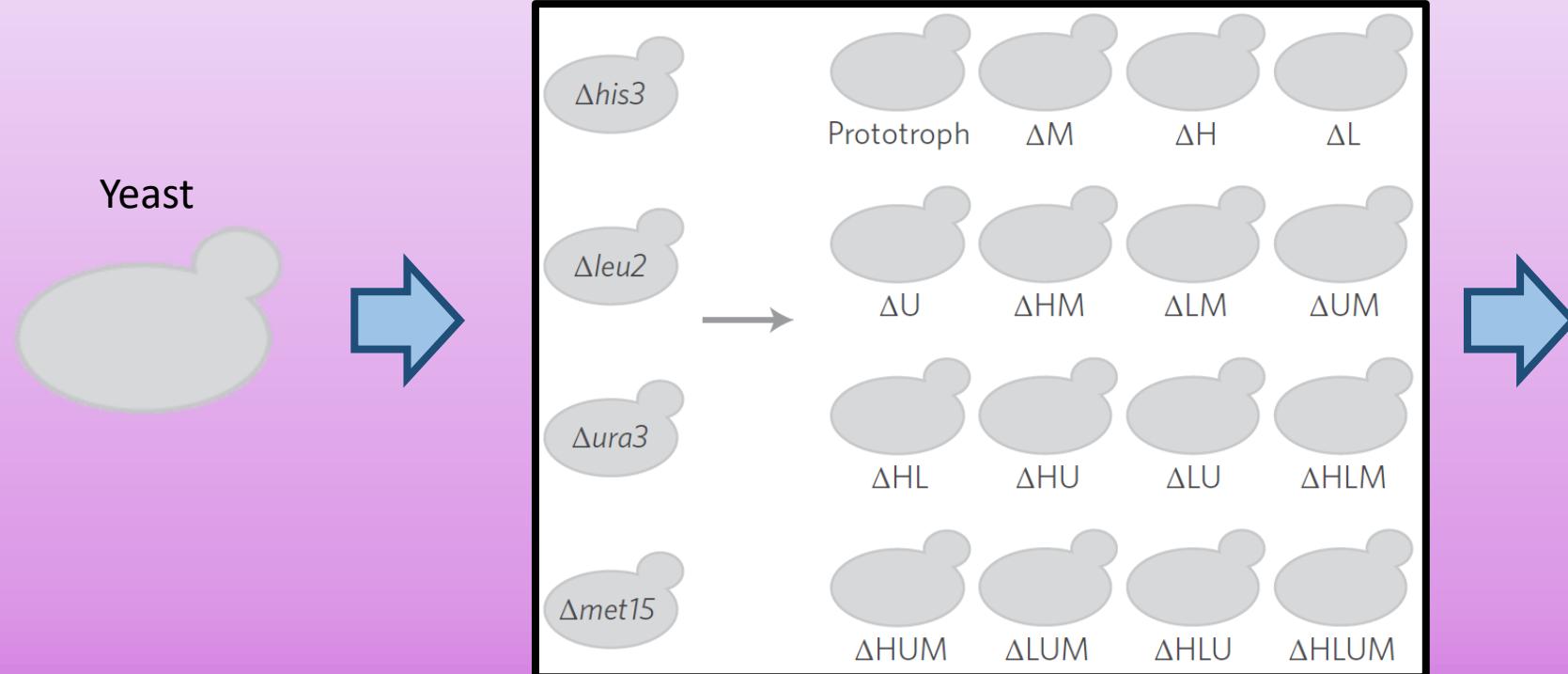
*Dr. Iddo Friedberg*

IOWA STATE UNIVERSITY

# Overview

- Background and introduction
- Dimensionality reduction (PCA, T-SNE, UMAP)
- Network
- Differential expression
- GO functional analysis
- Transcriptome-proteome data integration
- Conclusion
- Reference

# Background and Introduction



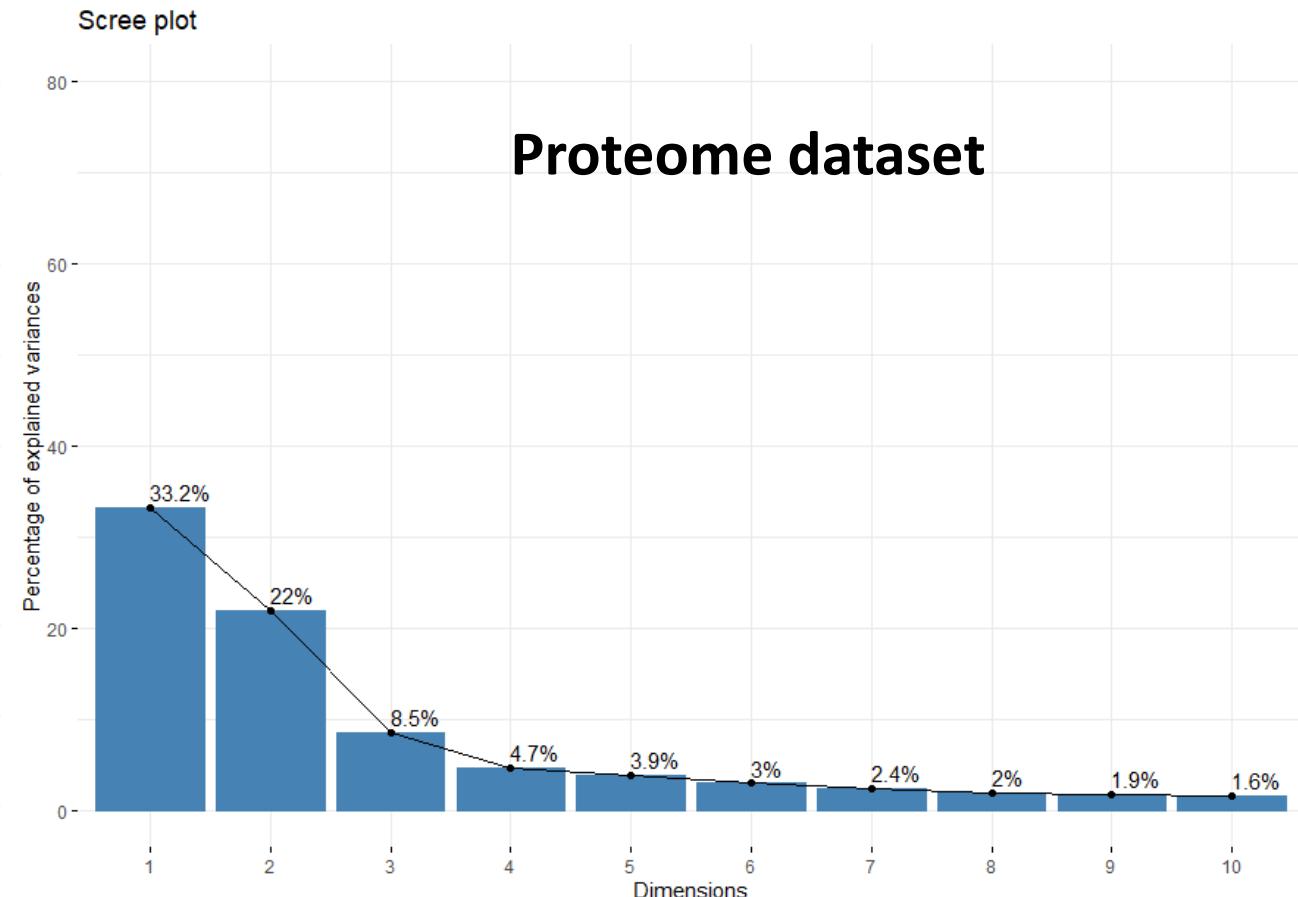
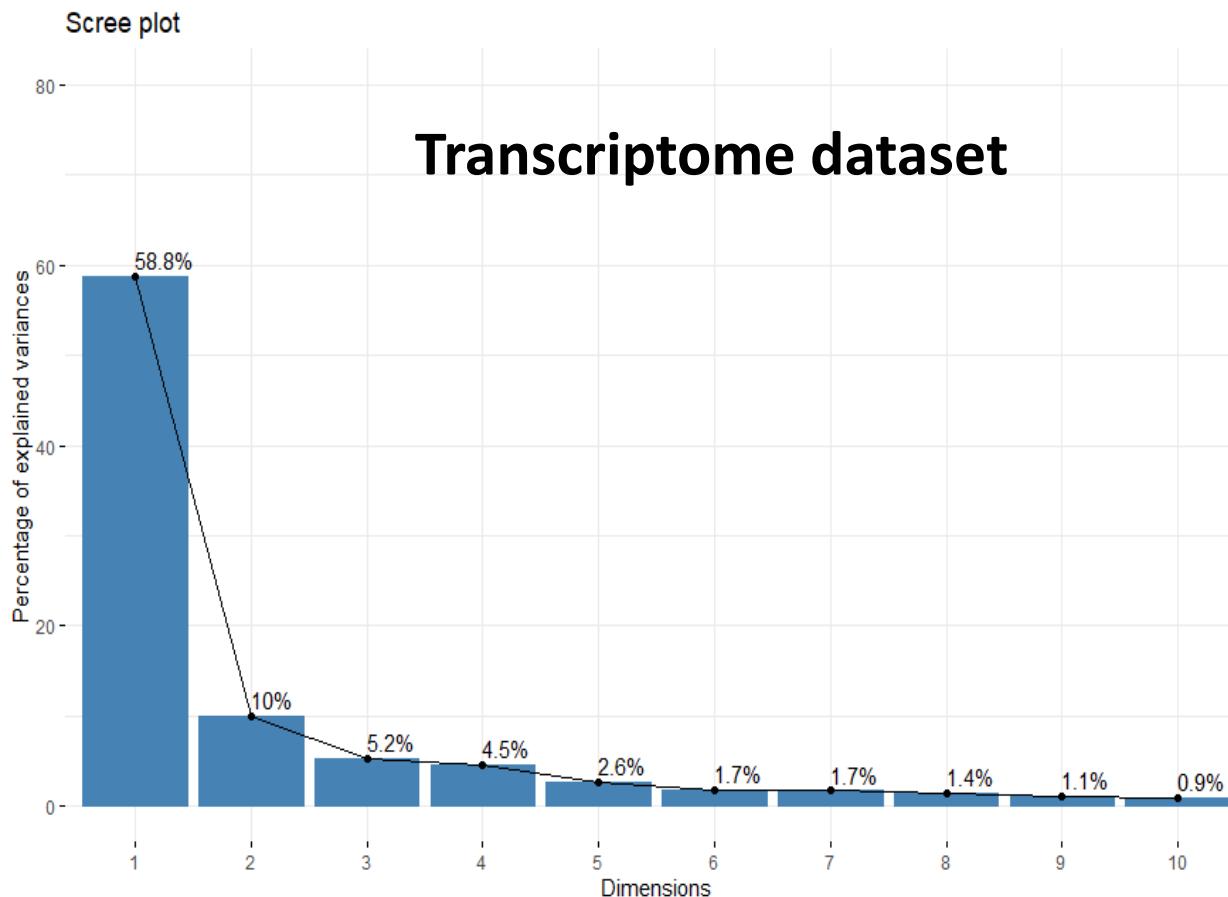
**Transcriptome dataset**

