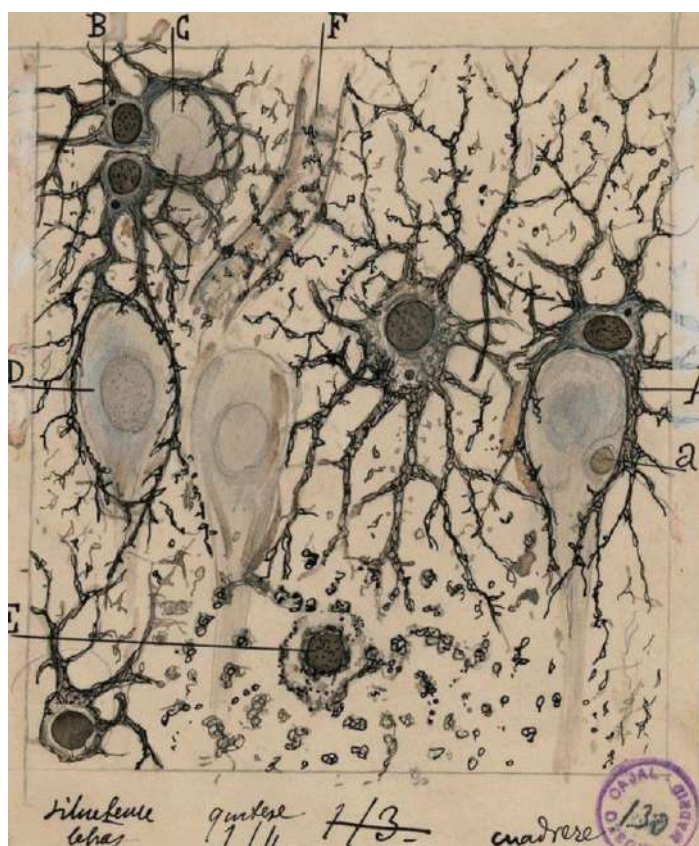# Integrative Analysis of Transcriptomics and Proteomics Data in the Astrocytes

Dr. Viktorian Miok

Postdoctoral fellow
Institute for Diabetes and Obesity
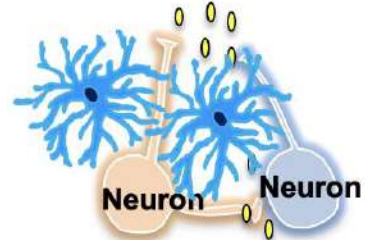Helmholtz Diabetes Center

Astrocytes

Cajal's drawing showing "neuroglia" (Cajal Institute, Madrid, Spain)
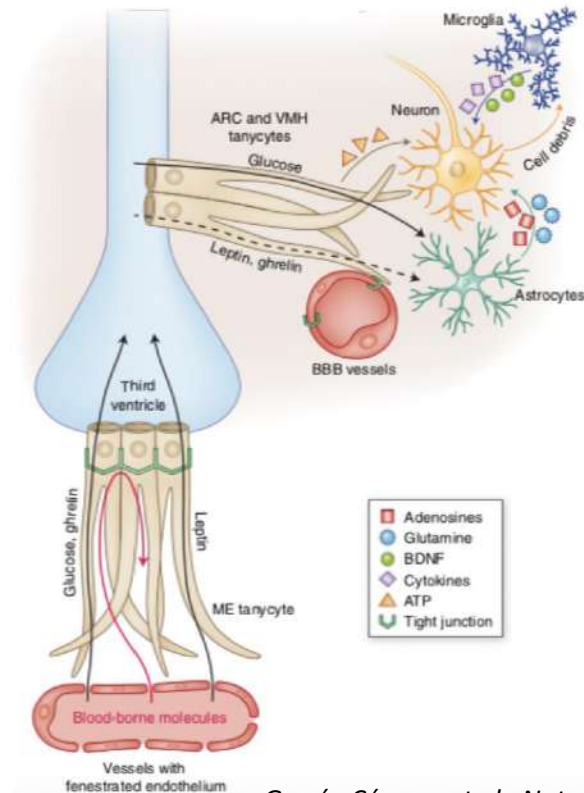*Ramón y Cajal, Nobel Prize in Medicine with Camillo Golgi in 1906*
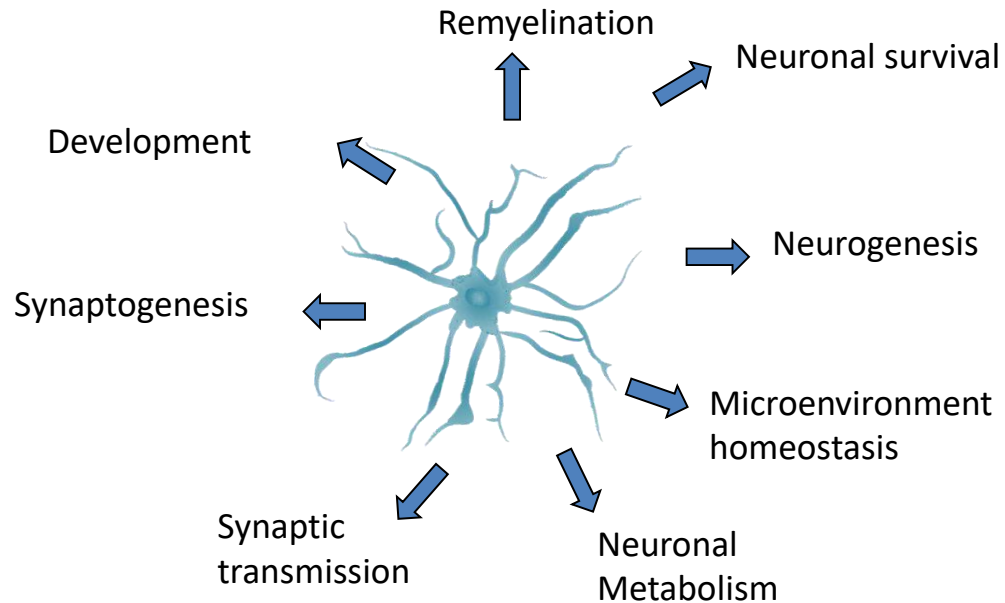

"Neurocentric View"

"Multipartite Synapsis View"

