

ncRNA Network Modeler (NMM)

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1 Introduction

The purpose of this system is to provide users with the construction of non-coding RNA to complete the simulation of non-coding RNA, mainly including two main functions:

- (1) non-coding RNA modeling and visualization;
- (2) dynamic model management and viewing.

Among them, non-coding RNA modeling and visualization is based on those nodes and lines that users use when drawing and modeling, then generate xml type files. Dynamic model management and viewing refers to saving and managing models through input information in the software.

This software provides biomolecular modeling and simulation functions for researchers in the field of systems biology.

1.1 Non-Coding RNA

A non-coding RNA (ncRNA) is a functional RNA molecule that is transcribed from DNA but not translated into proteins. Epigenetic related ncRNAs include miRNA, siRNA, piRNA and lncRNA. In general, ncRNAs function to regulate gene expression at the transcriptional and posttranscriptional level. Those ncRNAs that appear to be involved in epigenetic processes can be divided into two main groups; the short ncRNAs (<30 nts) and the long ncRNAs (>200 nts). The three major classes of short non-coding RNAs are microRNAs (miRNAs), short interfering RNAs (siRNAs), and piwi-interacting RNAs (piRNAs). Both major groups are shown to play a role in heterochromatin formation, histone modification, DNA methylation targeting, and gene silencing.

1.2 NMM tool

1.2.1 Main functions

This software mainly includes two main functions: (1) non-coding RNA modeling and visualization (2) dynamic model management and viewing. The following lists all the sub-templates of the two templates:

- (1) Non-coding RNA modeling and visualization:
 - 1) Use the drawing module in the software for biological modeling and drawing
 - 2) Modify various attributes in the figure
 - 3) Save and delete the model
 - 4) Import a new non-coding RNA model
 - 5) Node external database link
 - 6) Network analysis function
- (2) Dynamic model management and viewing:
 - 1) Manage model database entries
 - 2) View and search the model database

1.2.2 Architecture

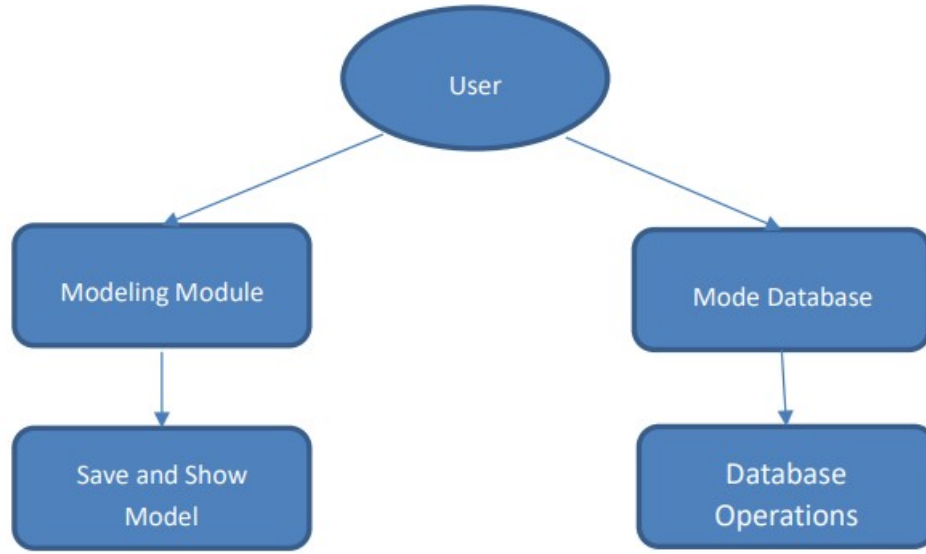


Figure 1: The architecture of NMM tool.

- 1) User-friendly non-coding RNA icon, Protein icon, cell icon, etc.
- 2) Easy to build a strong non-coding RNA network.
- 3) Formal analysis based on graph theory.
- 4) Link non-coding RNA to Kinetic model based on Snoopy.

2 Modeling

This section will present a general step-by-step procedure for how to construct an ncRNA network model. This part of the model is just to show the function, without specific practical significance.

2.1 Main interface

Figure 2 shows the main interface of the software. The menu and tool bar is on the top. The tools from left to right include “File”, “Edit”, “Options”, “View”, “Tool”, “Search”, and “Help”. Click “New” to create a new file, click “Save” to save the current page, and click “Open” to import the existing model of the computer.

