FROM SOCIAL TO MOLECULAR NETWORKS: EXTRACTING INFORMATION FROM THE INTERACTION IN BIOLOGICAL SYSTEMS

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Introduction and objectives

The understanding of complex biological systems requires the integration of experimental and computational research, namely a Systems Biology approach [1]. An elegant way for the representation of the relationship between biological molecules in Systems Biology is the use of networks, since this resource helps to represent different interactions among the molecules involved in representative biological processes such as those happening in the so-called *disease state* [2]. It is well known how difficult is to extract information from complex systems but, with the development of friendly computational approaches to deal with genomic and proteomic datasets, building and analyzing biological networks is now a tractable exercise [3], also applicable to investigate social media.

We studied eight complex disorders following a Systems Biology approach: Alzheimer disease, Alport syndrome, Amyotrophic Lateral Sclerosis (ALS), Asperger syndrome, depressive disorder, parasomnia, stomach neoplasms, and Tourette syndrome.

Our purpose was to detect the biological processes underlying these pathologies and to find highly connected genes that could be proposed as molecular targets in Biomedicine.

Methods

Getting data from public databases
https://phgkb.cdc.gov/HuGENavigator

Bibliometric mapping
https://www.vosviewer.com/

Obtaining molecular interactions
http://string-db.org

Network construction and analysis
http://www.cytoscape.org

Functional enrichment analysis
https://david.ncifcrf.gov

Results

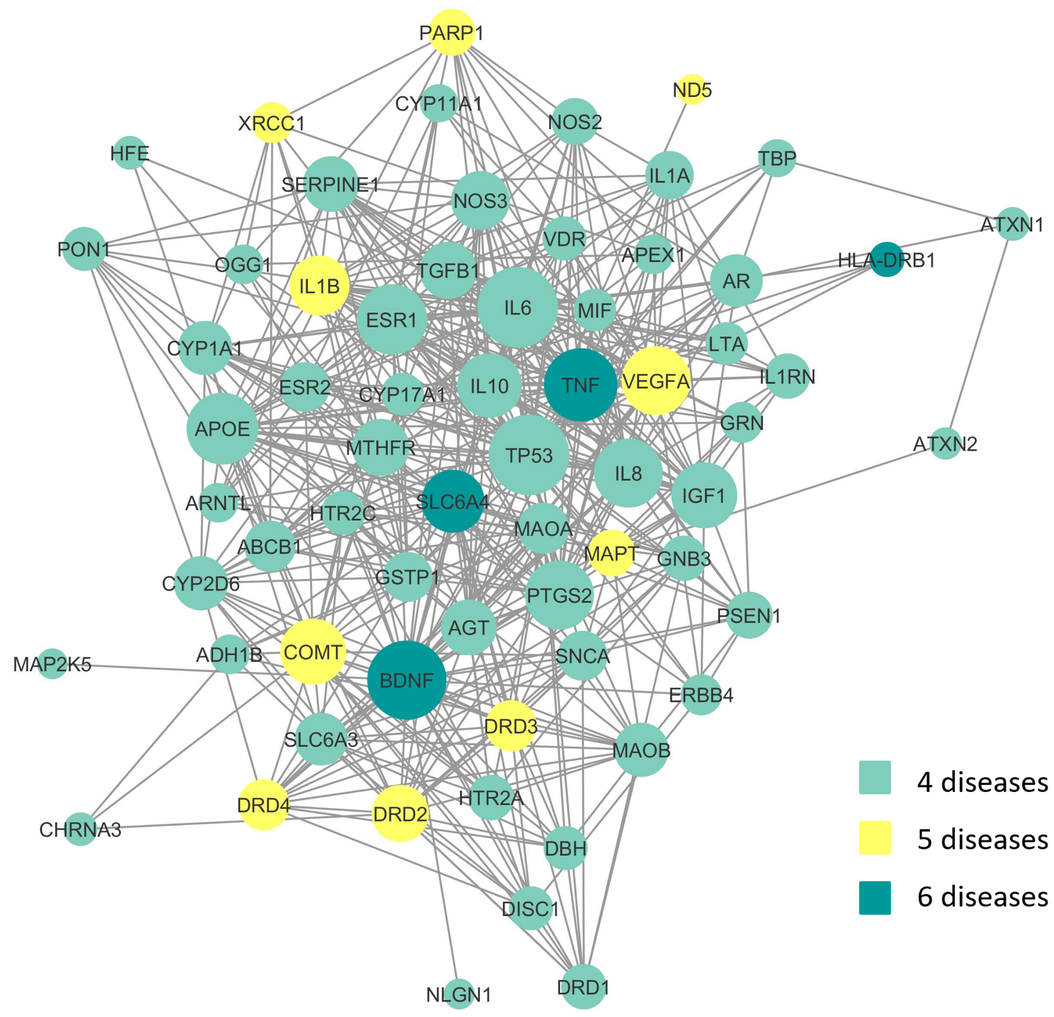

Figure 1. Network showing the 66 genes shared among four or more diseases. It has been built using Cytoscape v 3.6.0. Note that the size of the nodes increases as the *degree* does.

Table 1. Gene ontology analysis showing the main biological processes (BP), cellular components (CC) and molecular functions (MF) the most representative genes are enriched in.

Category	Item	Genes involved	FDR
BP	Response to drug	*IL6, DRD1, PTGS2, DRD3, CYP1A1, DRD2, SLC6A3, MAOB, SLC6A4, SNCA, ABCB1, COMT, XRCC1, IL10, TGFB1, MTHFR, OGG1, APEX1, HTR2C, LTA, HTR2A*	1.18E-16
	Dopamine catabolic process	*SLC6A3, MAOA, MAOB, COMT, DBH*	1.59E-06
	Regulation of transcription	*IL6, AR, TNF, ERBB4, ESR1, TP53, IGF1, TBP, ESR2, ARNTL, IL10, TGFB1, PSEN1, AGT, IL1B*	1.07E-05
	Aging	*IL6, CYP1A1, AGT, SLC6A3, SNCA, OGG1, APEX1, TGFB1, IL10, HTR2A*	1.98E-05
	Response to hypoxia	*MTHFR, CYP1A1, DRD2, ND5, SLC6A4, VEGFA, NOS2, XRCC1, TGFB1, LTA*	2.85E-05
CC	Extracellular space	*IL6, TNF, IL1RN, SNCA, NLGN1, HFE, IGF1, DBH, IL10, TGFB1, MIF, APOE, AGT, GRN, SERPINE1, VEGFA, PON1, IL1B, IL1A, GSTP1, LTA*	2.13E-05
	Axon	*CYP17A1, PSEN1, DRD2, MAPT, SLC6A3, SNCA, COMT, TGFB1, DISC1, HTR2A*	9.49E-05
MF	Cytokine activity	*IL6, TNF, GRN, VEGFA, IL1RN, IL1B, TGFB1, IL10, IL1A, LTA, MIF*	2.00E-06
	Drug binding	*DRD3, DRD2, SLC6A3, DRD4, CYP2D6, HTR2C, GSTP1, HTR2A*	2.38E-05

FDR: *False Discovery Rate*.

Conclusions

Systems Biology is a powerful tool to understand the molecular complexity underlying the *disease state* and it could be applied in the research of biomarkers and pharmacological targets. The representation of the molecular interactions using networks is a useful way to unravel the hidden connections between relevant genes.

Acknowledgements / Funding

References

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[3] Miryala SK et al. *Gene*. 2018; 642: 84-94.