Neuron-Neuron crosstalk

Astrocyte-Neuron crosstalk

Neuron   Neuron

Neuron   Neuron

Microglia

ARC and VMH tanycytes
Glucose

Neuron

Cell debris

Leptin, ghrelin

Astrocytes

BBB vessels

Third ventricle

Glucose, ghrelin

Leptin

ME tanycyte

	Adenosines
	Glutamine
	BDNF
	Cytokines
	ATP
	Tight junction

Blood-borne molecules

Vessels with fenestrated endothelium

García-Cáceres et al., Nature Neuroscience 2019

Functions of the Astrocytes

Remyelination

Neuronal survival

Development

Neurogenesis

Synaptogenesis

Microenvironment
homeostasis

Synaptic
transmission

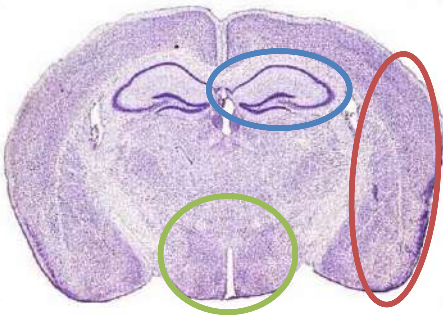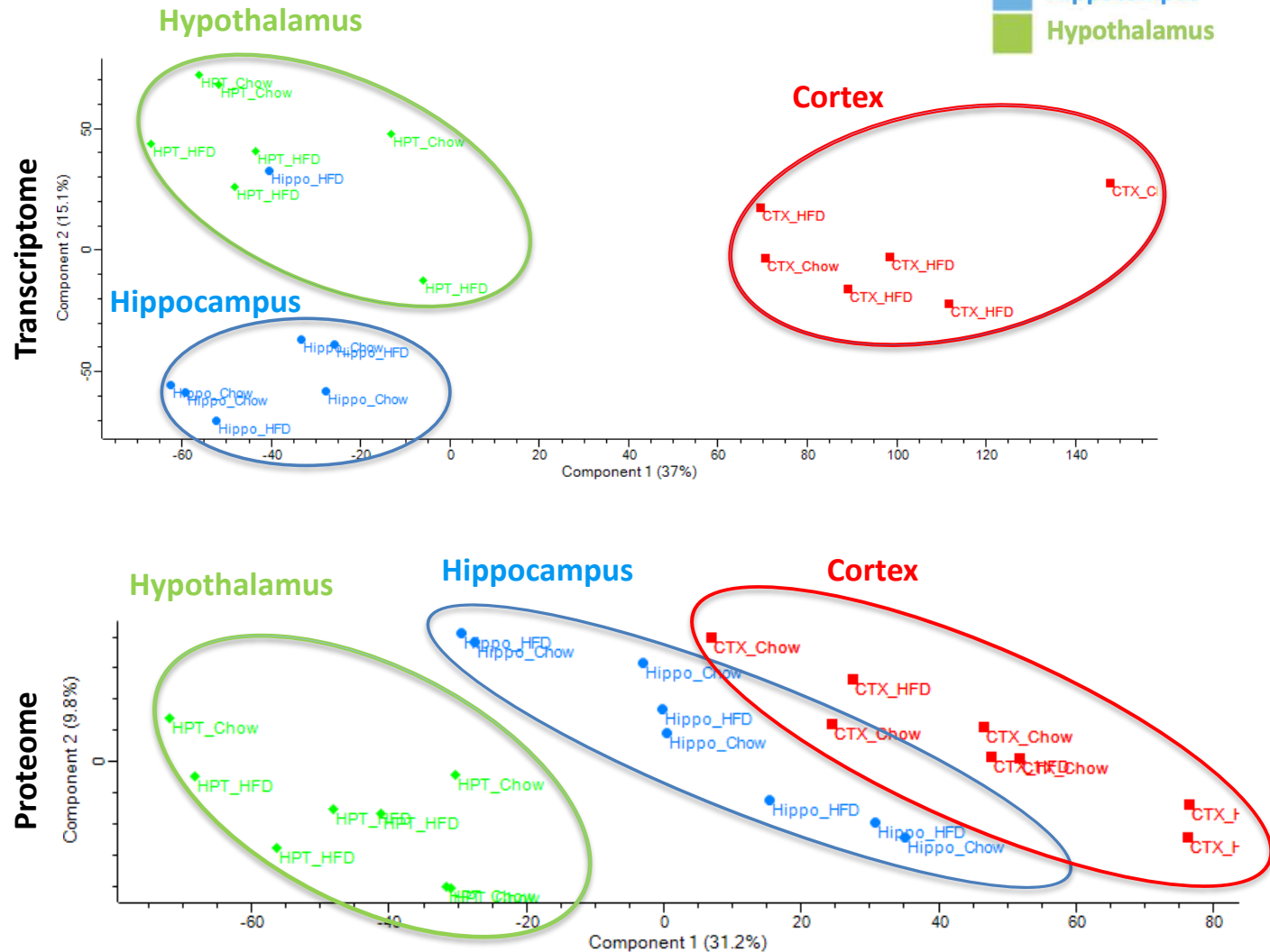Neuronal
Metabolism

Questions:

Are astrocytes a heterogeneous cellular population?

How astrocytes from different location in the brain respond to the
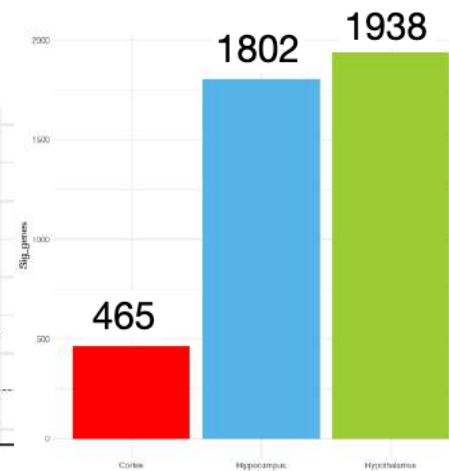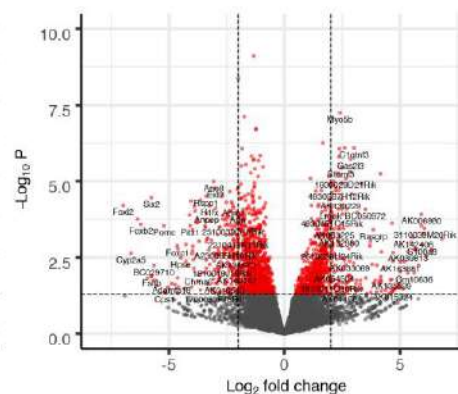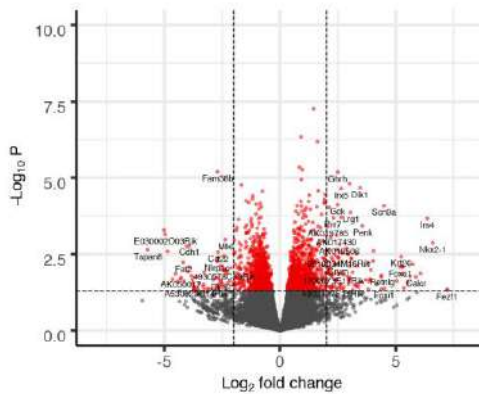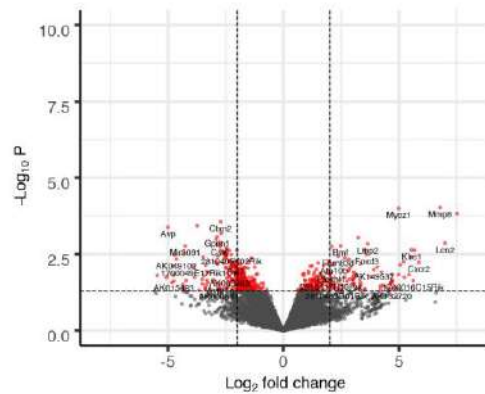hypercaloric diet?