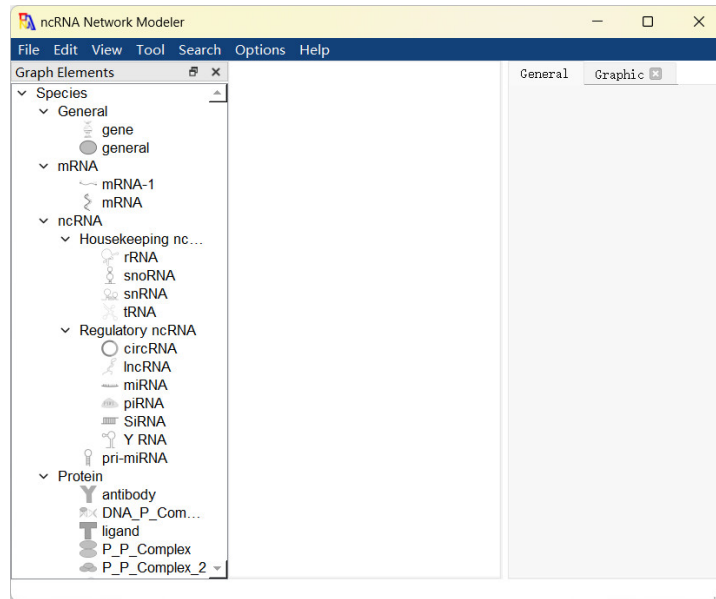


Figure 2: Main interface of NMM tool.

2.2 Add nodes

Click on the element on the left side of the page to draw. There are two ways to add a node, one is to click the node (add one by one), or double-click the node (add continuously).

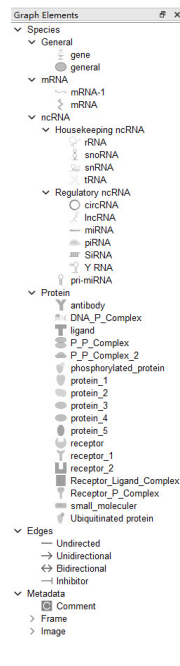


Figure 3: Graph elements

2.3 Node attributes

After adding a node, there is general attributes of the node on the right as show in Figure 4. Then user can change some attribute as show in Figure 5. The ID, Sub type and Type (marked in red) in the attribute cannot be modified. Name, Alias Name and name label visibility (blue label) in the attribute can be changed. Among them, different names of Alias Name need to be separated by semicolon ";". Logic attribute bar binds multiple attributes together, only their positions are different, all other attributes are the same, including the name. Node Graphic attributes are show in Figure 6. Node's graphic attributes can be modified to fit in the actual situation.

General Graphic

Number of items selected: 1
Priority type: node

ID 4

Name mRNA_4

☒ Show

Alias Name mRna;No4;

Sub Type mRNA

Type mRNA

Gene

Search gene

Logic ☐

Comment

Figure 4: Node General attributes

ID 4

Name mRNA_4

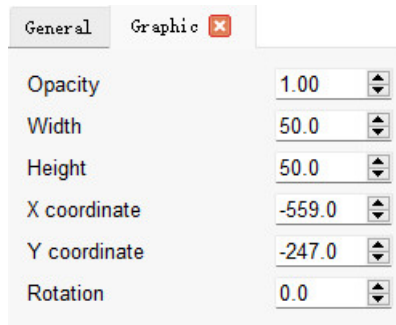
☒ Show

Alias Name mRna;No4;

Sub Type mRNA

Type mRNA

Figure 5: The ID, Sub type and Type (marked in red) in the attribute cannot be modified. Name, Alias Name and name label visibility (blue label) in the attribute can be changed. Among them, different names of Alias Name need to be separated by semicolon ";".



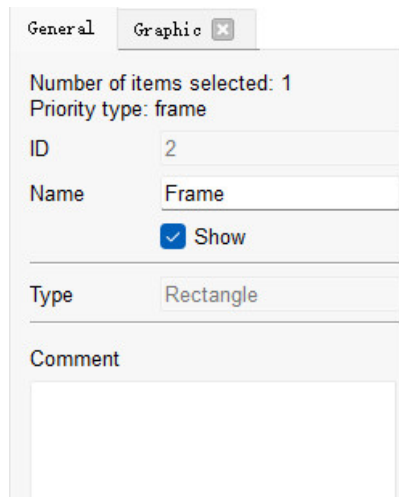
General Graphic ✕

Opacity	1.00	⬆ ⬇ ⬆
Width	50.0	⬆ ⬇ ⬆
Height	50.0	⬆ ⬇ ⬆
X coordinate	-559.0	⬆ ⬇ ⬆
Y coordinate	-247.0	⬆ ⬇ ⬆
Rotation	0.0	⬆ ⬇ ⬆

Figure 6: Node Graphic attributes

2.4 Frame attributes

Frame has no name by default, users can define the name. The type and ID of frame cannot be changed. The height and width of the frame can be changed by dragging frame on graphic scene or directly modifying the size attributes of the frame