Genes	Samples		
	S1	S2	S3

**Proteome dataset**

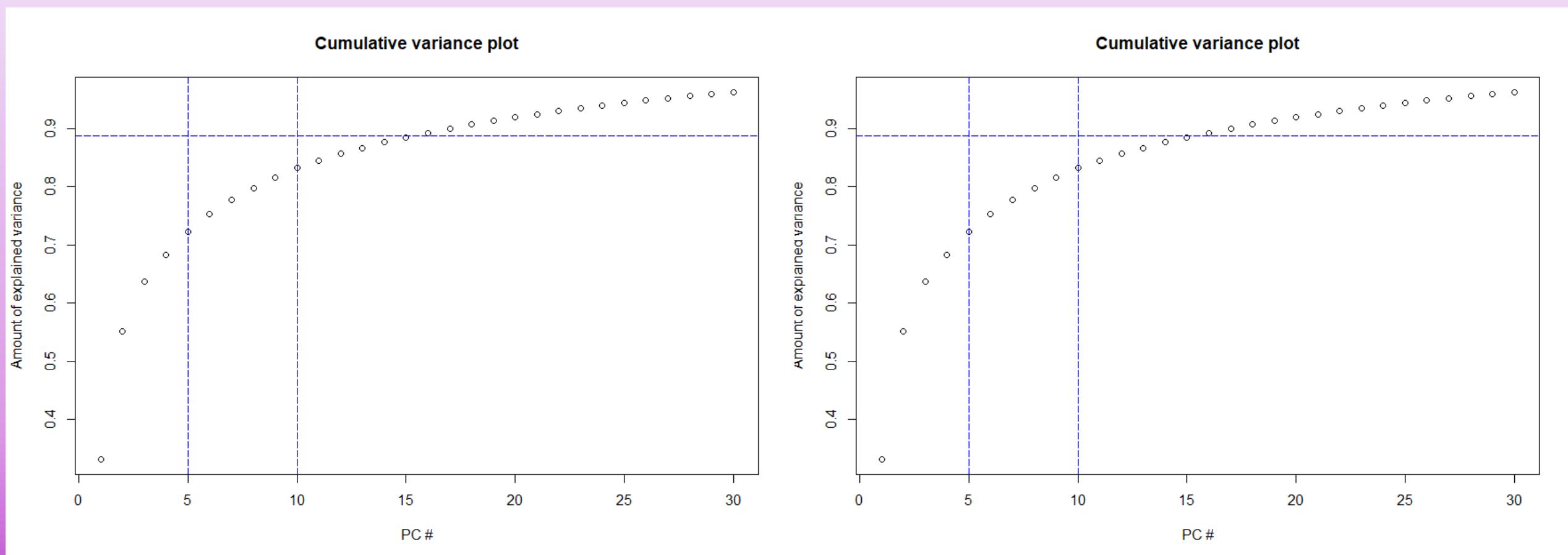
Proteins	Samples		
	S1	S2	S3

# Dimensionality Reduction (PCA) - Scree Plot

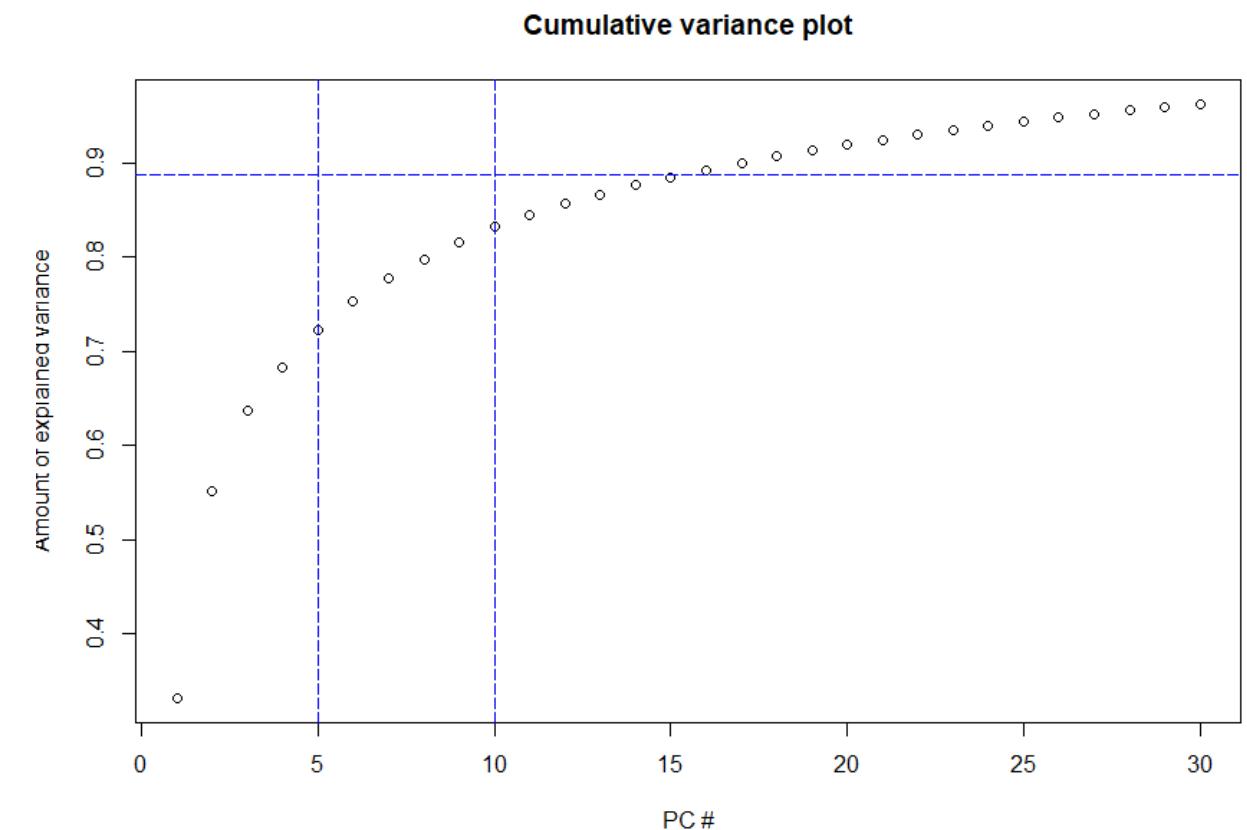


# Dimensionality Reduction (PCA) -Cumulative Variance Plot

Transcriptome dataset

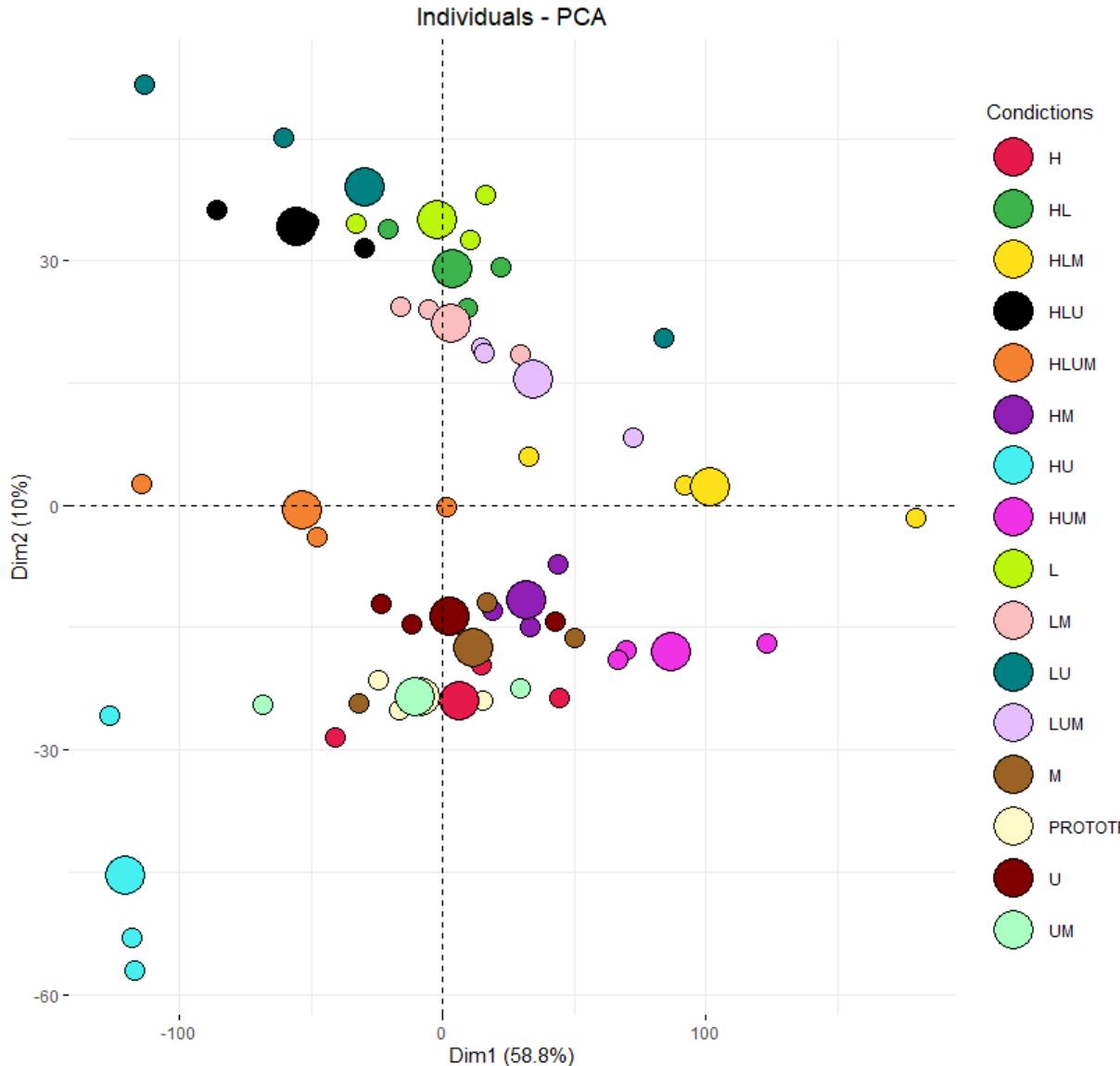


Proteome dataset