Heterogeneity in the Brain Areas

- Astrocytes are isolated using ACSA-2 antibody and MACS sorting

- Astrocytes are measured at transcriptome and proteome levels
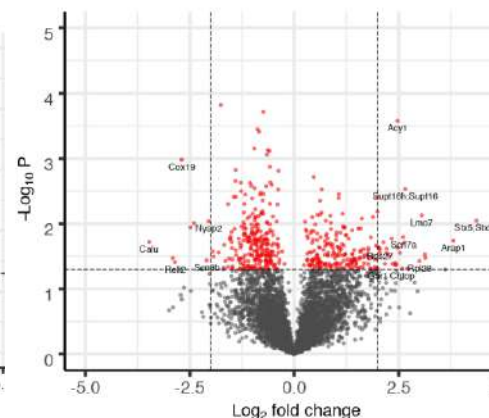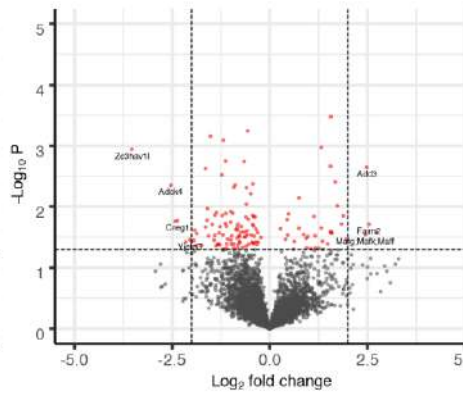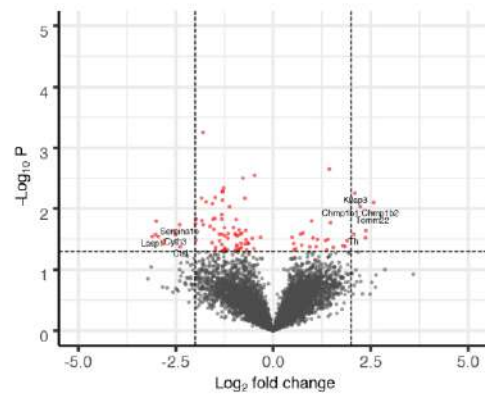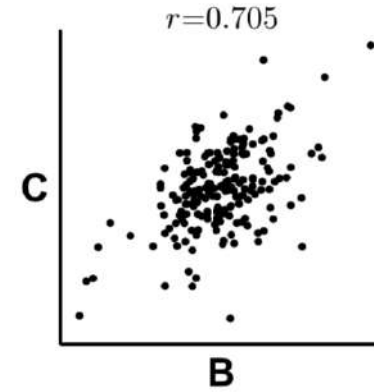
Quantitative Effect of a Diet

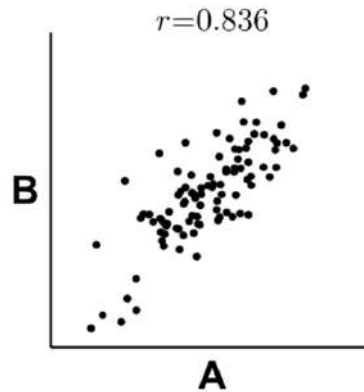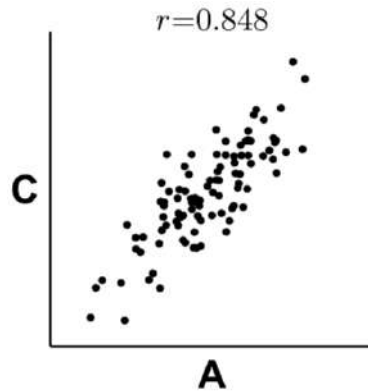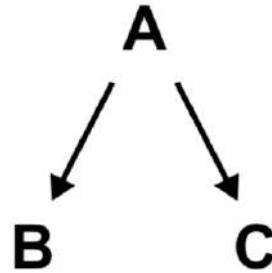## Transcriptome
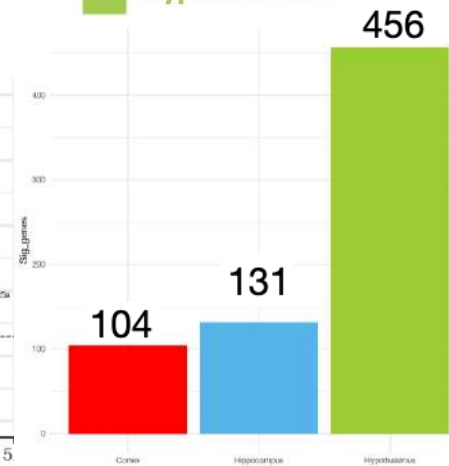
Proteome