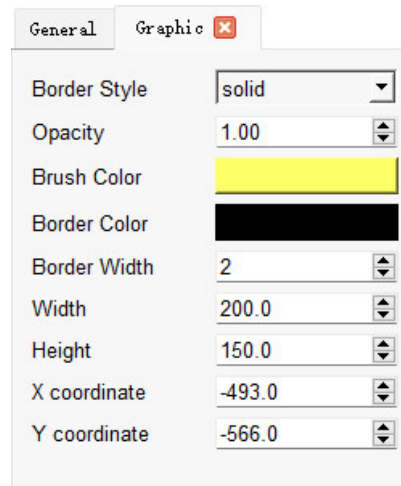


General Graphic ✕

Number of items selected: 1
Priority type: frame

ID	2
Name	Frame
	<input checked="" type="checkbox"/> Show
Type	Rectangle
Comment	

Figure 7: Frame General attributes

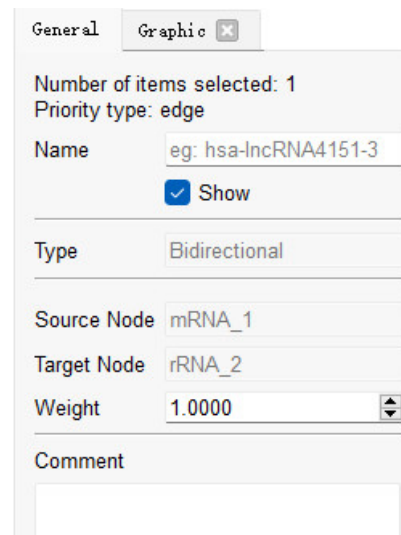


Attribute	Value
Border Style	solid
Opacity	1.00
Brush Color	Yellow
Border Color	Black
Border Width	2
Width	200.0
Height	150.0
X coordinate	-493.0
Y coordinate	-566.0

Figure 8: Frame Graphic attributes

2.5 Line attributes

Line has no name by default, users can define the name. Line's general attributes can show the line's type, and the source node and target node connected by it. Line's weight can be modified to represent different relevance. In graphic attributes can modify some line style.



Attribute	Value
Number of items selected	1
Priority type	edge
Name	eg: hsa-lncRNA4151-3
Show	<input checked="" type="checkbox"/>
Type	Bidirectional
Source Node	mRNA_1
Target Node	rRNA_2
Weight	1.0000
Comment	

Figure 9: Line General attributes

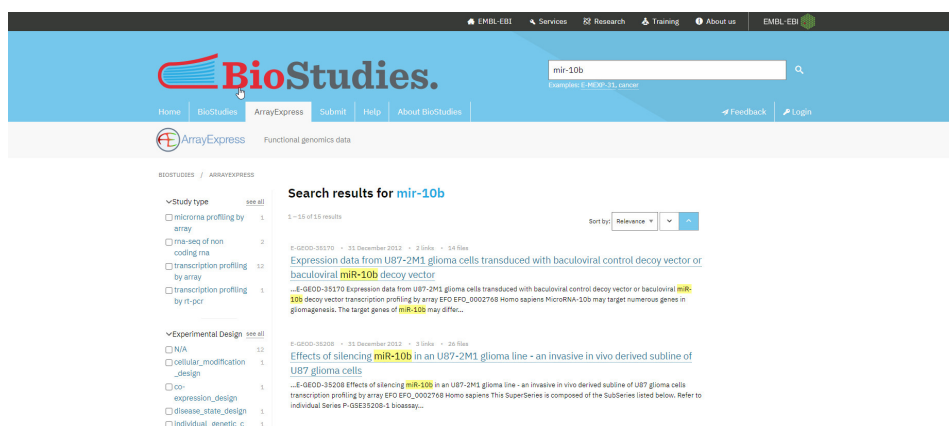


Figure 12: External database on web.

2.7 Preference / Molecular information sheet

Click the “Options” action on the top menu bar, then click on the “Preference” in the submenu, you can open the preference editor and view the analysis Molecular information table as Figure 13. In the preference editor, custom options of canvas style and font style can be set. Shown in Figure 14 and Figure 15.

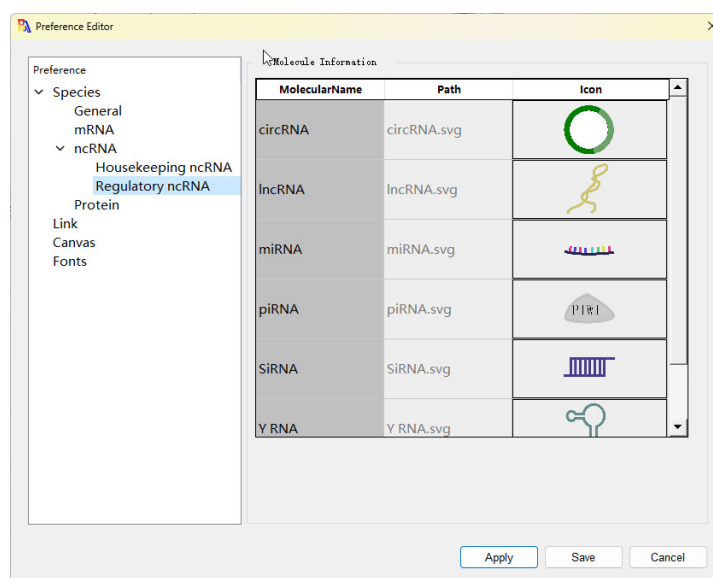


Figure 13: Molecular information sheet.