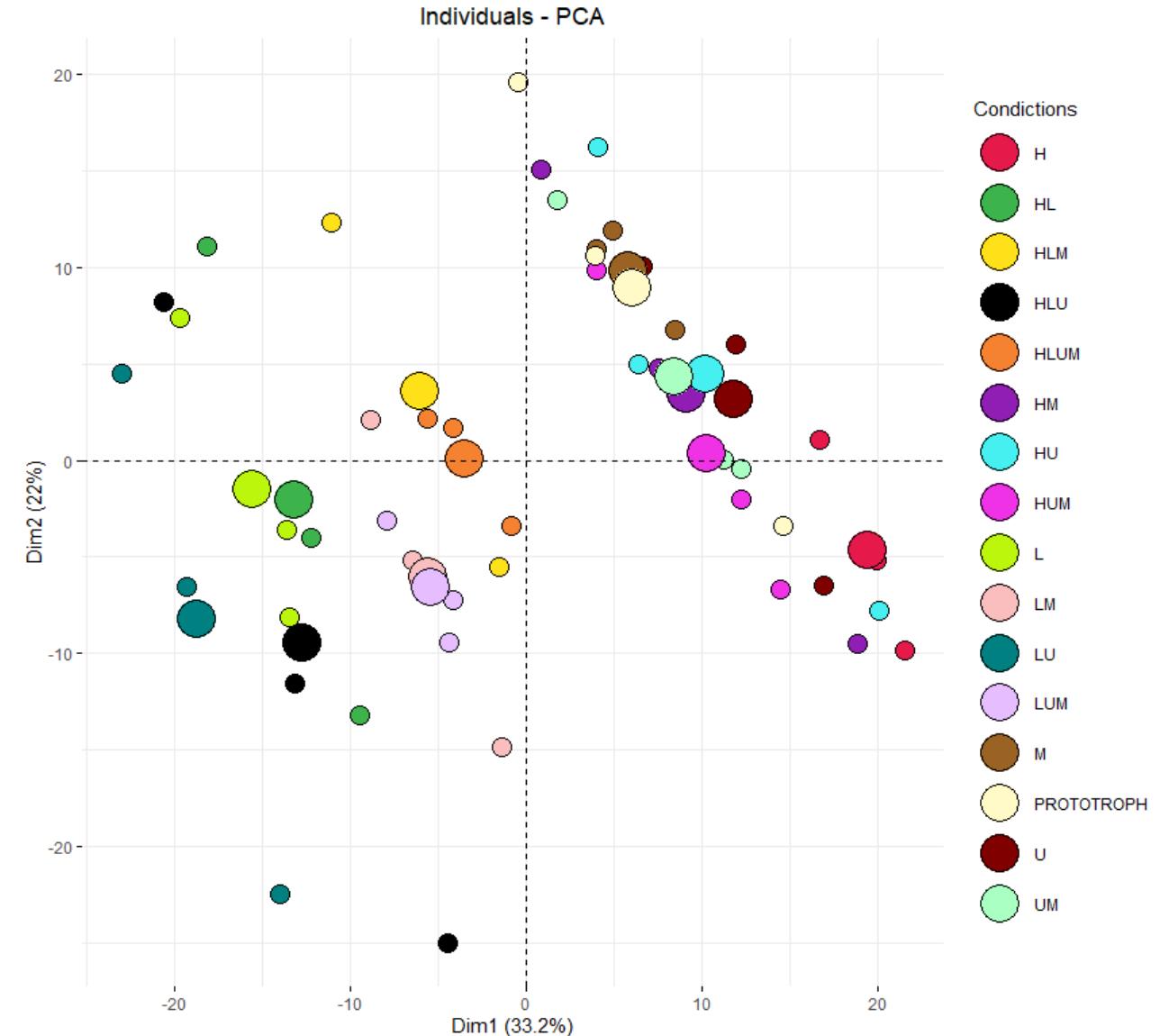


# Dimensionality Reduction (PCA) - Plot

Transcriptome dataset

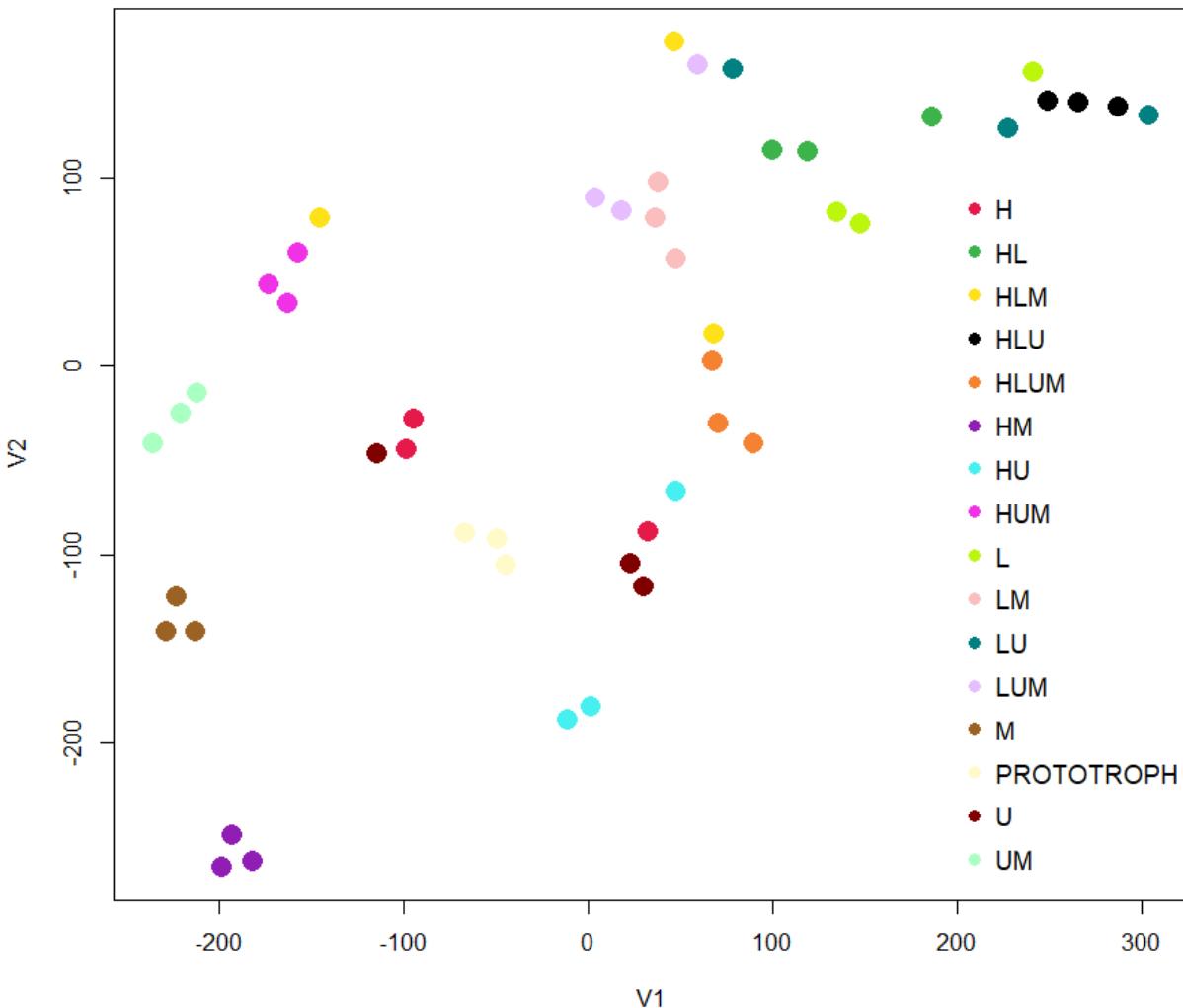


Proteome dataset

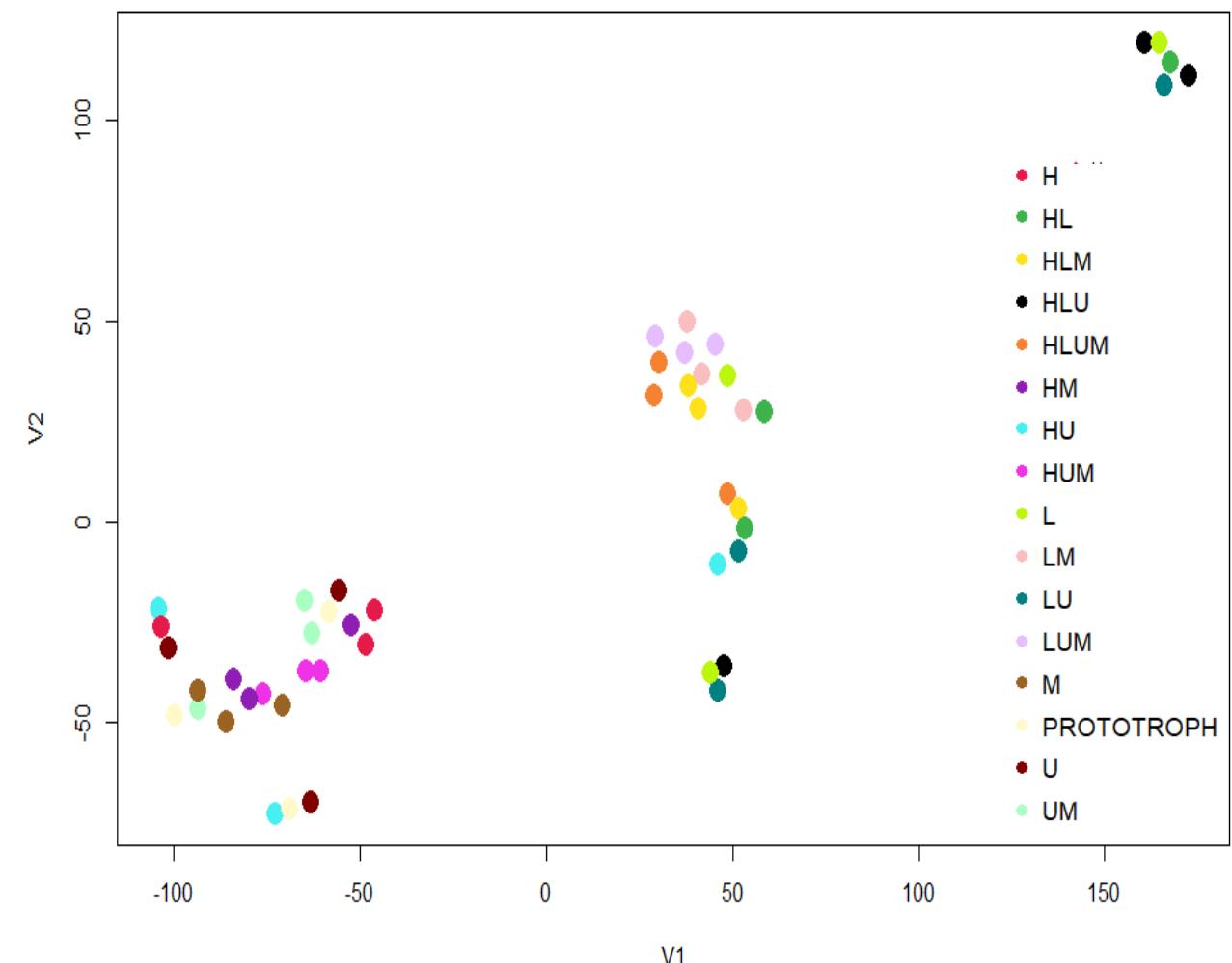


# Dimensionality Reduction (t-SNE)

Transcriptome dataset

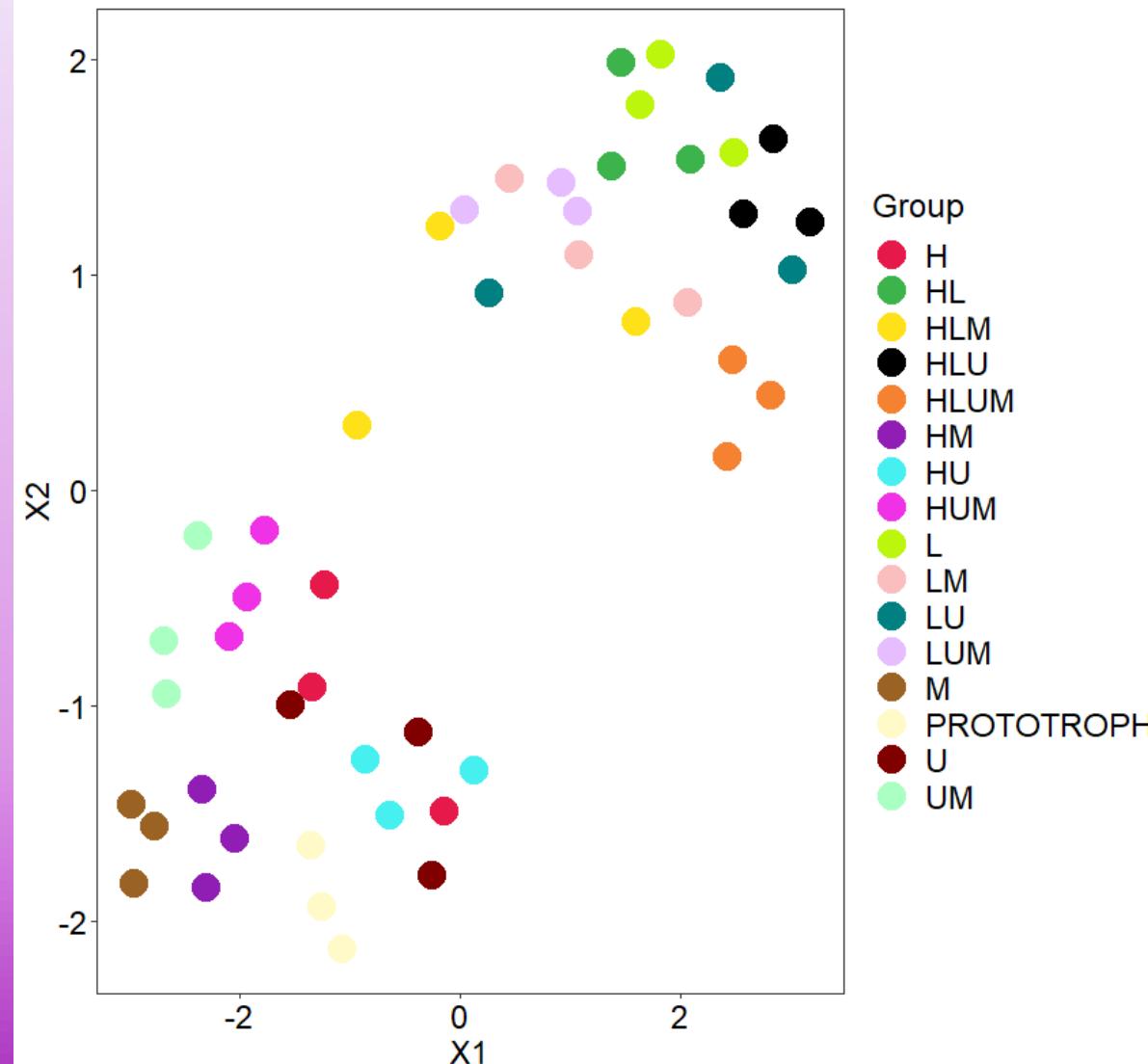


Proteome dataset

