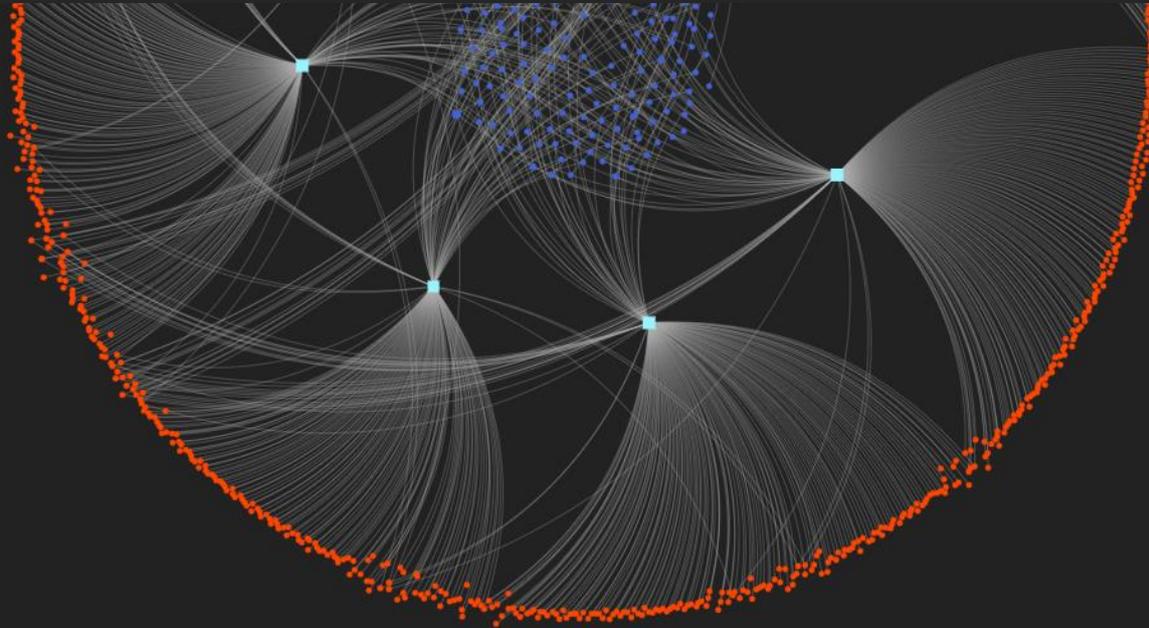miRNet 2.0 Tutorial 2

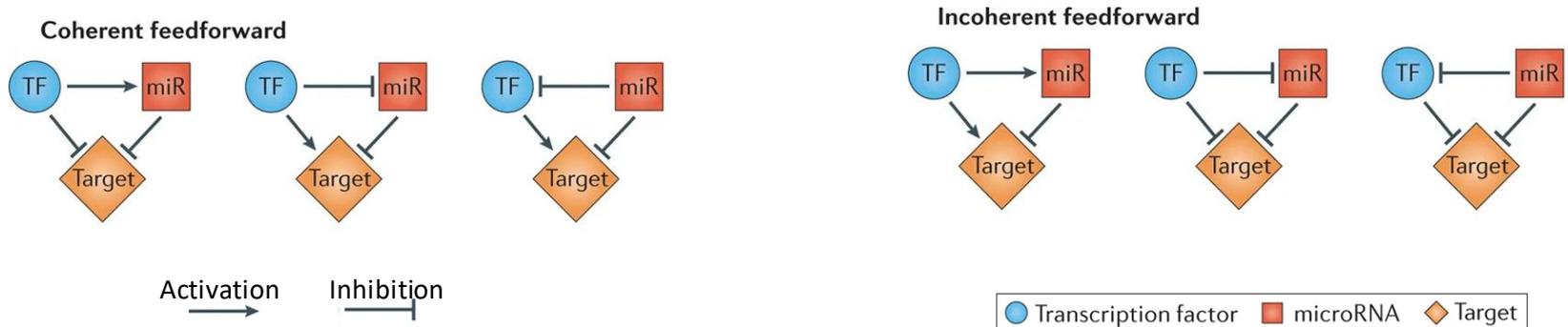# Transcription factor-microRNA feed-forward loop analysis

Computer and Browser Requirements

- A modern web browser with JavaScript enabled
  - Supported browsers include Chrome, Safari, Firefox, and Internet Explorer 9+
- For best performance and visualization, use:
  - Latest version of Google Chrome
  - A computer with at least 4GB of physical RAM
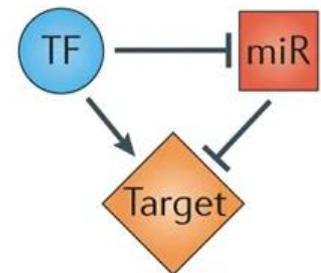 - A 15-inch screen or bigger (larger is better)

Background

What is TF-miRNA feed-forward loop (FFL)?