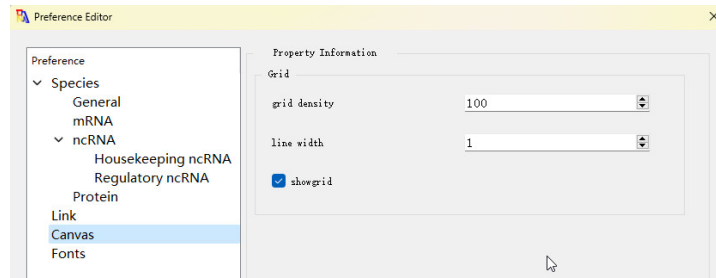


Figure 14: Canvas settings.

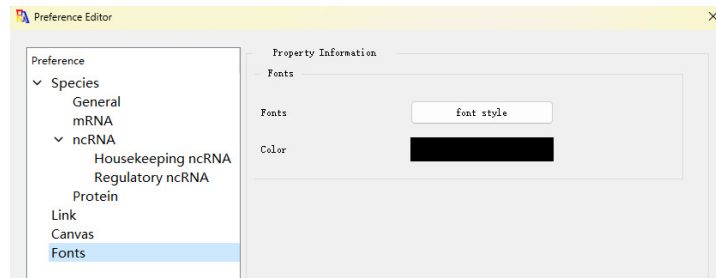


Figure 15: Fonts style settings.

2.8 Network analysis

Click the “Network Analyzer” button on the “Tool” menu to perform the network analysis. There are two methods for network analysis: Directed network analyze and Undirected network analyze. There are the number of nodes, the number of discrete nodes, and the number of connected devices.

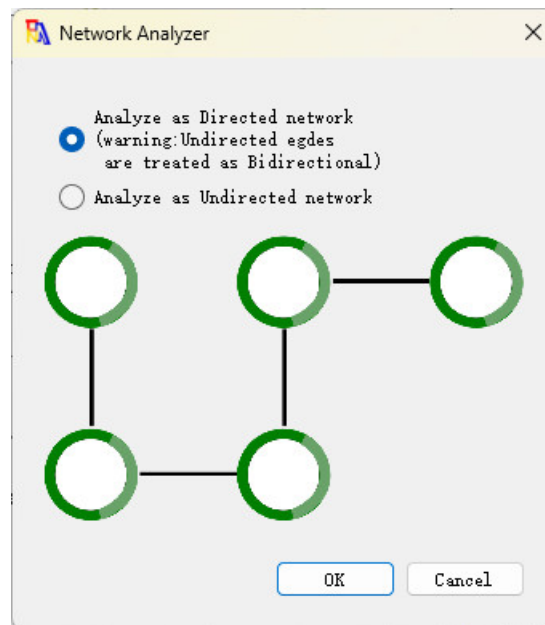


Figure 16: Network analyzer.

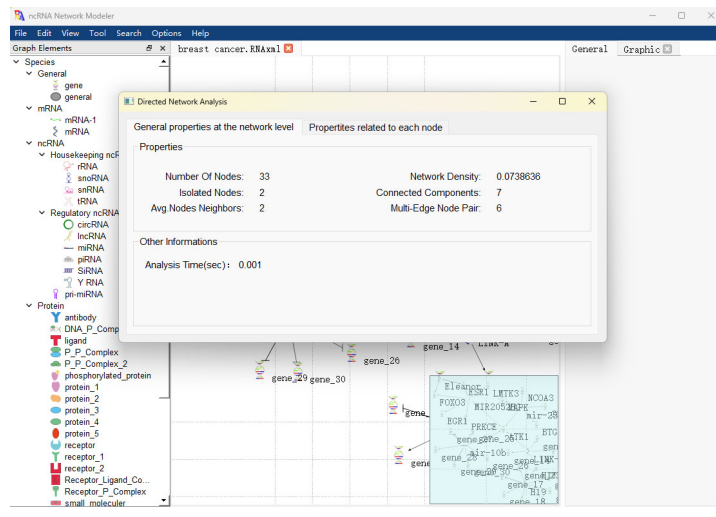


Figure 17: Network analysis function (Directed).

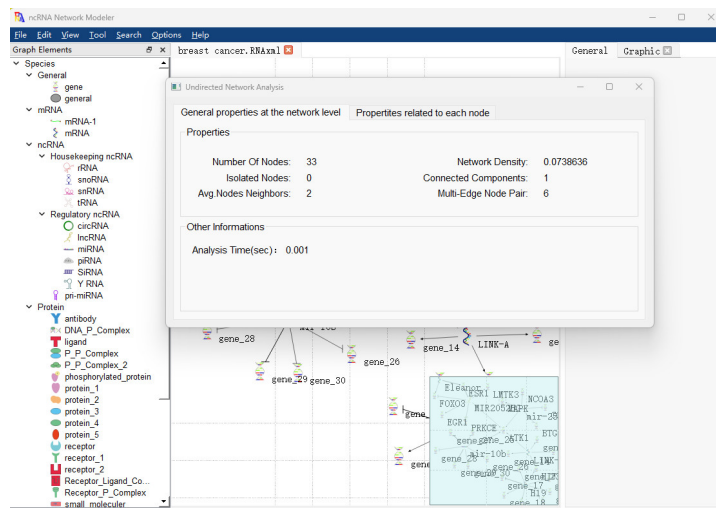


Figure 18: Network analysis function (Undirected).