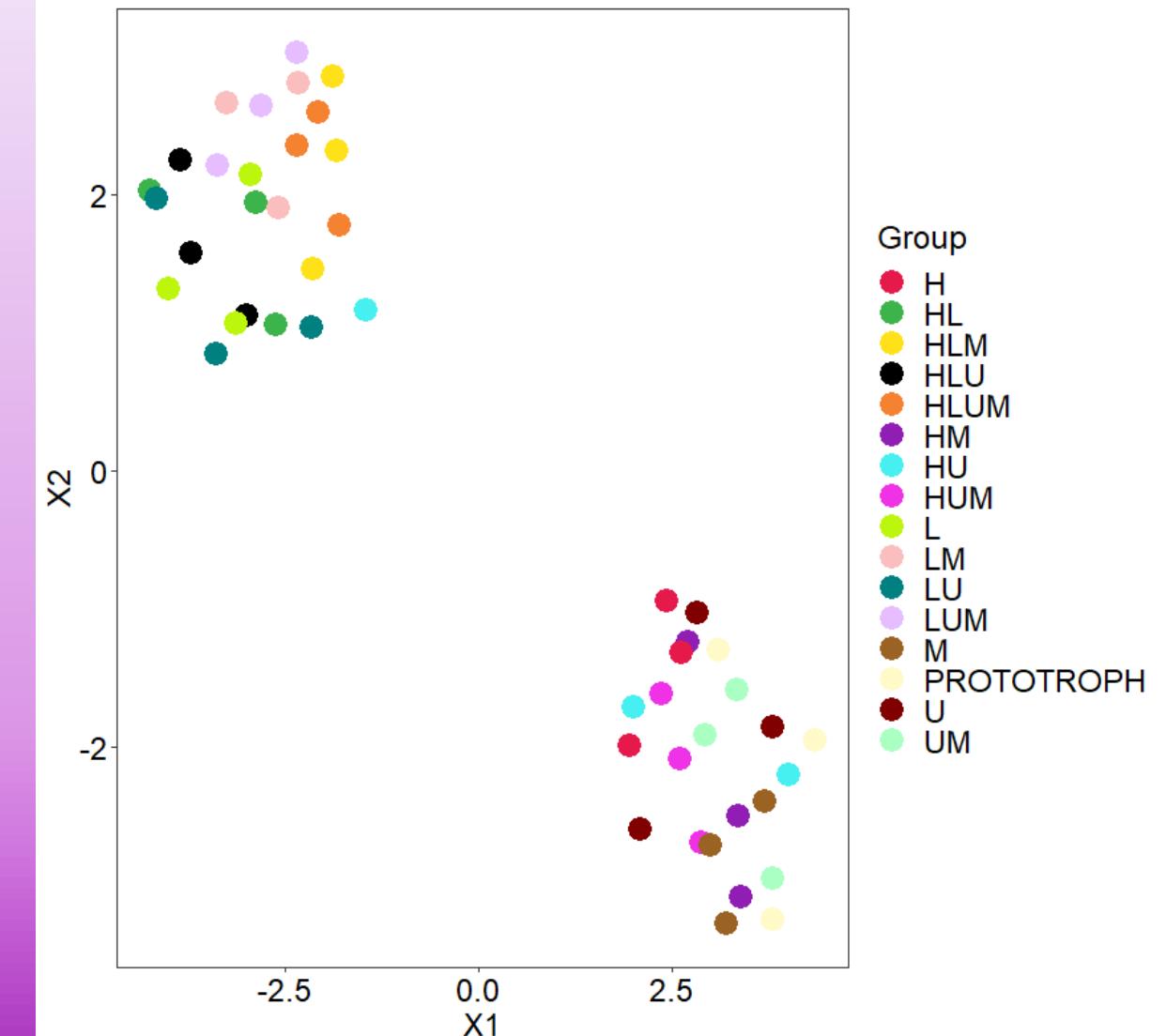


# Dimensionality Reduction (UMAP)

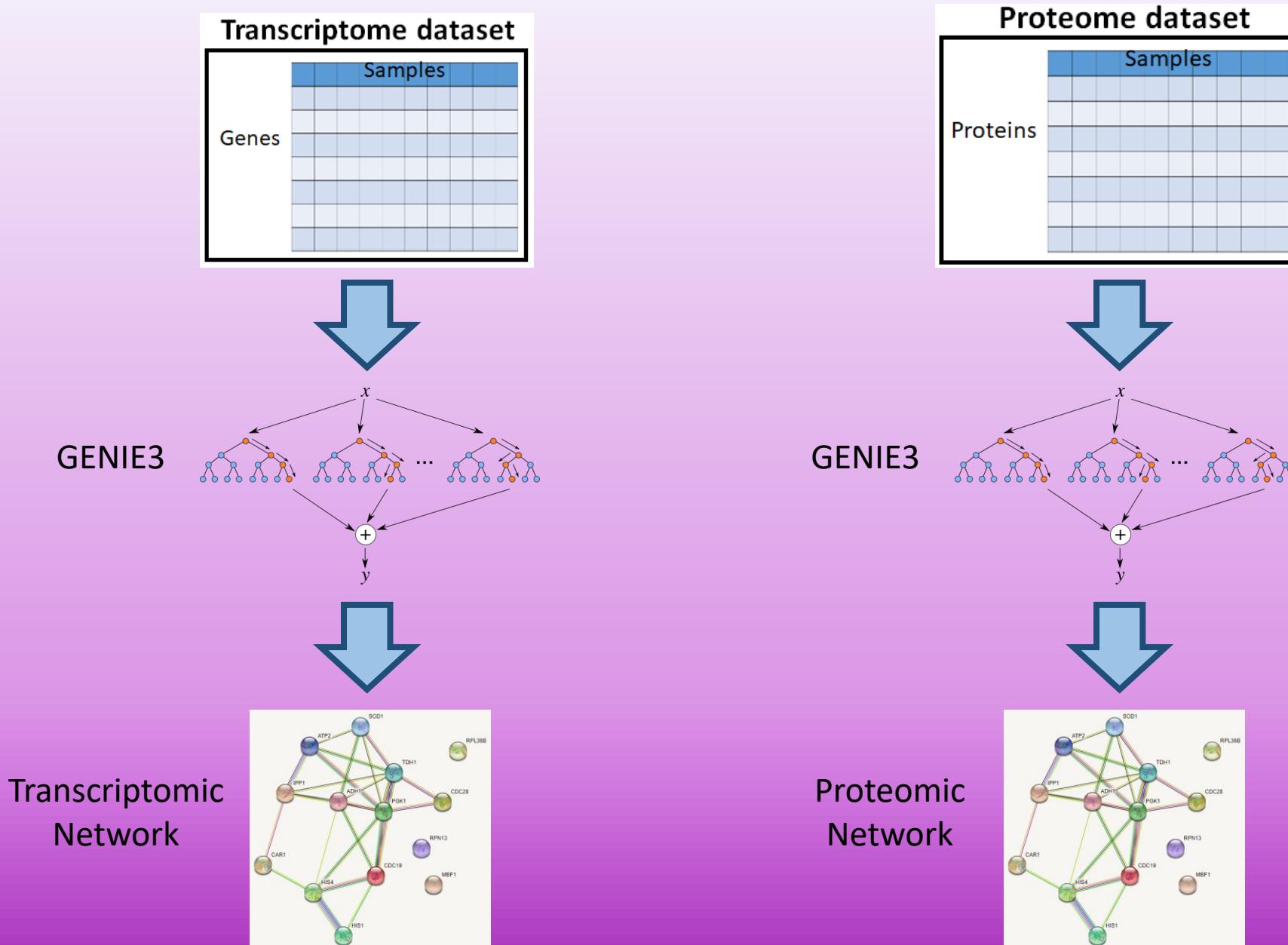
Transcriptome dataset



Proteome dataset

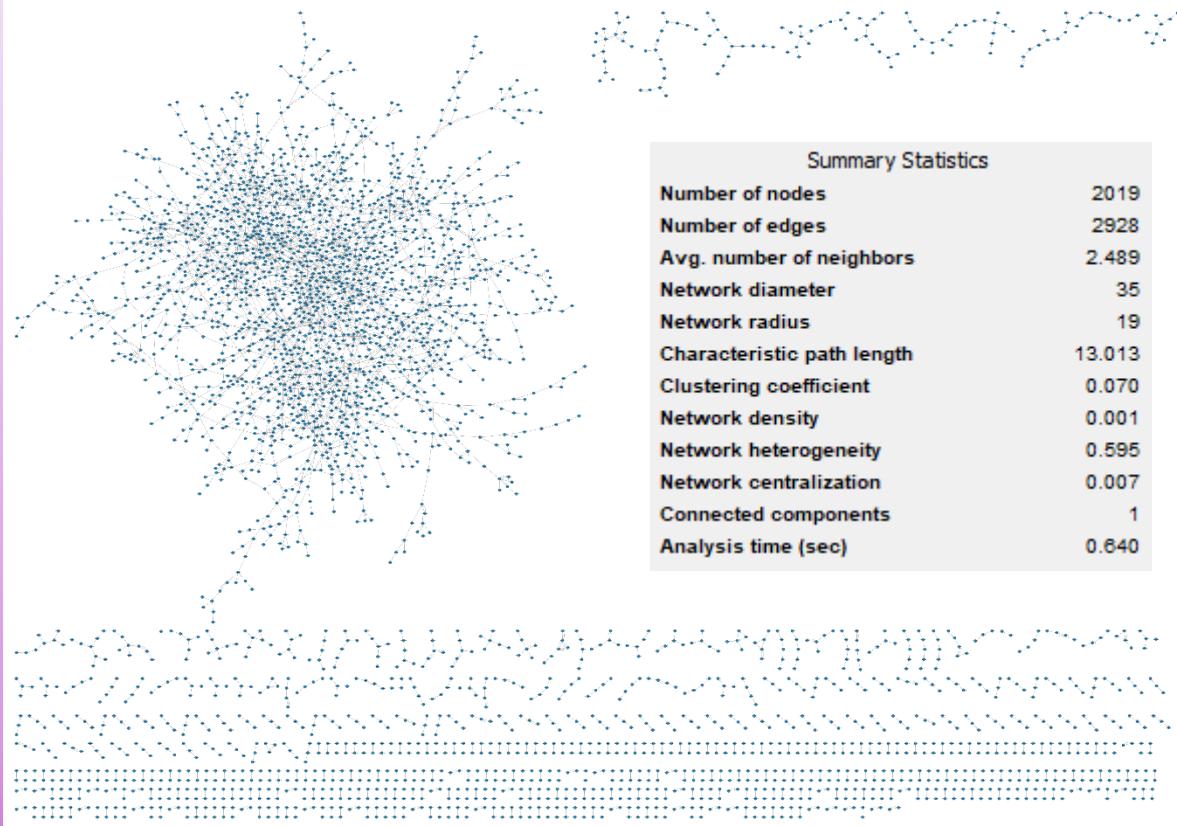


# Network building

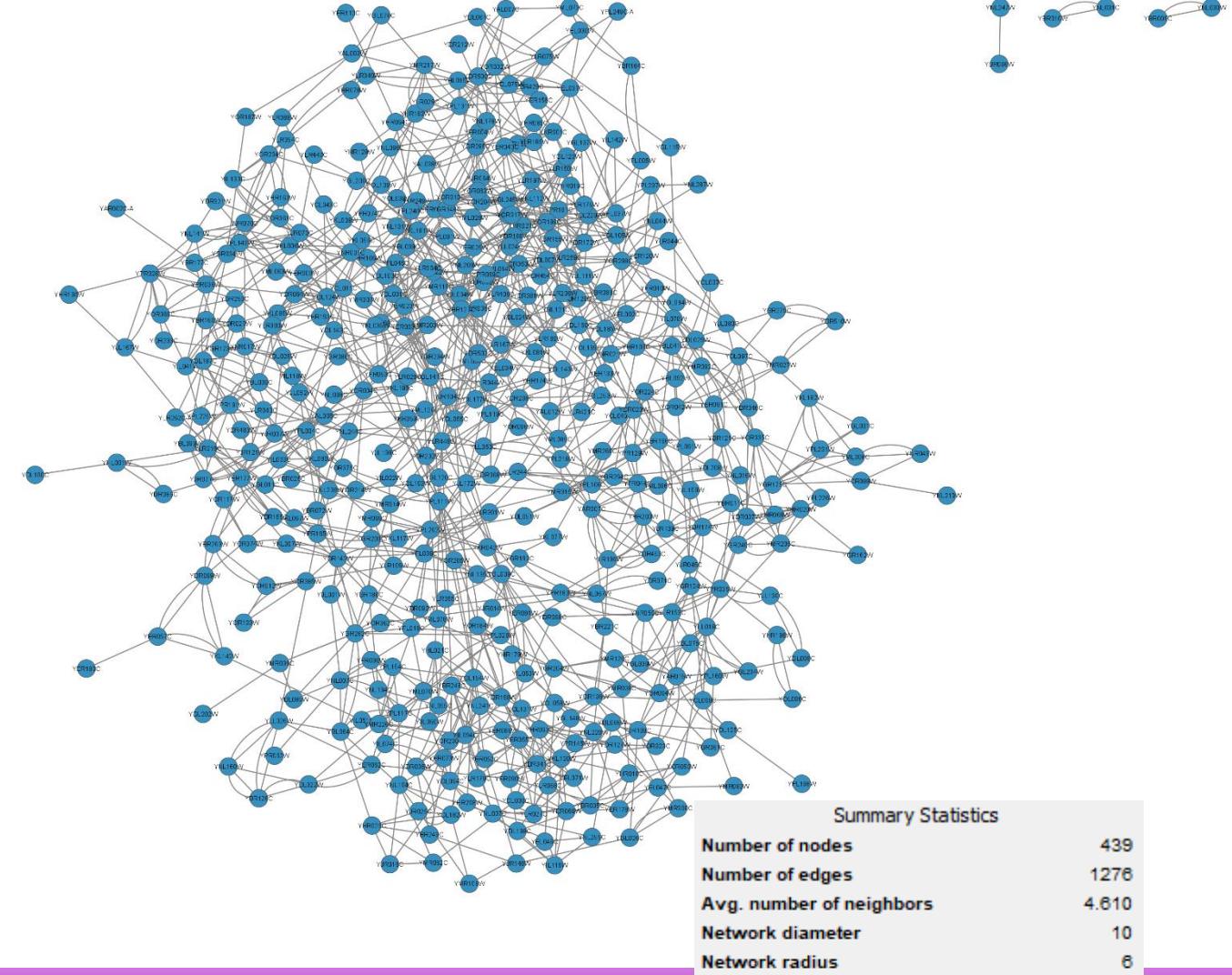


# Network

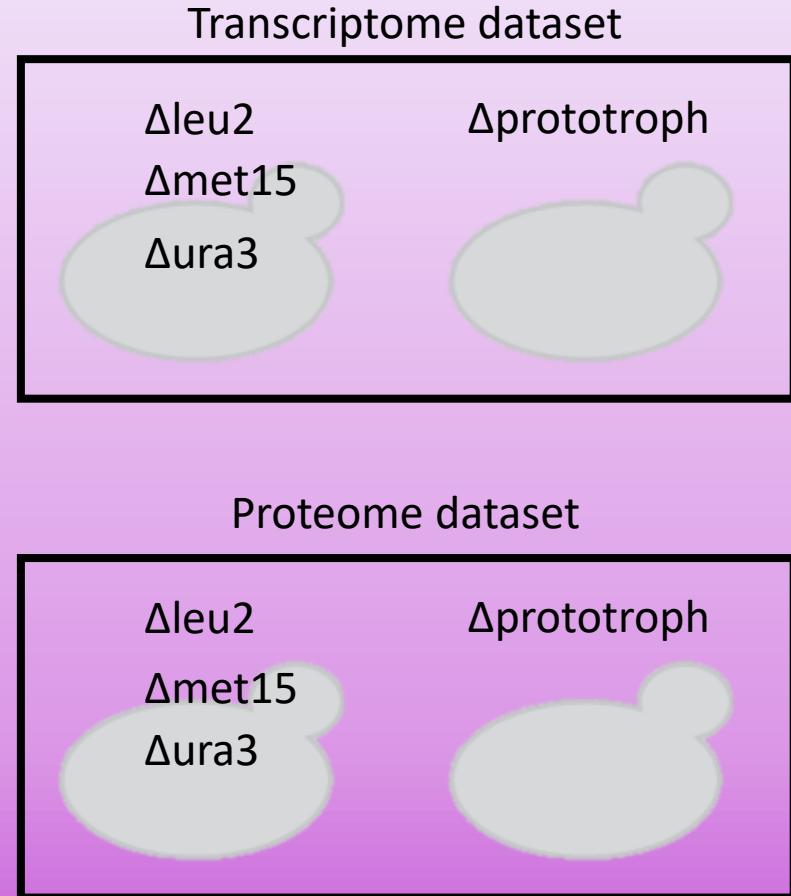
## Transcriptome (Score > 0.05)