Integration of Transcriptomics and Proteomics Data
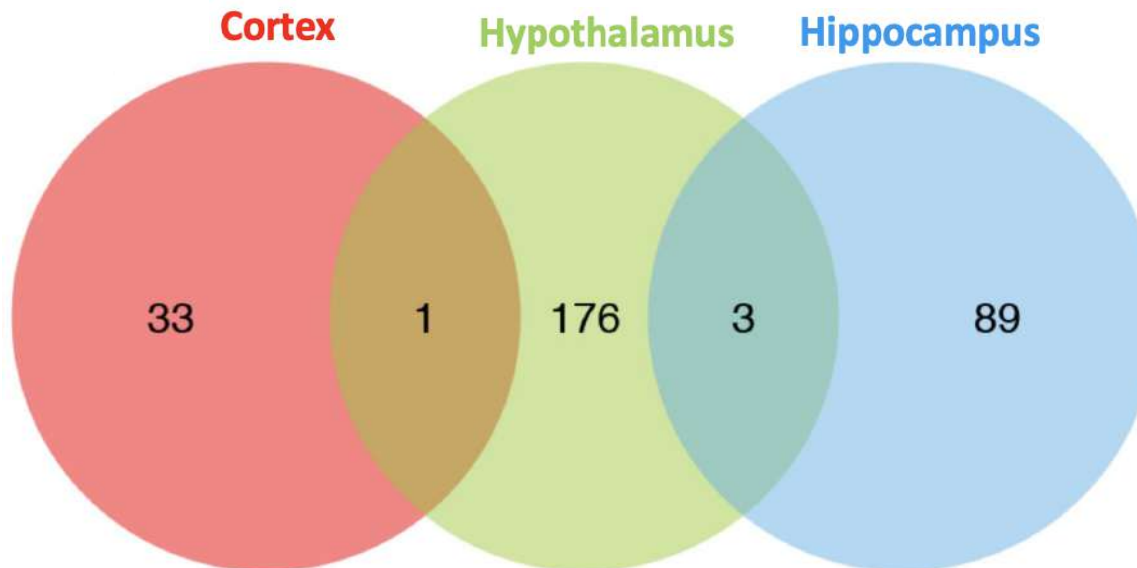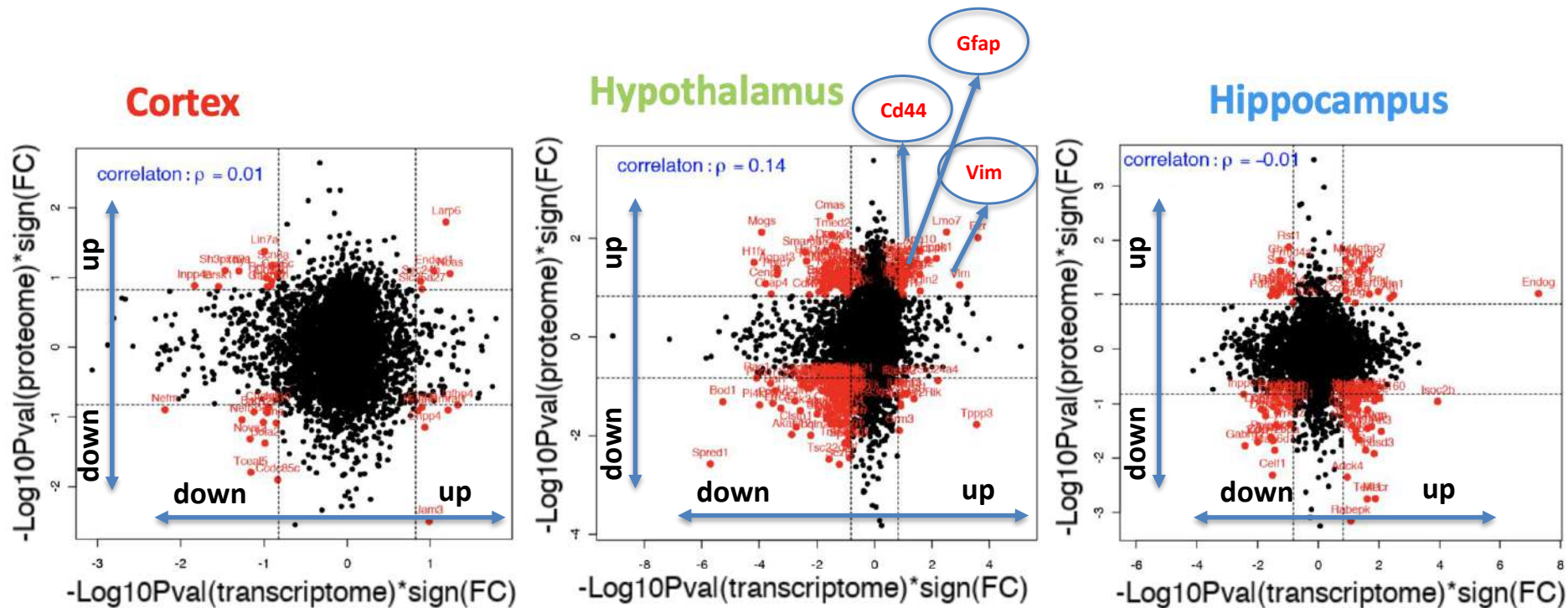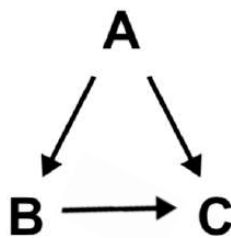
Correlation vs. Partial Correlation