2.9 Node analysis

Click the DegreeAnalyzer button to view the node analysis results. You can choose to show the degree of nodes by size and color.

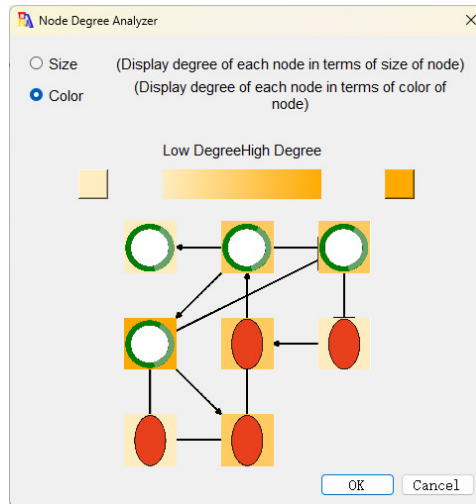


Figure 19: Node analysis function.

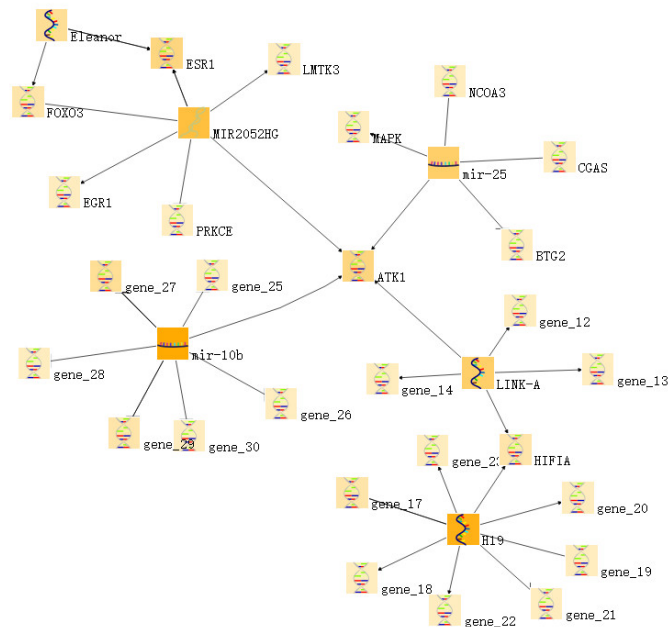


Figure 20: Node degree analysis example.

2.10 Search Kenitic Repository

Select node and click the “Search in Kenitic model repository” button. All kenitic model containing this mRNA/ncRNA/Protein can be listed.

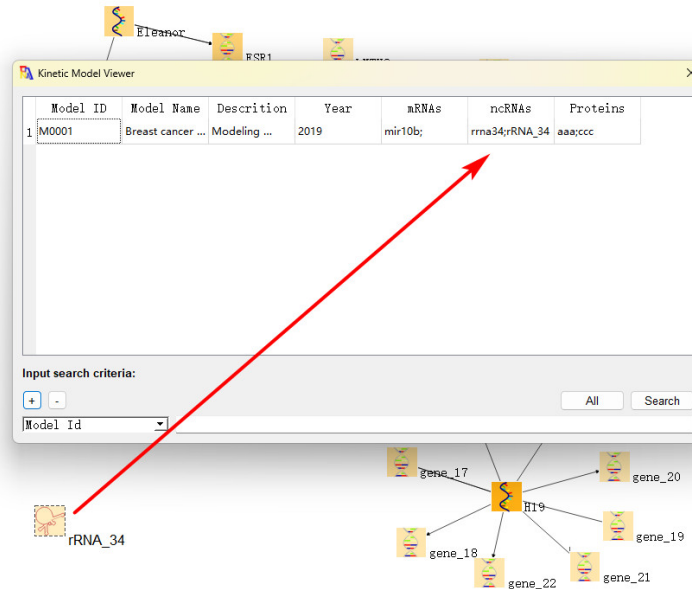


Figure 21: Search Kenitic Repository function.

2.11 Layout

Layout is in the “View” menu, users can freely choose four layout modes. Including grid layout, circle layout, degree sorted circle layout and tree layout. Note that the tree layout can only be used when there is only one root node.