## Proteome (Score > 0.05)



# Differential expression

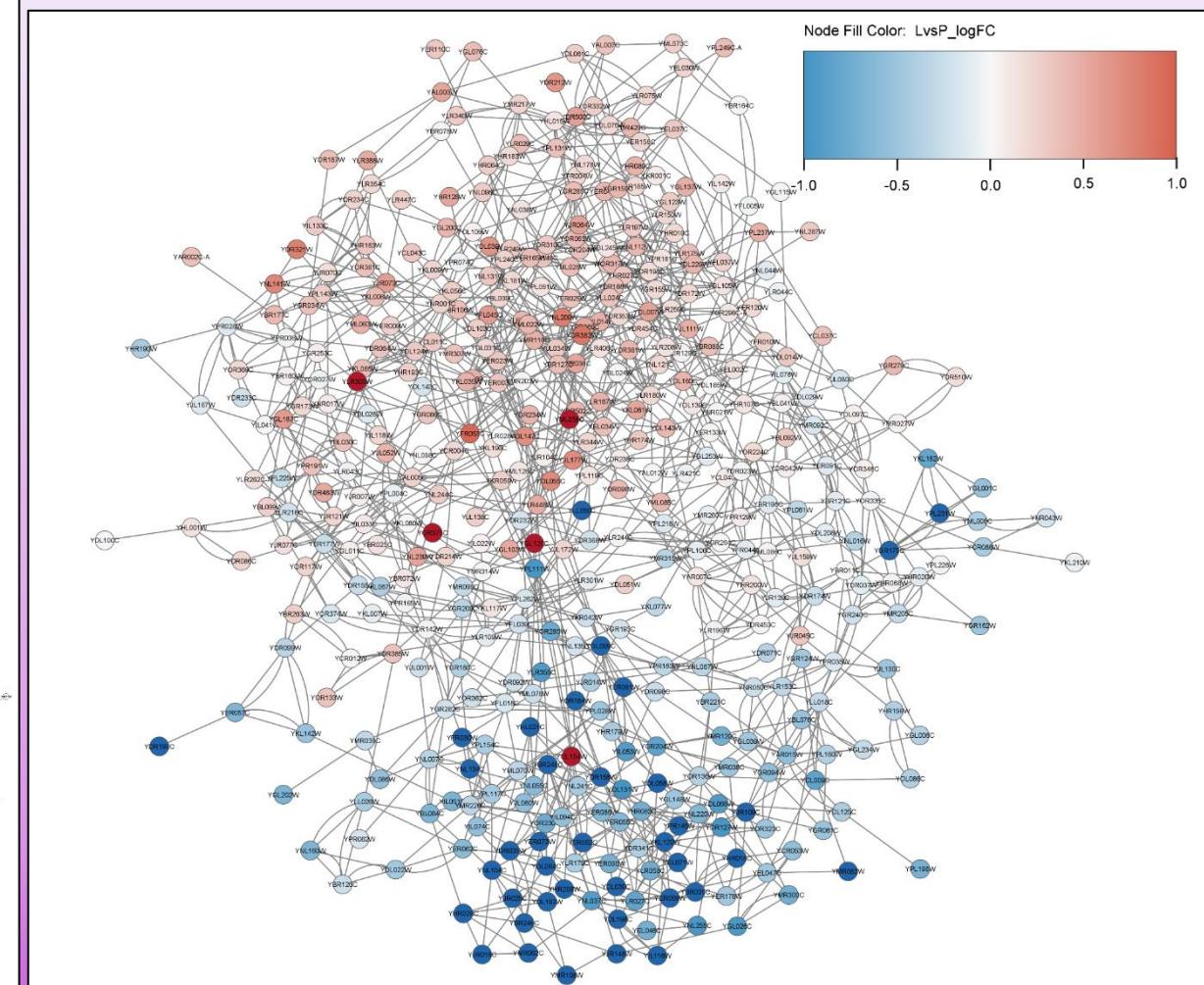
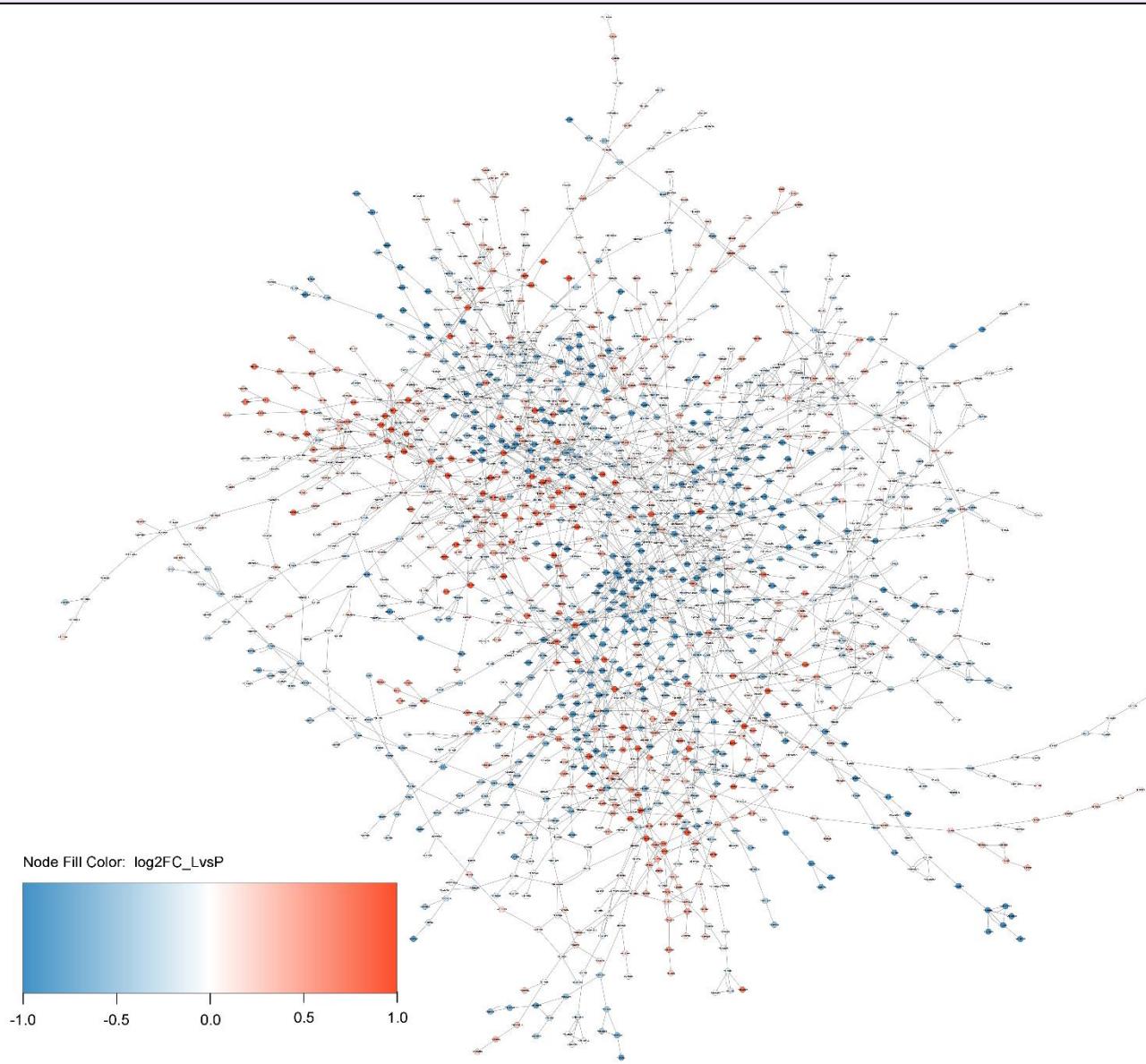


R  
DESeq2

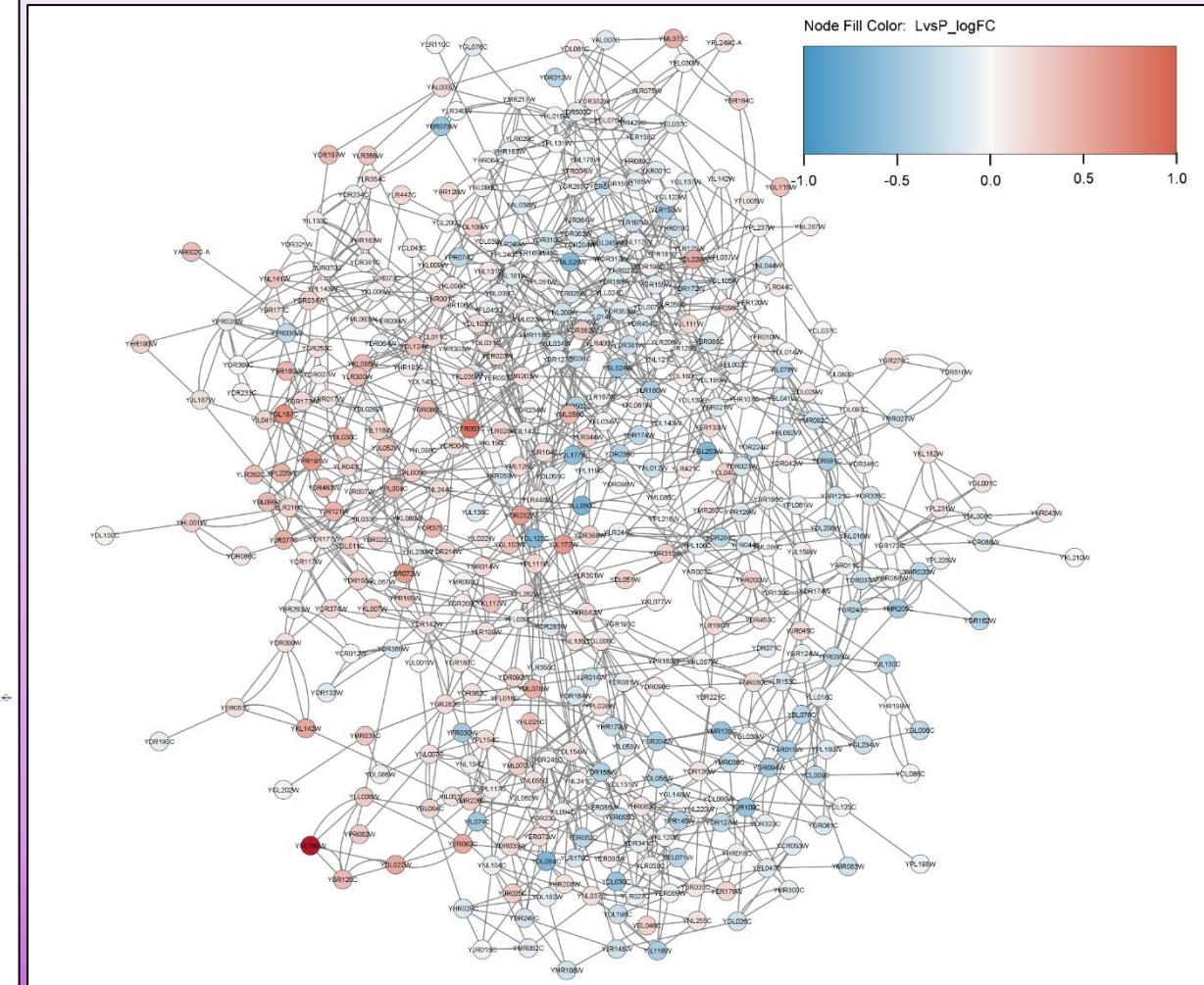
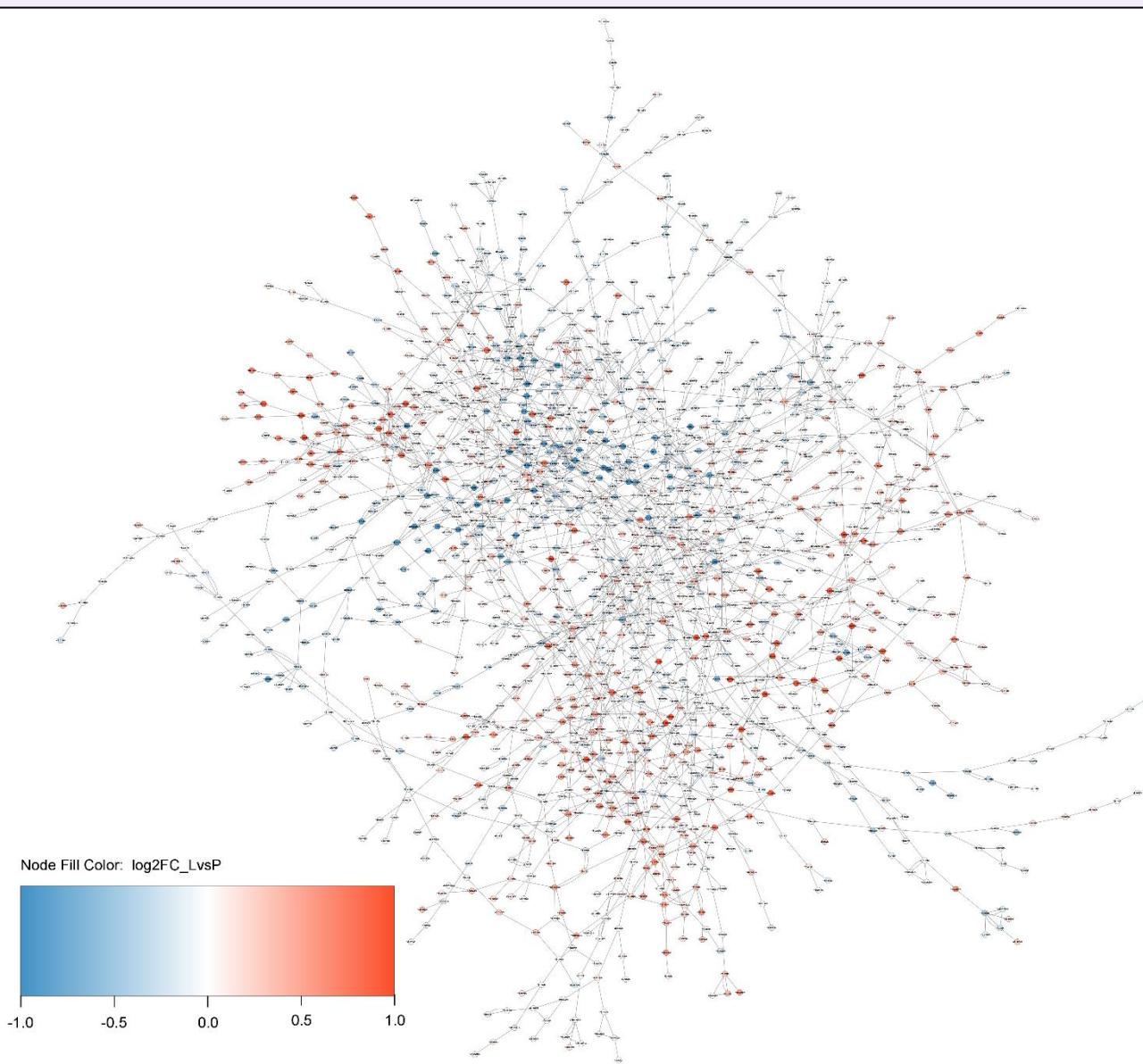
Transcriptome	Log2 fold change	Adjusted P-value