True relationship

Correlation Matrix
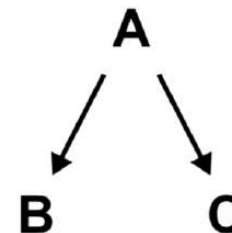
```
        A      B      C
A  1.000  0.848  0.836
B  0.848  1.000  0.705
C  0.836  0.705  1.000
```
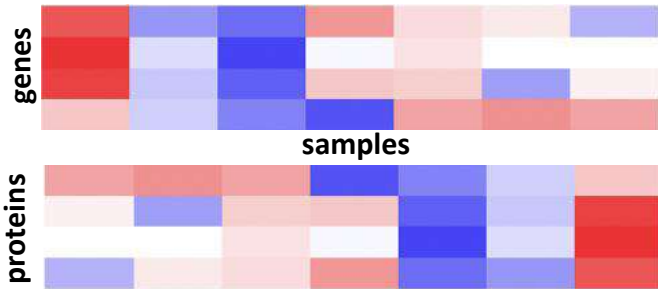
Partial Correlation Matrix

```
        A      B      C
A  1.000  0.848  0.836
B  0.848  1.000  0.000
C  0.836  0.000  1.000
```
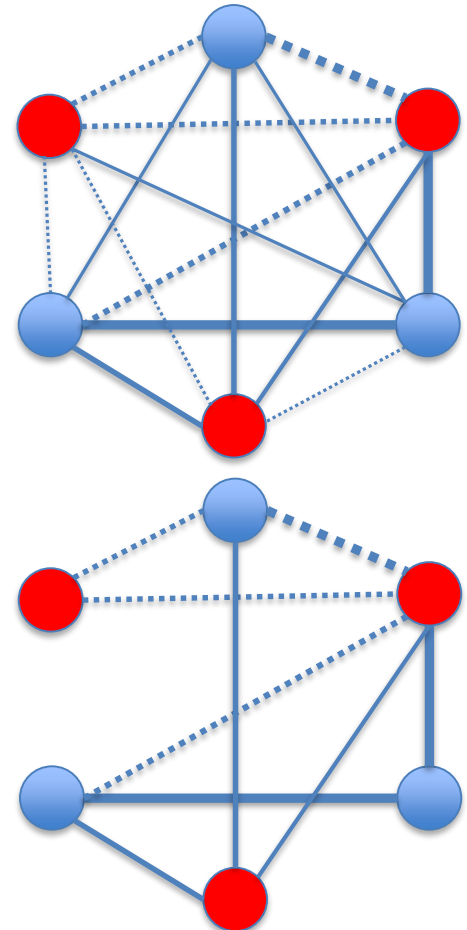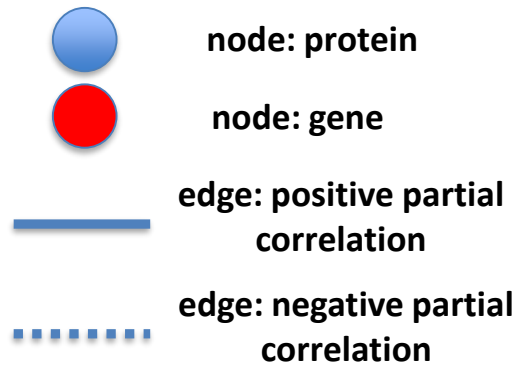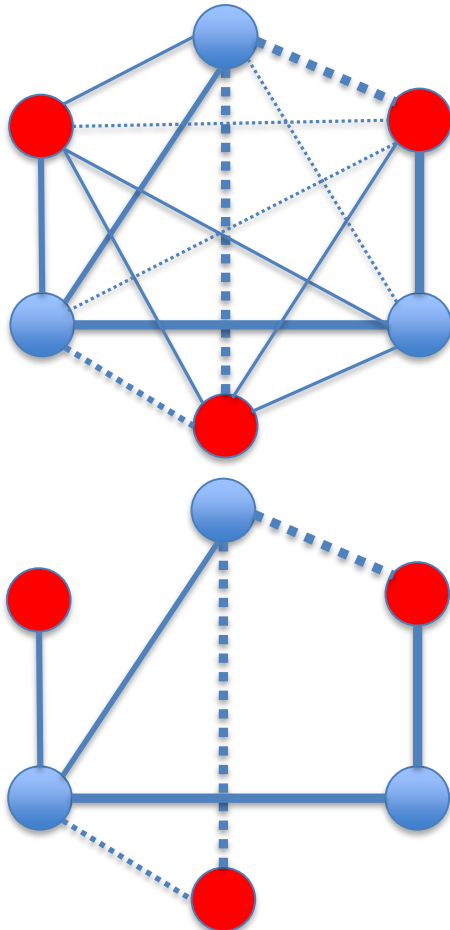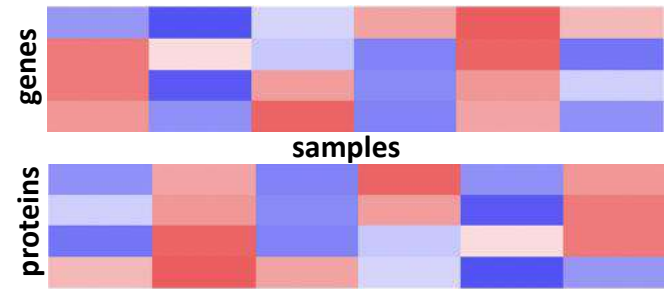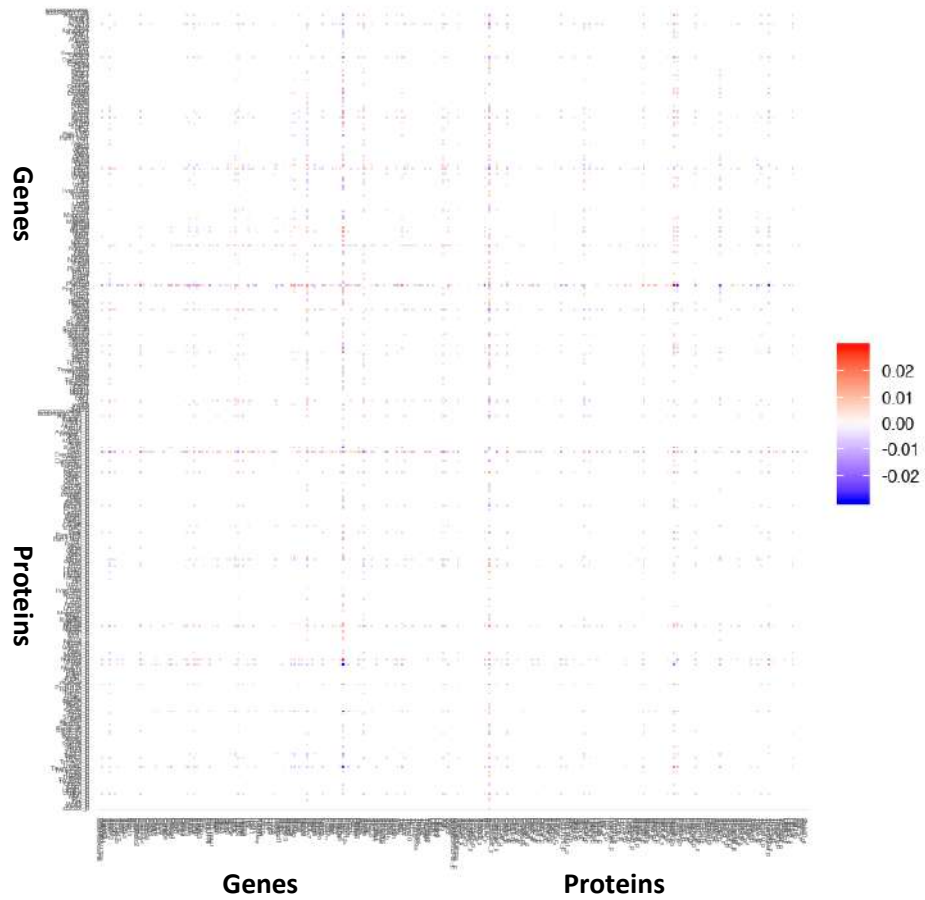
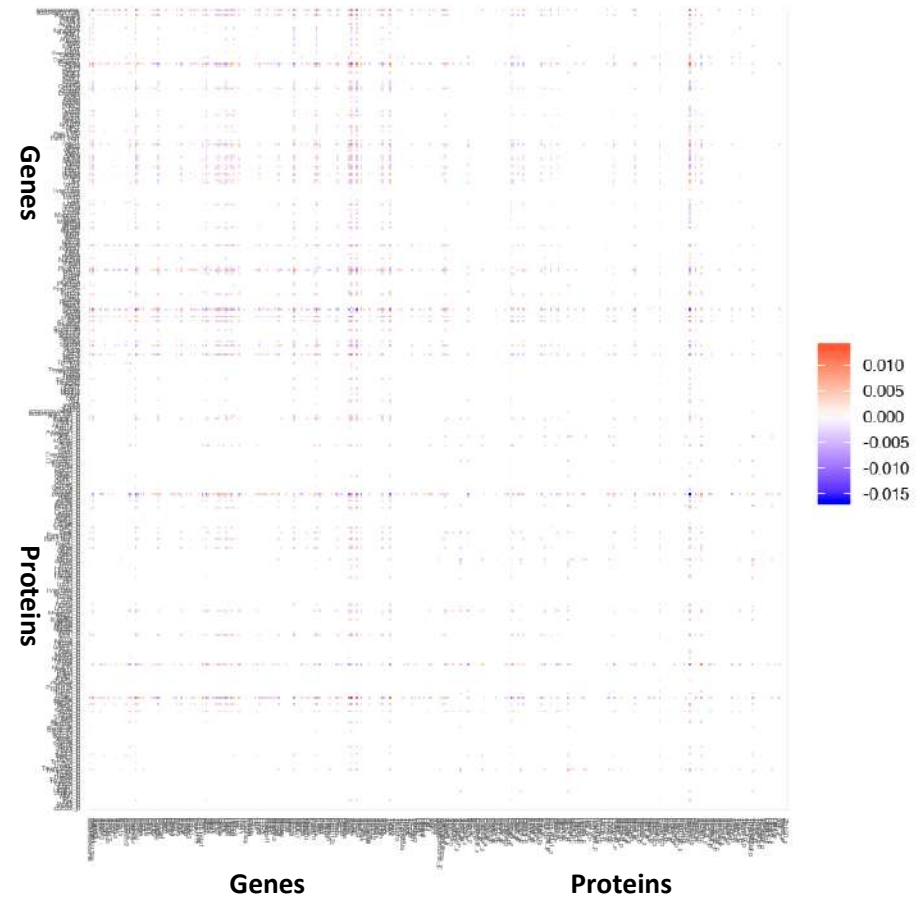# Gene-Protein Regulatory Network Reconstruction