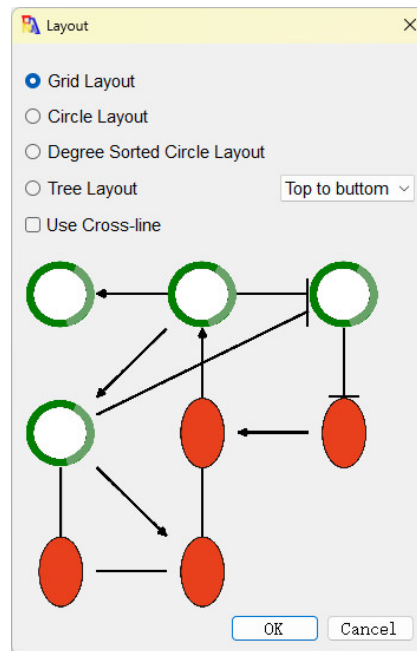


Figure 22: Layout function.

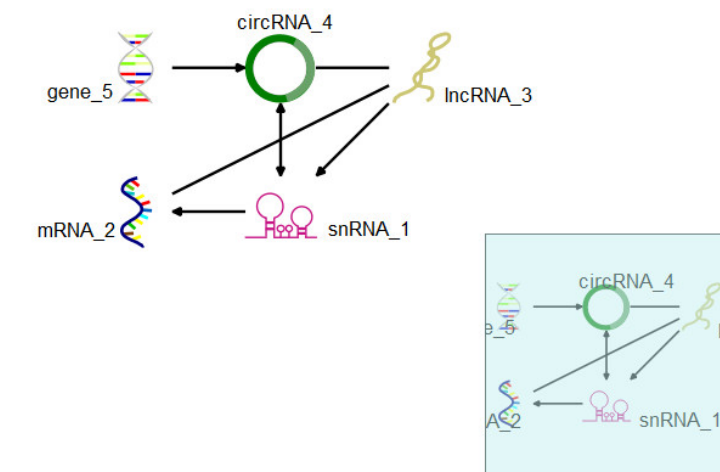


Figure 23: Grid Layout.

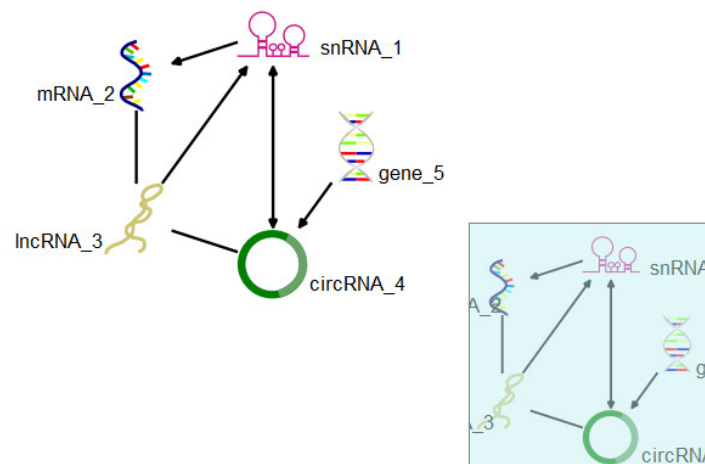


Figure 24: Circle Layout.

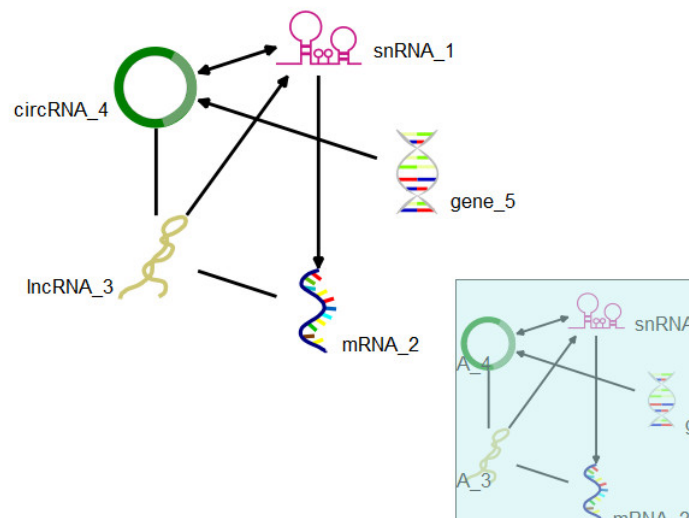


Figure 25: Degree Sorted Circle Layout.