- In TF-miRNA feed-forward loops, TF and miRNA **co-regulate** the target genes
  - **Coherent feed-forward loops**: the TF and miRNA have the *same* effects on their common targets
  - **Incoherent feed-forward loops:** the TF and miRNA carry out *opposing (buffering)* effects, which precisely fine-tune gene expressions to minimize noise and maintain stability (*Bracken et al., Nat Rev Genet. 2016*)

Goal for This Tutorial

- How to perform transcription factor (TF)-miRNA feed-forward loop analysis

Choose a Module

Go to the miRNet home page (www.mirnet.ca) and click "**Multiple query types**" to enter the module

Input 1: Choose Molecular Types

Select "miRNAs" and "Transcription factors", then click "OK" to proceed

Input 2: Upload miRNA Data

Example data: Qin,et al.,(2020)

Input 3: Upload TF Data

After data uploaded for both miRNAs and TFs, click "**Proceed**"

Network Creation

Network Viewer

Change layout to Circular Bipartite/Tripartite

Functional enrichment analysis

A TF-miRNA-gene network. The blue nodes (central zone) represent miRNAs, red nodes (middle layer) represent target genes and green nodes (outer layer) represent TFs.

Subnetwork Extraction

1) Choose "Node-neighbours"

3) Click "Extract" icon

2) Double click on node of interest

A few TFs and miRNAs regulate a large number of target genes. You can extract a subnetwork to further investigate.

TF-miRNA Feed-forward Loops
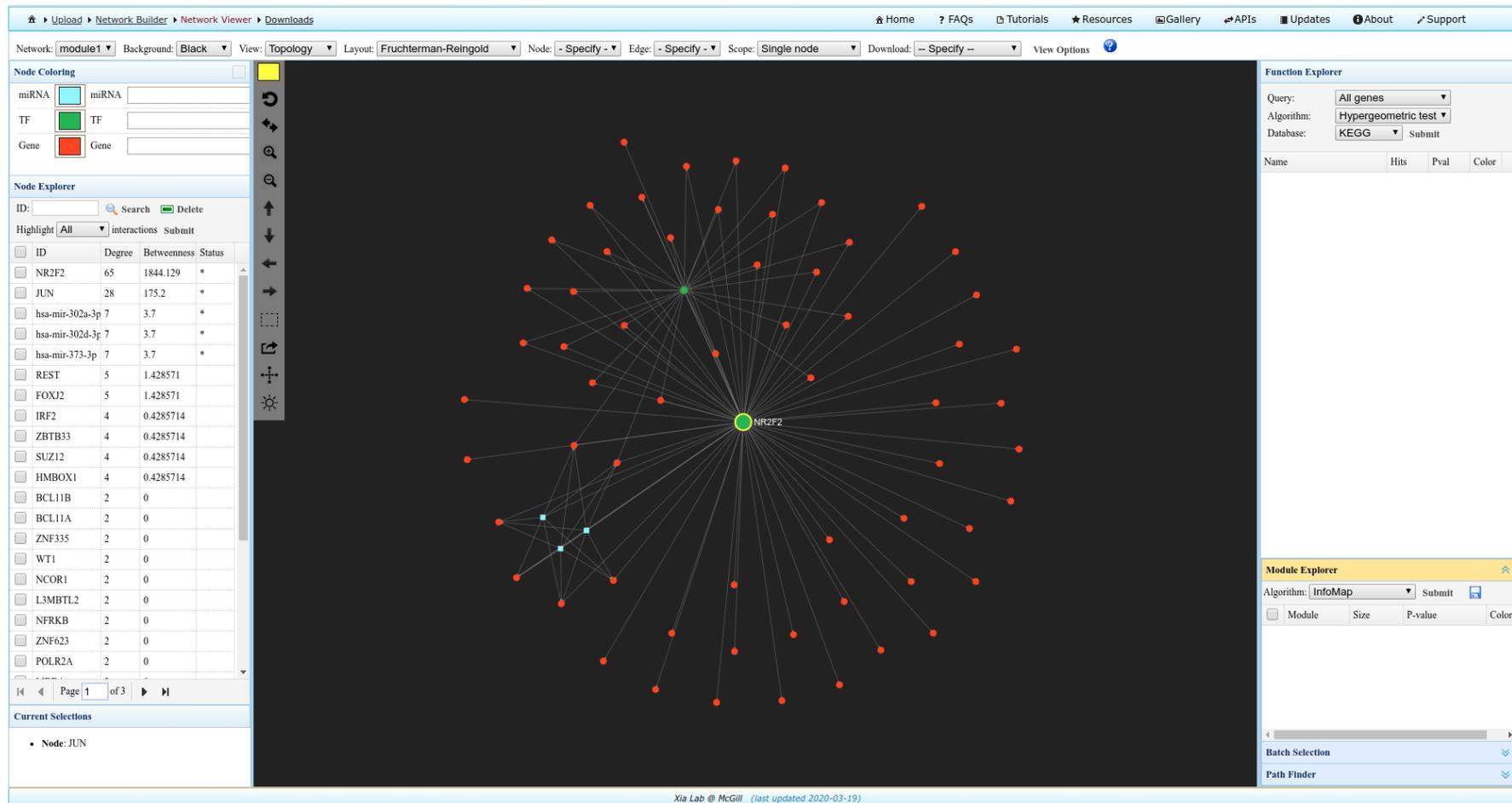
An example subnetwork containing TF-miRNA feed-forward loops (FFL). *NR2F2* is a TF-coding gene, which activates gene expression; whereas the miRNAs (hsa-miR-302a-3p, hsa-miR-302d-3p, hsa-miR-373-3p) repress gene expression, suggesting that the FFL might have a significant role in pathogenesis of testicular germ cell tumors (example data: Qin,et al.,2020).

==END==