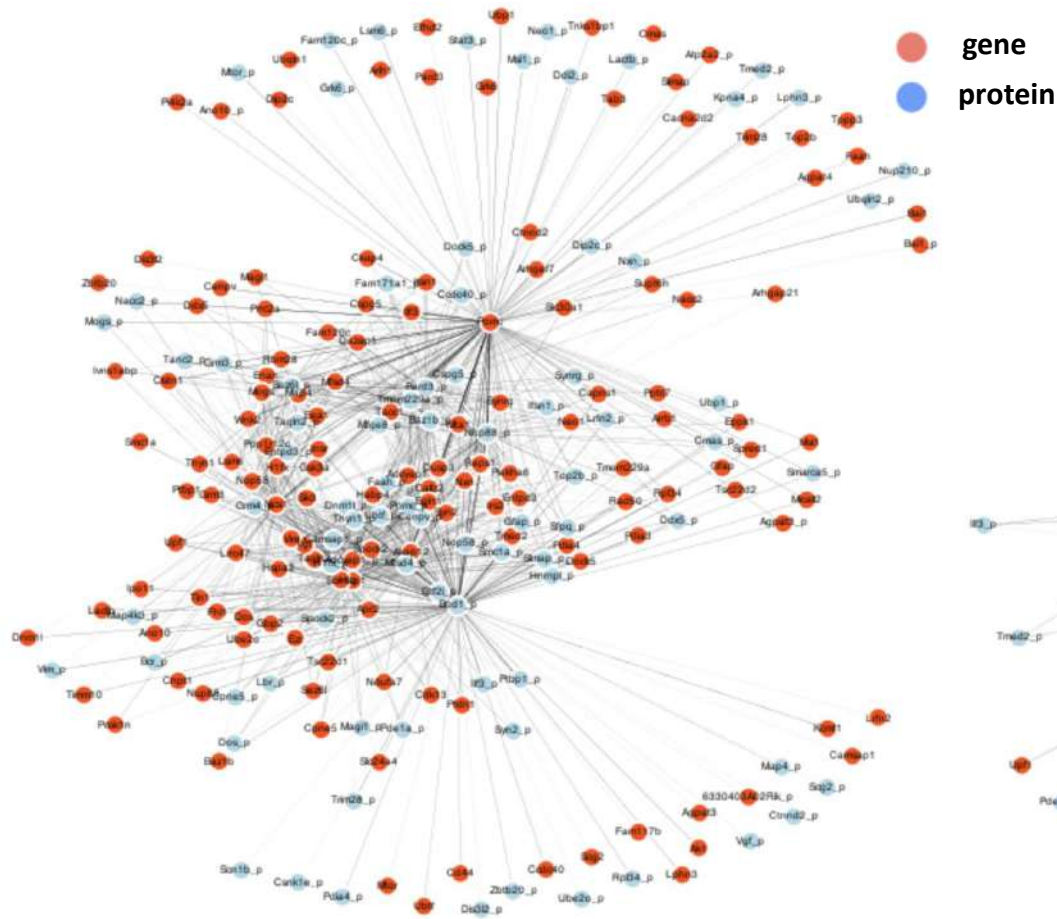# Inverse Covariance Matrix

Chow Diet Data

HFHS Diet Data
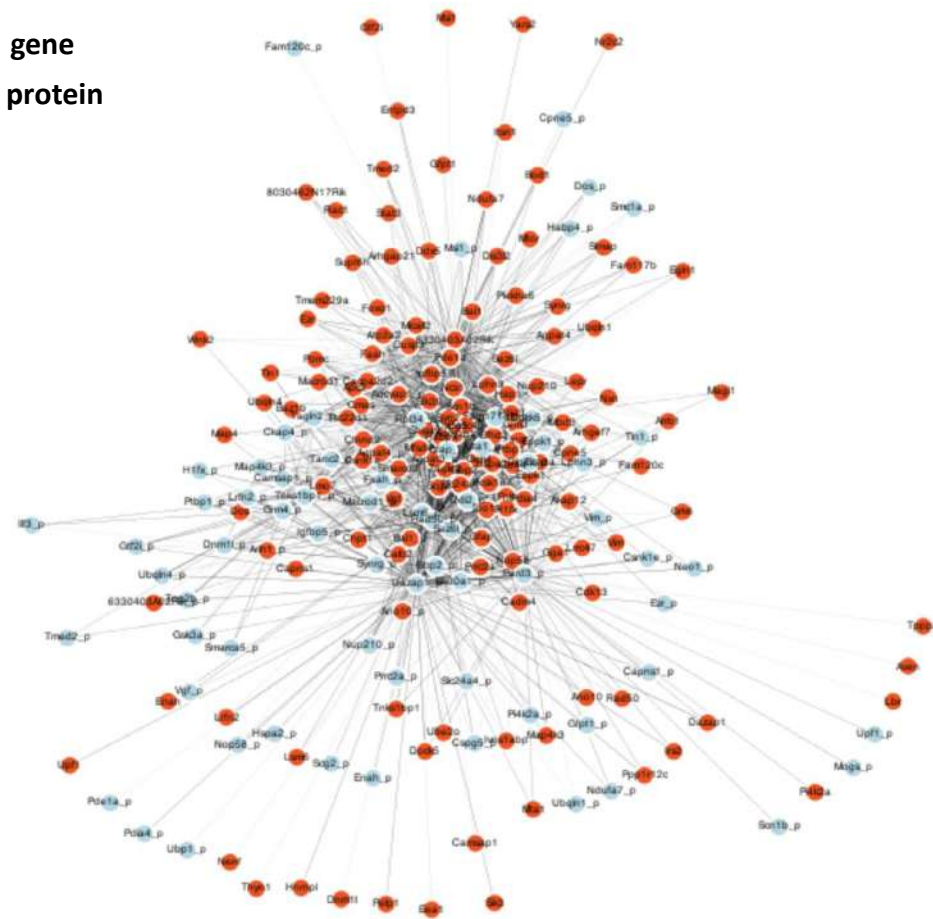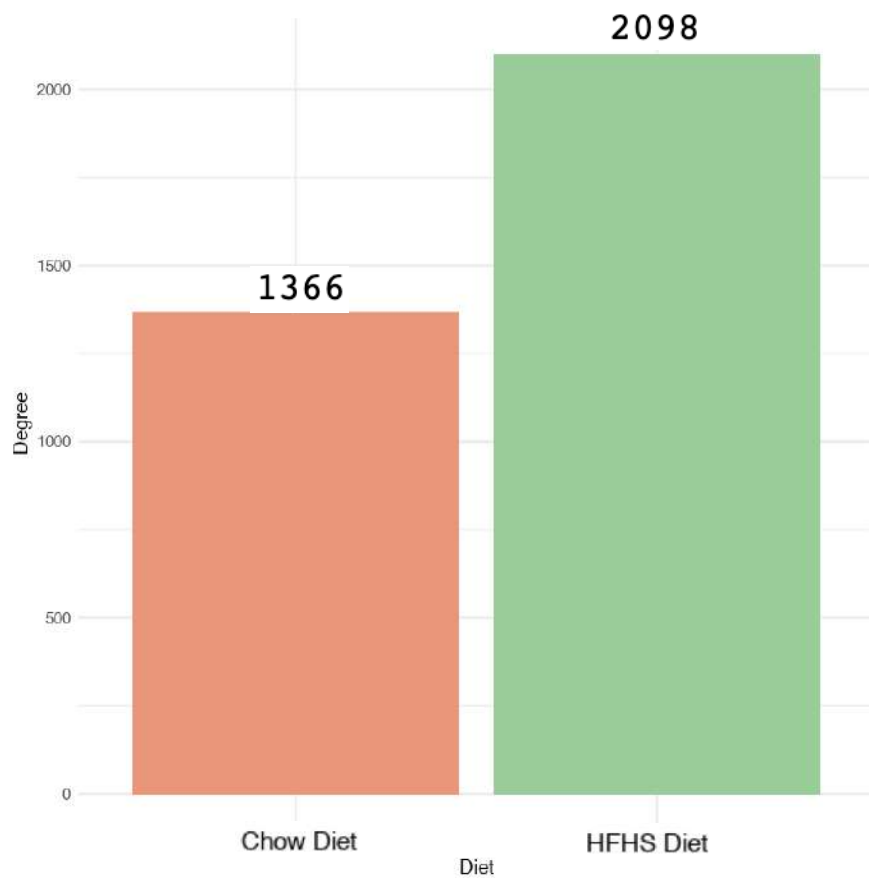