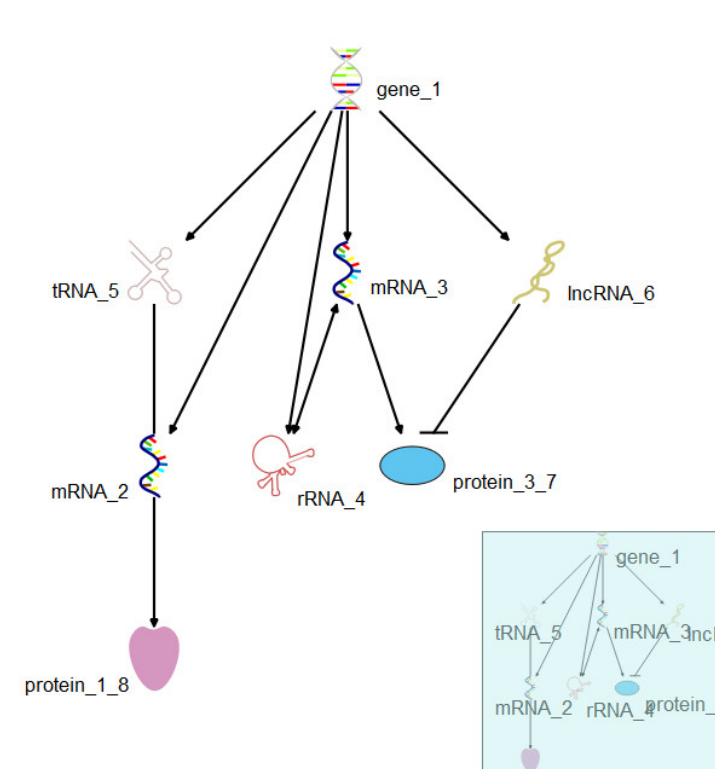


Figure 26: Tree Layout.

2.12 Search Nodes

Search nodes function can be found in the top menu. With the searching nodes function, users can focus on a certain ncRNA, protein or gene node easily by giving name or ID of the node.

Let's use an example to show how to use this function. For example, when you want to focus on ncRNA

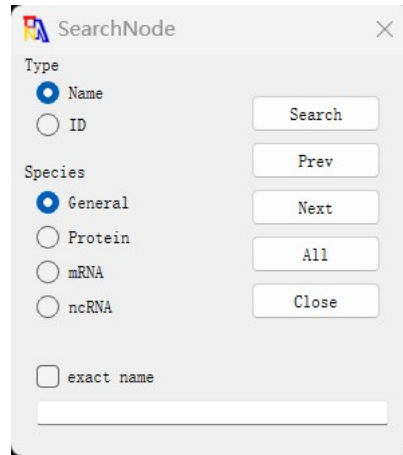


Figure 27: Search function.

nodes that names contain “uc”, you can select the species options of ncRNA and enter “uc” in the input field. Then click the “Search” button, a node with name contains “uc” will be selected as the Figure 28.

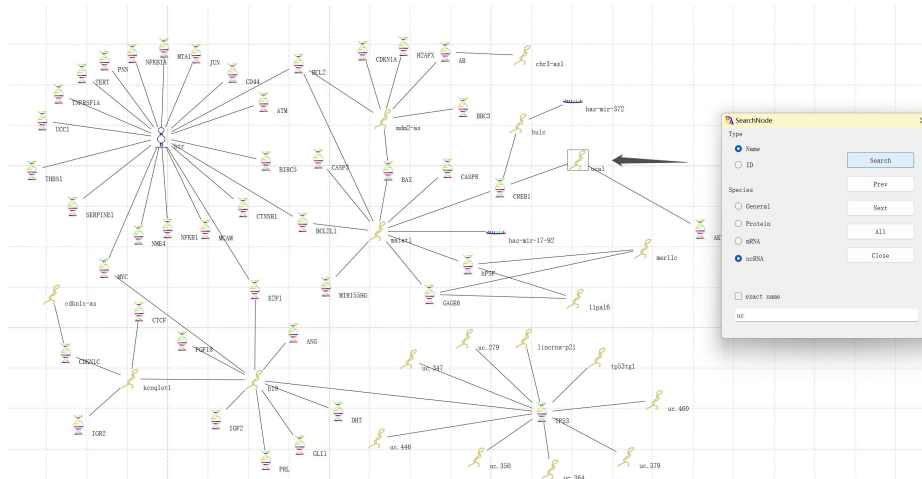


Figure 28: Search nodes example.

You can use more operation buttons to select different that were found by the previous search. Such as “All” button to select all nodes whose name contains “uc”

2.13 Welcome page

Welcome page is the first page the user sees after entering “ncRNA Network Modeler(NMM)”. The welcome page is mainly used to help users review the recently opened models and present some sample models. The welcome page is persented as the Figure 29.

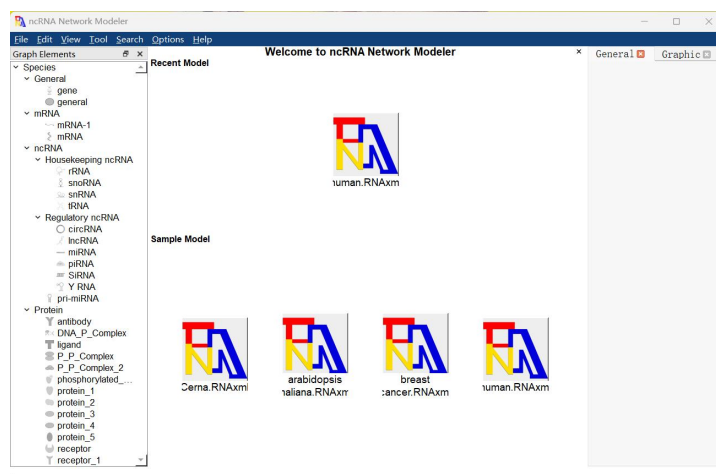


Figure 29: Welcome page.