Proteome	Log2 fold change	Adjusted P-value

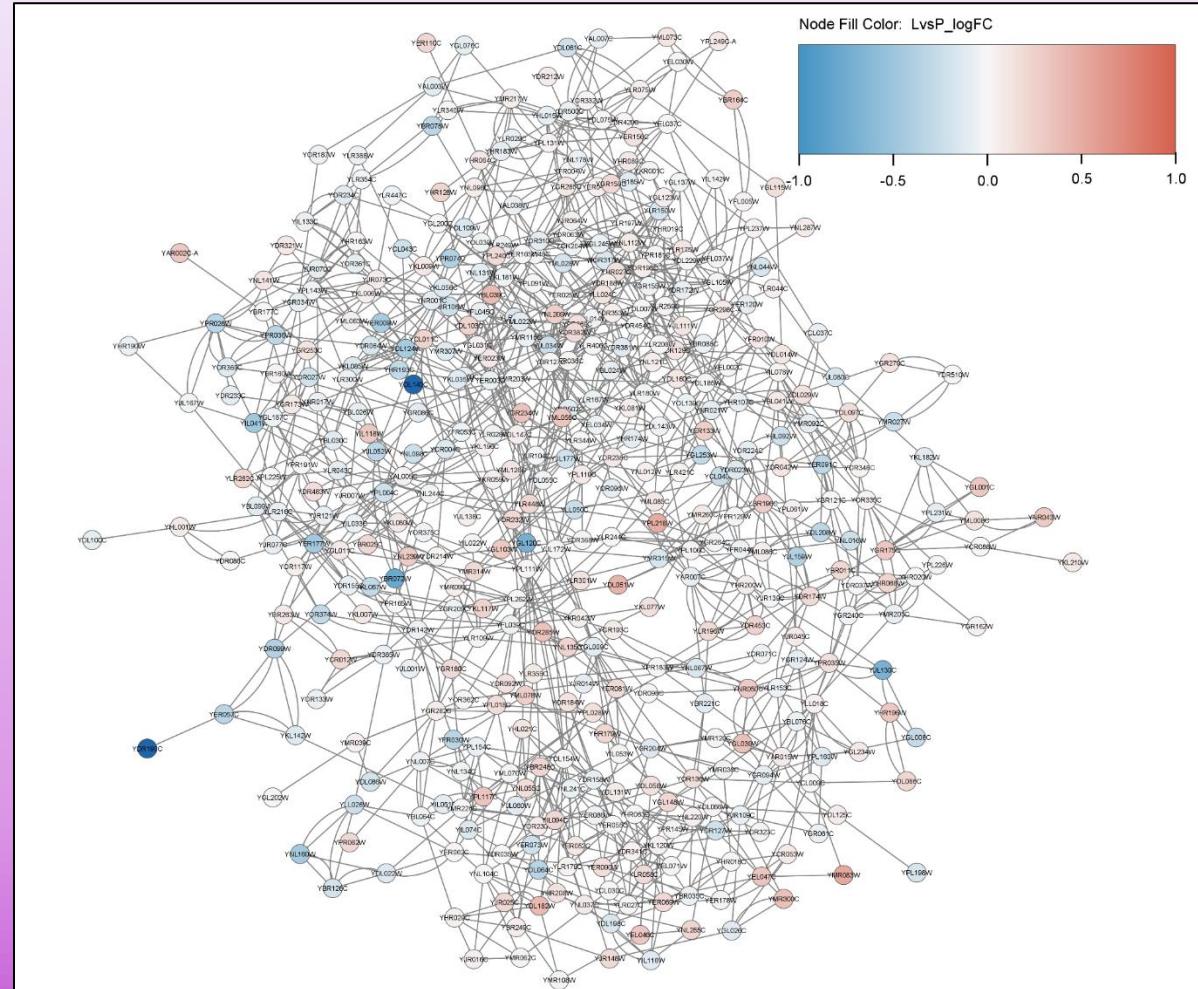
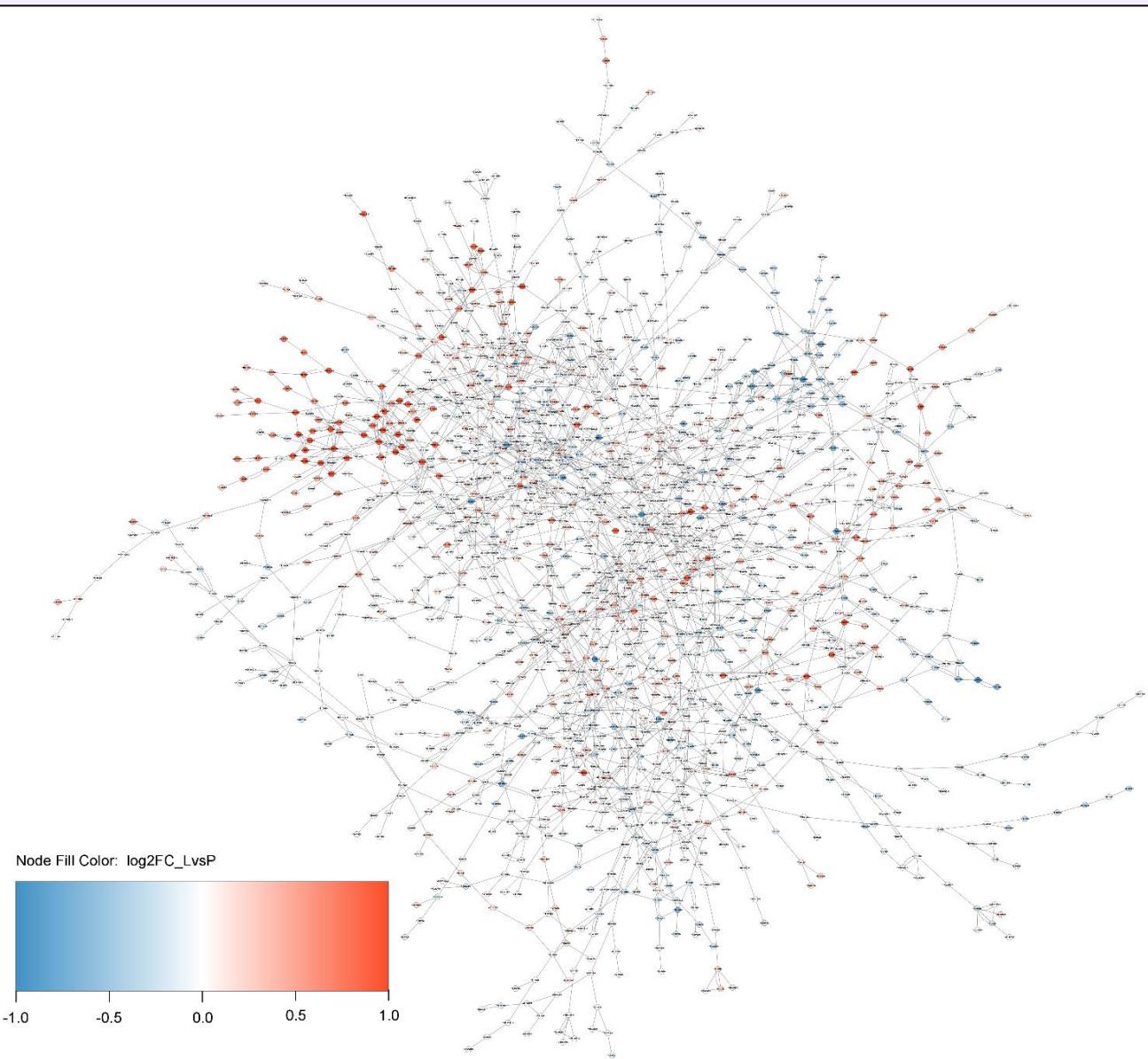
# Differential expression ( $\Delta$ leu2)



# Differential expression ( $\Delta$ met15)



# Differential expression ( $\Delta$ ura3)



# Differential expression ( $\Delta$ leu2)

## Transcriptome dataset

### Upregulated

#term ID	term description	observed gene count	background gene count	strength	false discovery rate
GO:0003735	Structural constituent of ribosome	116	220	0.44	3.45E-14
GO:0005198	Structural molecule activity	149	334	0.37	4.44E-14

### Downregulated

#term ID	term description	observed gene count	background gene count	strength	false discovery rate
GO:0016491	Oxidoreductase activity	131	333	0.25	2.44E-05
GO:0000981	DNA-binding transcription factor activity, RNA polymerase II-specific	60	134	0.31	0.0051
GO:0003700	DNA-binding transcription factor activity	69	167	0.27	0.0061
GO:0043169	Cation binding	242	821	0.13	0.0061
GO:0046872	Metal ion binding	238	814	0.12	0.0085

## Proteome dataset

### Upregulated

#term ID	term description	observed gene count	background gene count	strength	false discovery rate
GO:0005488	Binding	126	2877	0.25	1.72E-15
GO:1901363	Heterocyclic compound binding	101	1925	0.33	2.98E-15
GO:0097159	Organic cyclic compound binding	101	1936	0.33	3.03E-15
GO:0003723	RNA binding	57	669	0.54	1.04E-14
GO:0003735	Structural constituent of ribosome	33	220	0.79	9.89E-14

### Downregulated

#term ID	term description	observed gene count	background gene count	strength	false discovery rate
GO:0003824	Catalytic activity	121	2197	0.39	6.87E-29
GO:0016491	Oxidoreductase activity	45	333	0.78	4.49E-19
GO:0016614	Oxidoreductase activity, acting on ch-oh group of donors	20	82	1.03	1.77E-11
	Oxidoreductase activity, acting on the ch-oh group of donors, nad or nadp as acceptor	19	76	1.04	4.12E-11
GO:0036094	Small molecule binding	55	931	0.42	2.41E-09

# Differential expression ( $\Delta$ ura3)

## Transcriptome dataset

### Upregulated

#term ID	term description	observed gene count	background gene count	strength	false discovery rate
GO:0005215	Transporter activity	85	386	0.3	1.18E-05
GO:0015075	Ion transmembrane transporter activity	63	260	0.34	1.18E-05
GO:0015144	Carbohydrate transmembrane transporter activity	20	33	0.74	1.18E-05
GO:0015291	Secondary active transmembrane transporter activity	33	89	0.53	1.18E-05
GO:0015293	Symporter activity	23	46	0.66	1.18E-05