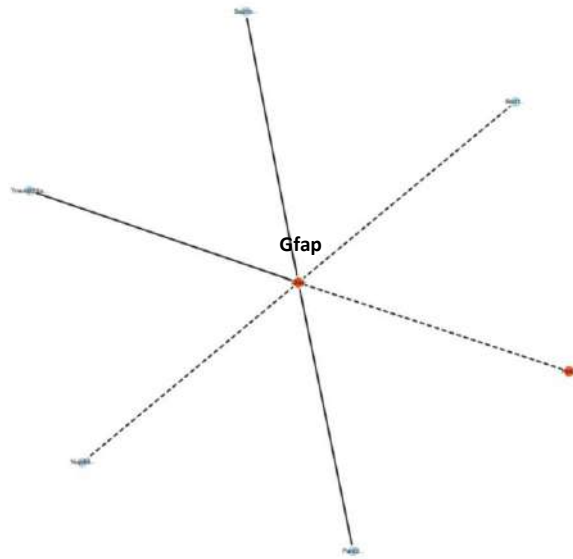# Integrative Regulatory Network

Chow Diet Data

HFHS Diet Data

- gene
- protein

Higher Entropy in HFHS Diet Data
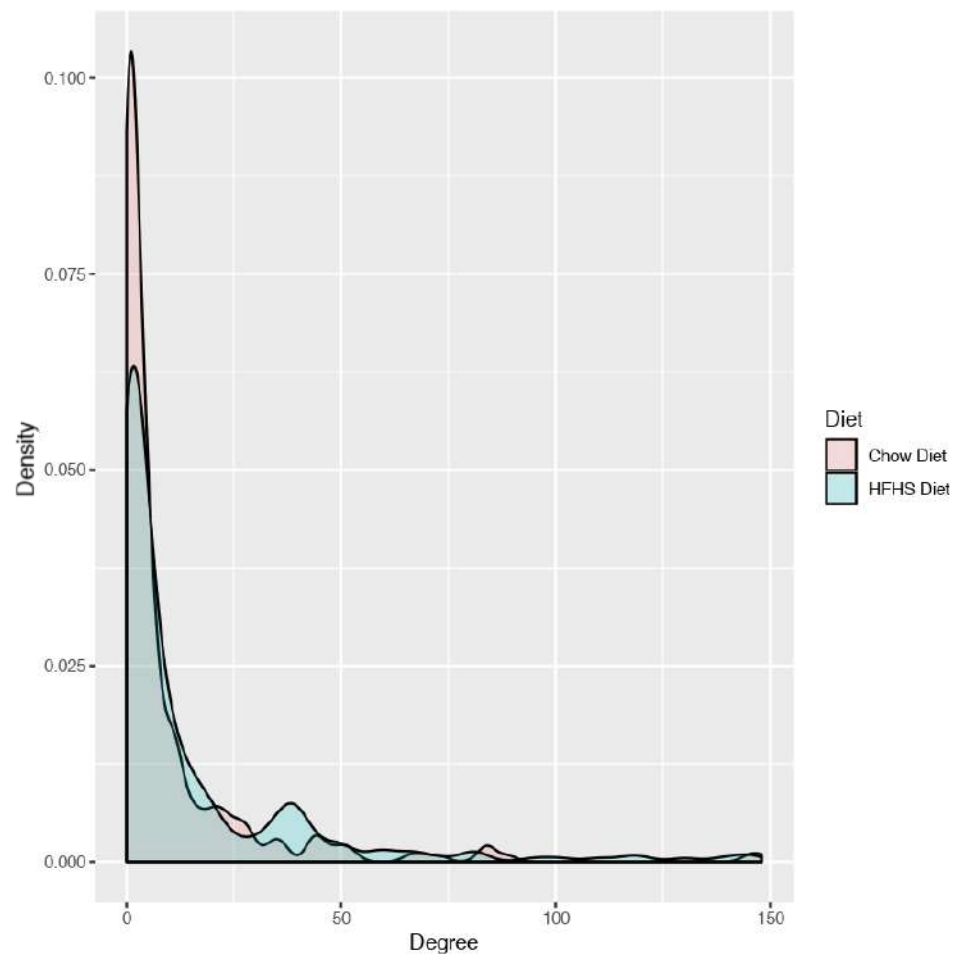
Zoom-in Network

Chow Diet Data

HFHS Diet Data

gene

protein

Gfap

Pomc
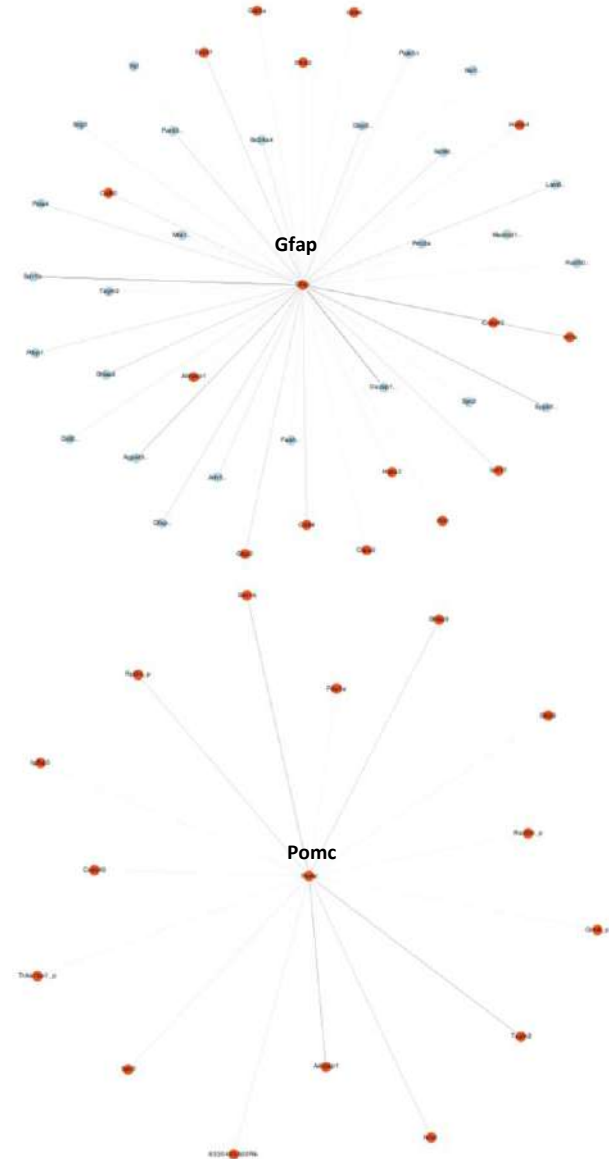
Regulatory Cascades
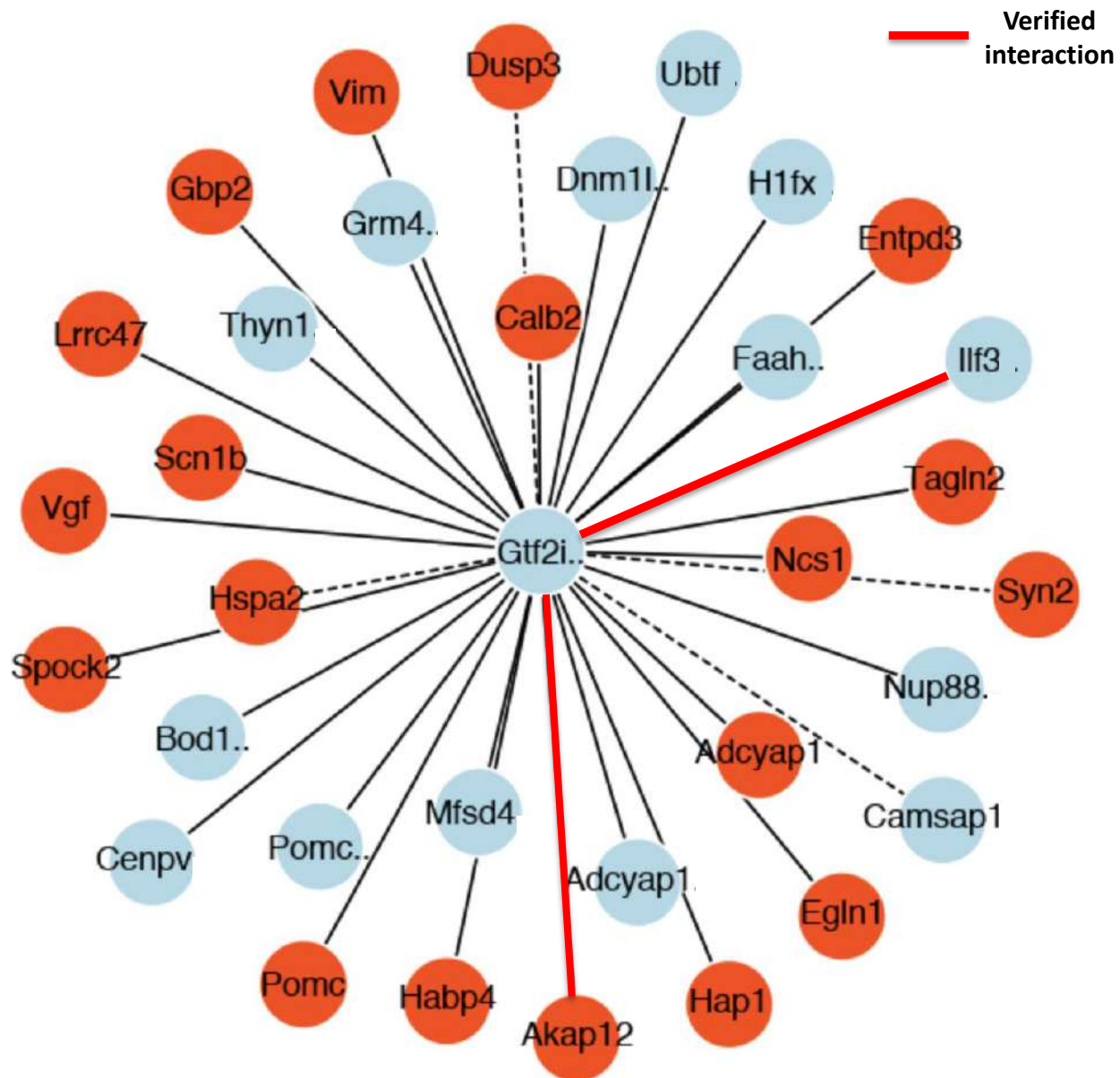
Future directions…

- Identify the regulatory cascades, motifs and communities of interest from the networks and verify them experimentally.

- Compare network from chow and HFHS diet data.

- Include prior knowledge from other experiments to improve estimation of the interactions.

- Extend and apply this methodology on single-cell RNA-seq data and on other types of data.

Acknowledgements

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Munich Cluster for Systems Neurology

erc

HELMHOLTZ RESEARCH FOR GRAND CHALLENGES