## Proteome dataset

### Upregulated

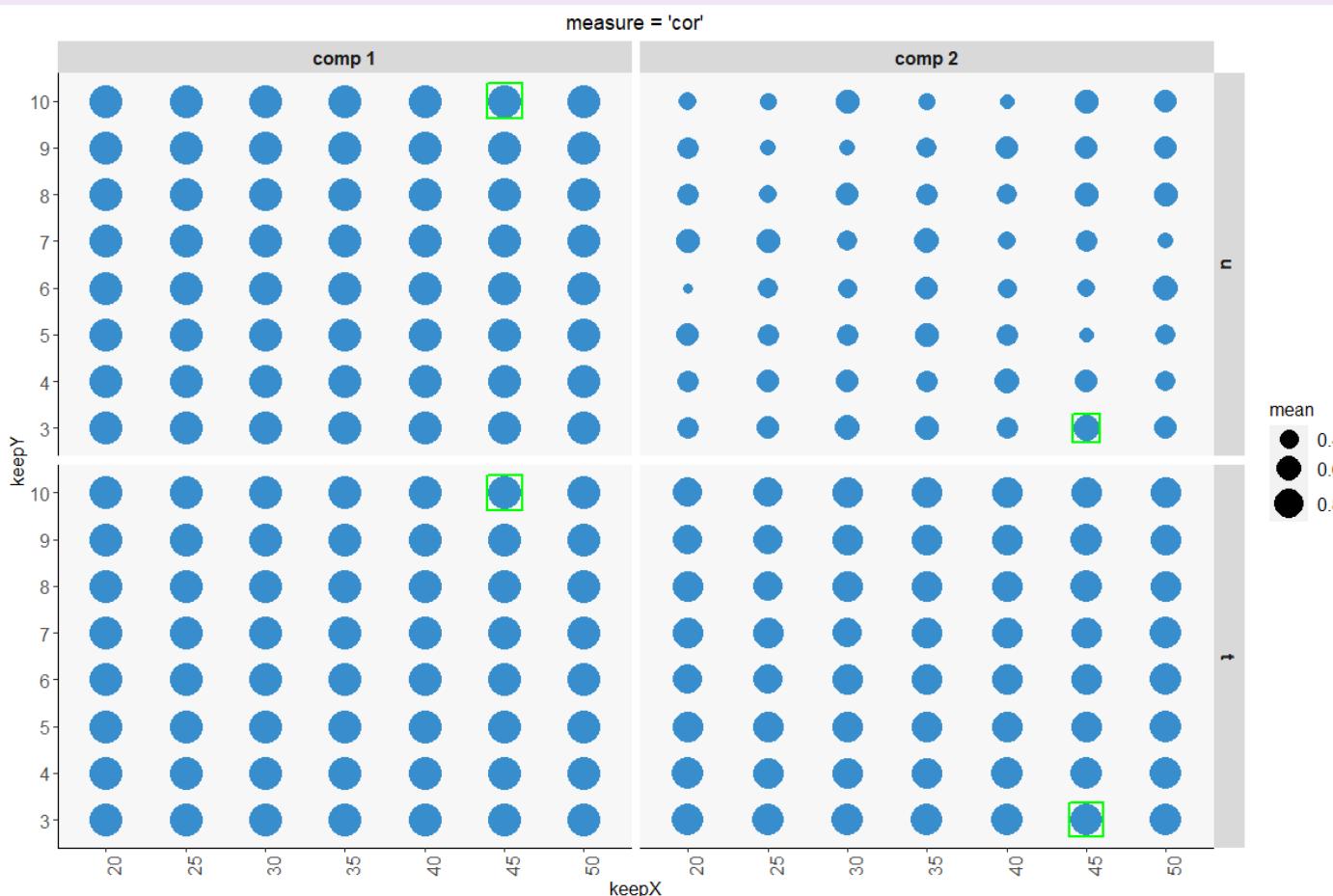
#term ID	term description	observed gene count	background gene count	strength	false discovery rate
GO:0003824	Catalytic activity	35	2197	0.36	3.74E-06
GO:0016491	Oxidoreductase activity	14	333	0.79	2.67E-05
GO:0016616	Oxidoreductase activity, acting on the ch-oh group of donors, nad or nadp as acceptor	6	76	1.06	0.008

### Downregulated

### Downregulated

#term ID	term description	observed gene count	background gene count	strength	false discovery rate
GO:0016903	Oxidoreductase activity, acting on the aldehyde or oxo group of donors	4	24	1.38	0.0486

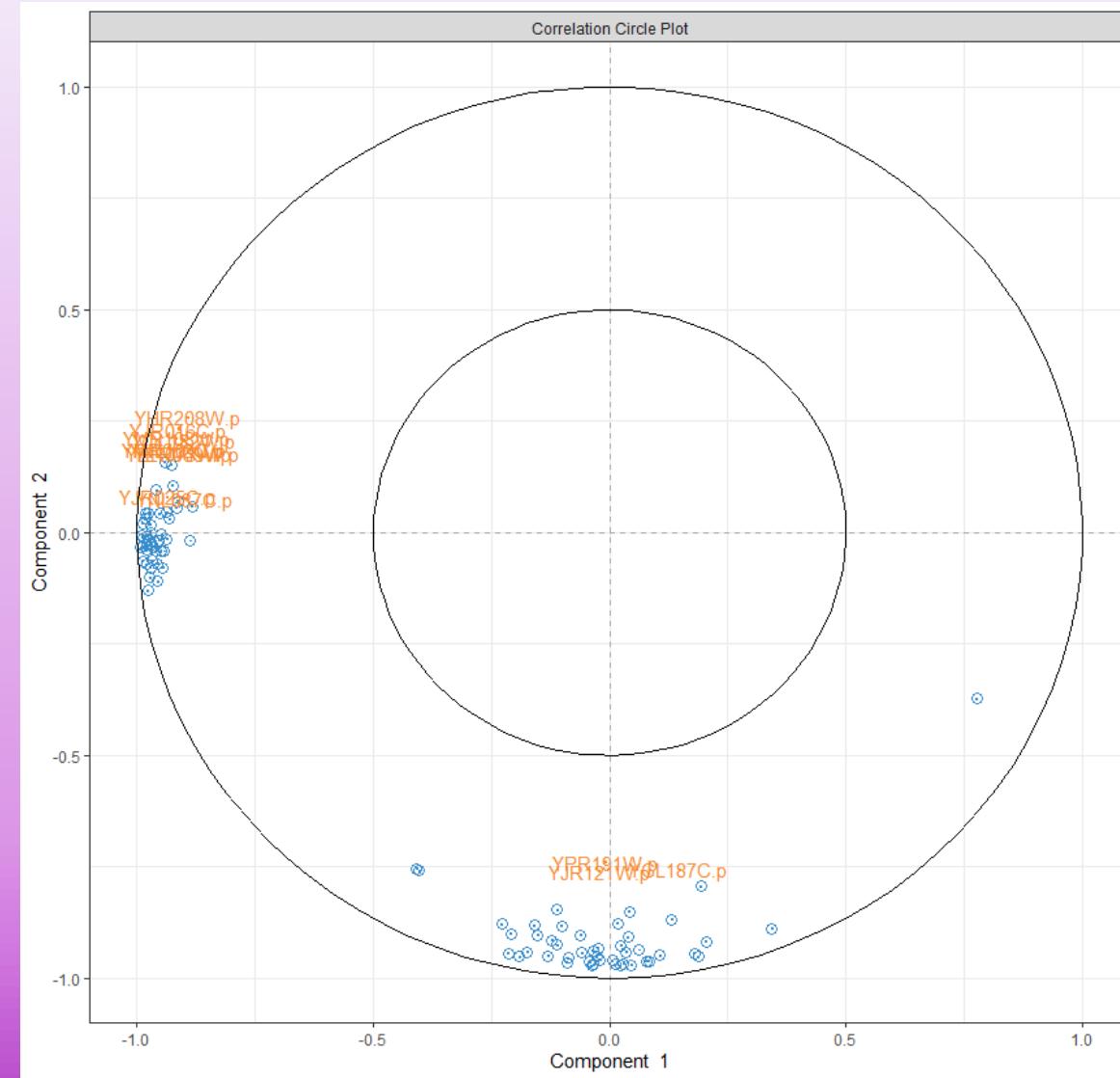
# Transcriptome-proteome integration (sPLS)



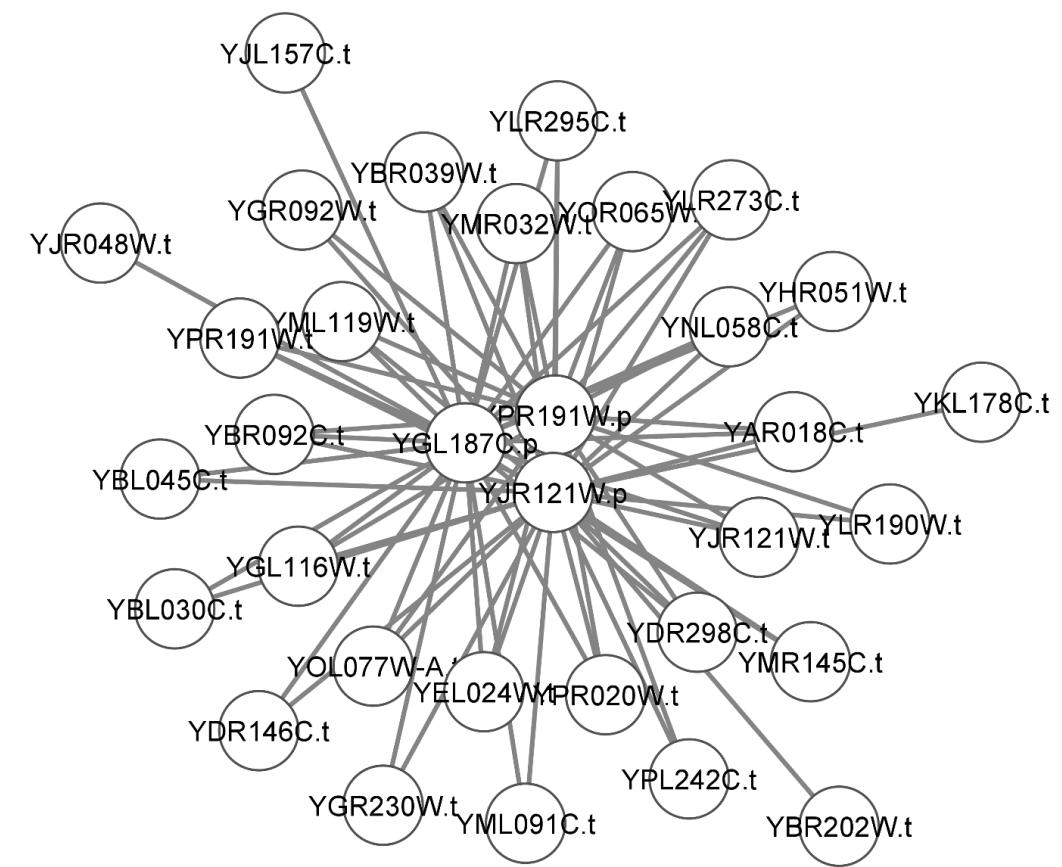
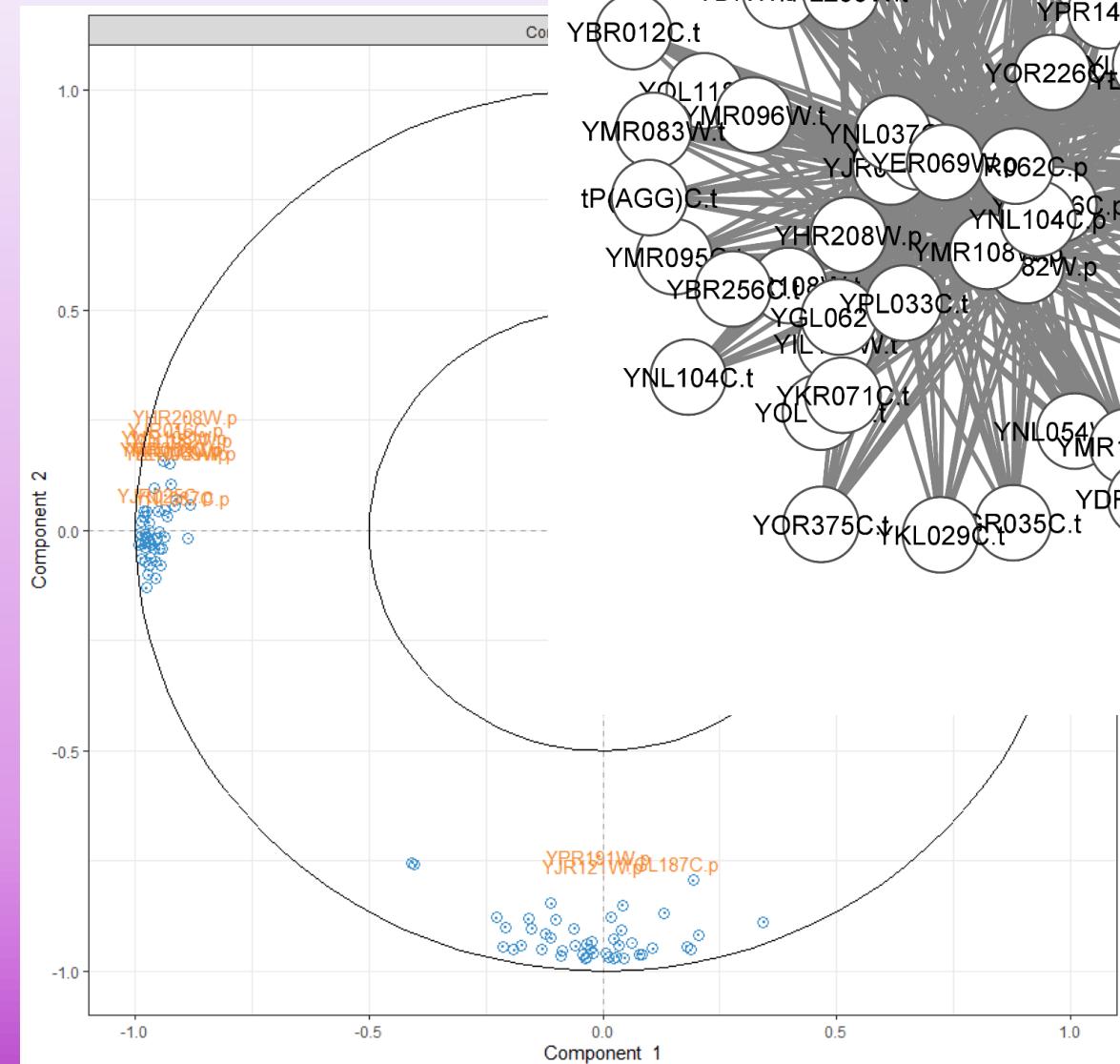
90 transcriptome × 13 proteome

	YJR121W.p	YGL187C.p	YNL104C.p	YPR191W.p	YMR108W.p	YNL037C.p	YHR208W.p	YJR016C.p
YAR018C	0.7393516	0.7377326	0.0000000	0.7195658	0.0000000	0.0000000	0.0000000	0.0000000
YBL030C	0.7095500	0.7004595	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000
YBL045C	0.7142865	0.7395548	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000
YBR012C	0.0000000	0.0000000	0.8565782	0.0000000	0.8593294	0.8393396	0.8379642	0.8567225
YBR039W	0.7307002	0.7265352	0.0000000	0.7109430	0.0000000	0.0000000	0.0000000	0.0000000
YBR047W	0.0000000	0.0000000	0.8937854	0.0000000	0.8982024	0.8691230	0.8791360	0.8967335
YBR092C	0.7350846	0.7348697	0.0000000	0.7155235	0.0000000	0.0000000	0.0000000	0.0000000
YBR202W	0.7200169	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000
YBR256C	0.0000000	0.0000000	0.8731556	0.0000000	0.8736136	0.8657130	0.8469902	0.8690575
YDL151C	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000
YDR146C	0.7188469	0.7038841	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000	0.0000000
YDR158W	0.0000000	0.0000000	0.8914577	0.0000000	0.8932815	0.8780047	0.8689119	0.8897273
YDR170W-A	0.0000000	0.0000000	0.8882012	0.0000000	0.8898861	0.8753680	0.8653315	0.8862380
YDR298C	0.7296843	0.7384806	0.0000000	0.7109799	0.0000000	0.0000000	0.0000000	0.0000000

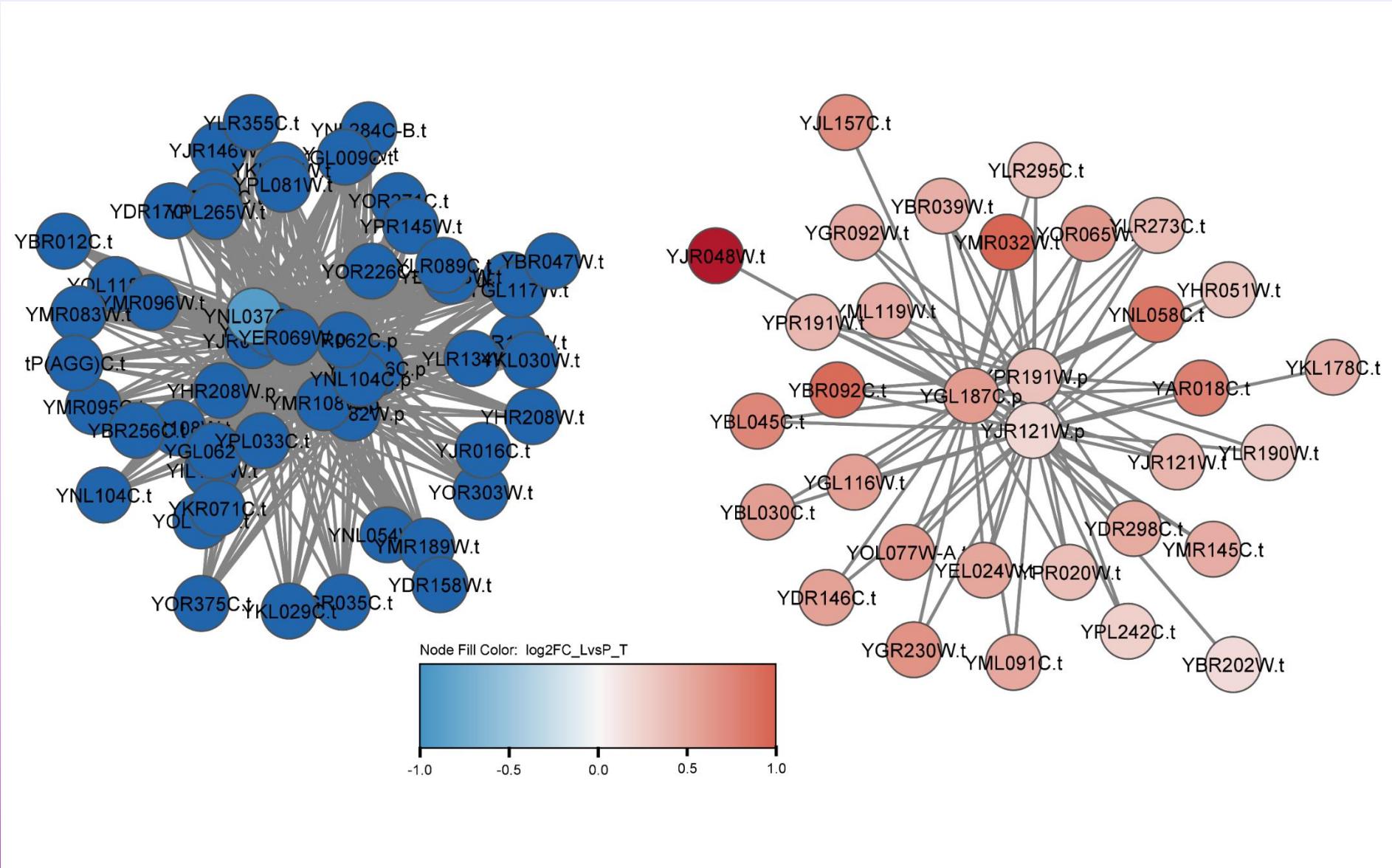
# Network



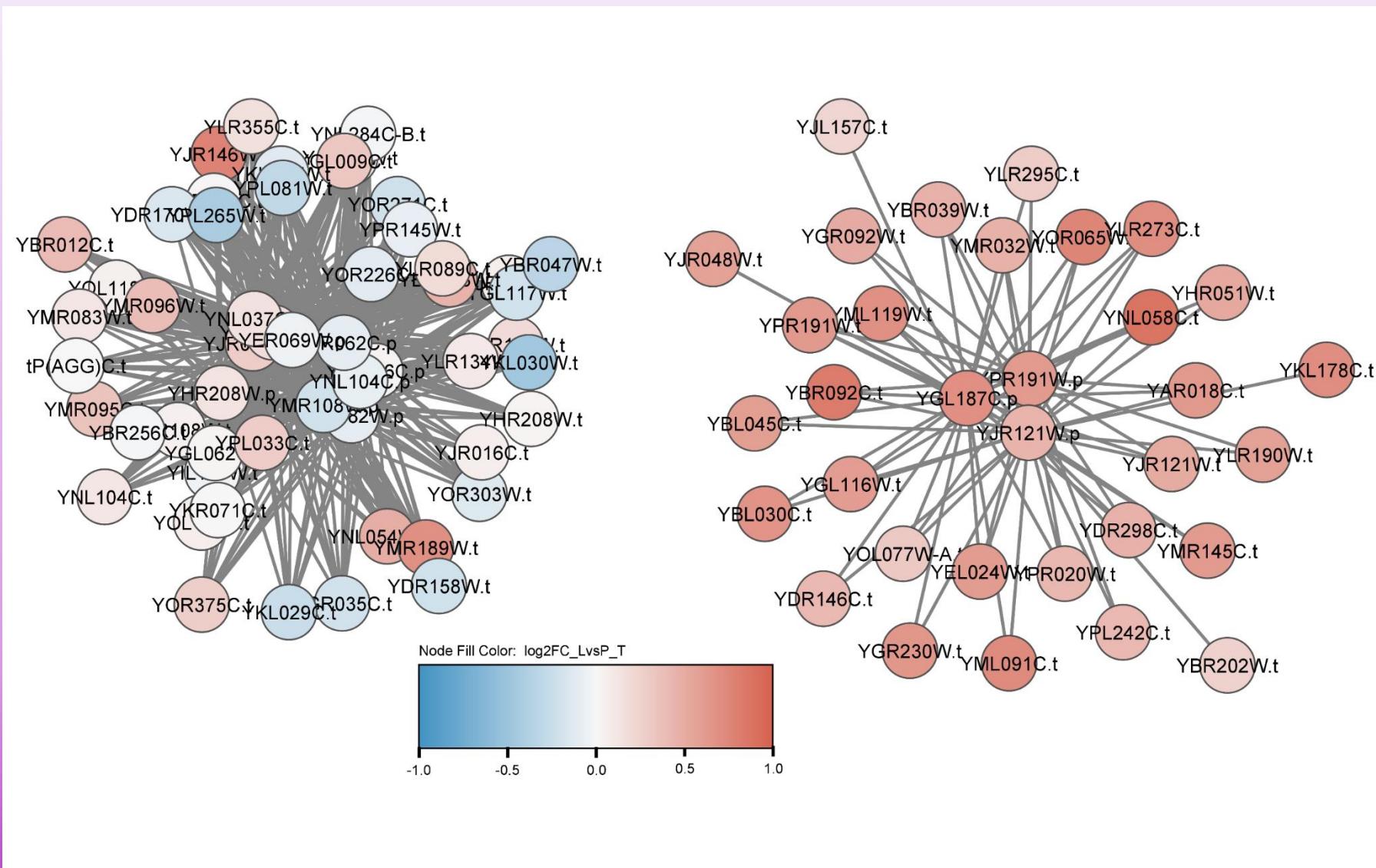
# Network



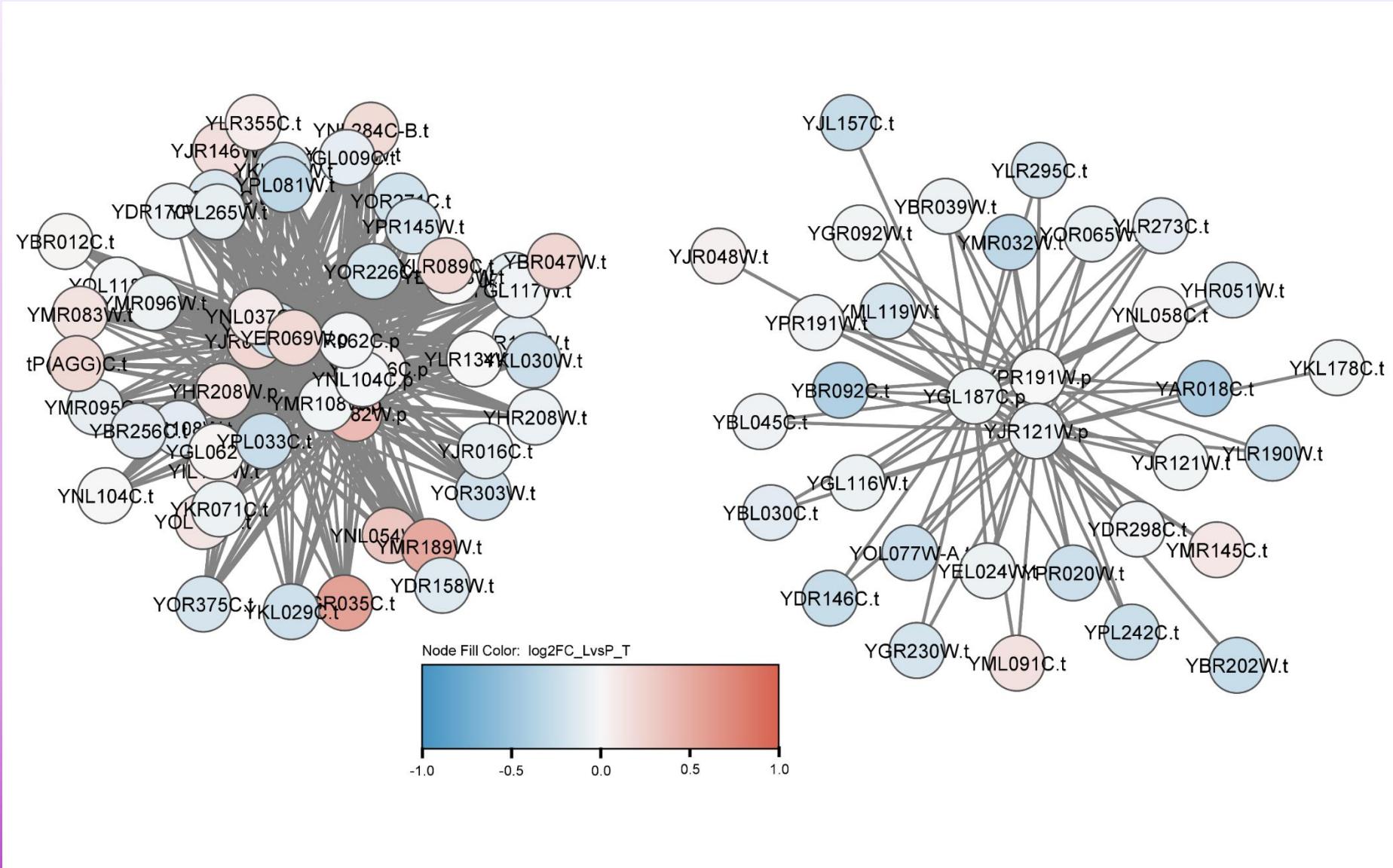
# Differential expression ( $\Delta$ leu2)



# Differential expression ( $\Delta\text{met15}$ )



# Differential expression ( $\Delta$ ura3)



# Conclusion

- Compared to prototroph, the  $\Delta$ leu2 auxotroph showed the most distinguishable properties, followed by  $\Delta$ met15 and  $\Delta$ ura3
- Integration of transcriptomic and proteomic dataset selects features from the two datasets to distinguish the classes

# Reference

- [1] M. T. Alam, A. Zelezniak, M. Mülleder, P. Shliaha, R. Schwarz, F. Capuano, J. Vowinckel, E. Radmaneshfar, A. Krüger, E. Calvani, S. Michel, S. Börno, S. Christen, K. R. Patil, B. Timmermann, K. S. Lilley and M. Ralser. *The metabolic background is a global player in *Saccharomyces* gene expression epistasis*, Nature Microbiology.
- [2] S. v. Dam, U. Vosa, A. v. d. Graaf, L. Franke, and J. P. d. Magalhaes. *Gene co-expression analysis for functional classification and gene–disease predictions*, Briefings in Bioinformatics.