3 Kinetic model viewing and management

Model database button are on the top of page as show in Figure 30. Click “Kinetic Model Viewer”to enter the database viewing page. Click “Kinetic Model Manager” to enter the database management page, then click add, fill in the information, add the database model, and finally click add to complete the addition of the dynamic model. To edit model, users can click “Kinetic Model Manager” to enter the database management page, then click specific items, click edit, modify the dynamic model information in the database here. Click on a specific entry and then click delete to delete the target model in the database. You can enter the target dynamic model data you want to query in the search bar below, then click Search to query the target dynamic model, or click the target dynamic model you want to view detailed information on this page to enter the target The detailed data page of the model.

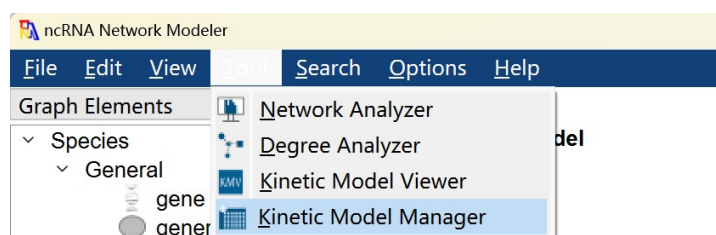


Figure 30: Model database button. Click “Kinetic Model Viewer” to enter the database viewing page.

Click “Kinetic Model Manager” to enter the database management page.

3.1 Kinetic Model Manager

Click “Kinetic Model Manager” to enter the database management page, then click “add”, fill in the information, add the database model, and finally click “add” to complete the addition of the dynamic model.

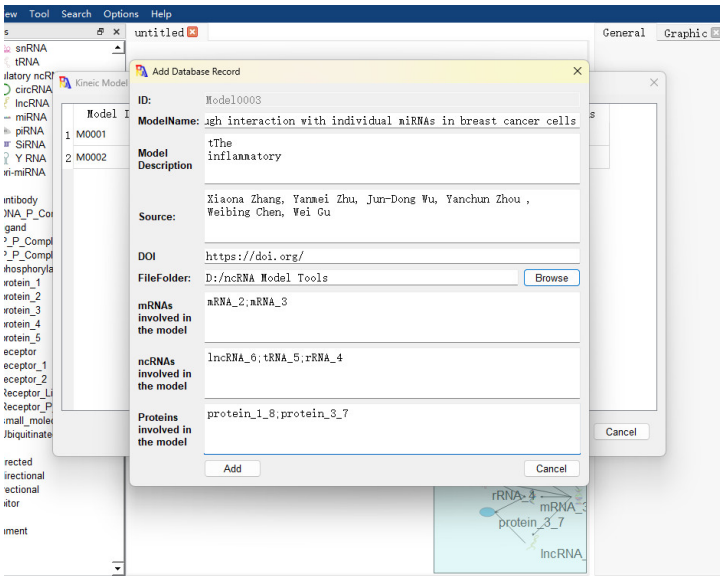


Figure 31: Add database model.

Click “Kinetic Model Manager” to enter the database management page, then click specific items, click edit, you can modify the dynamic model information in the database here.

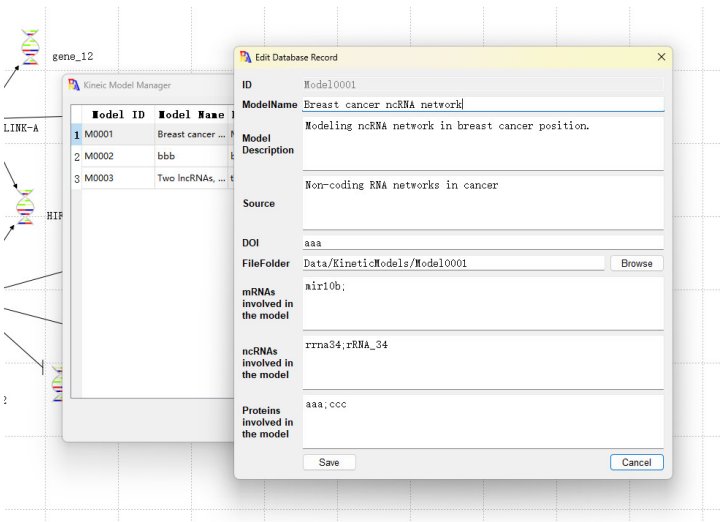


Figure 32: Edit database model.

Click a specific entry and then click Delete to delete the target model in the database

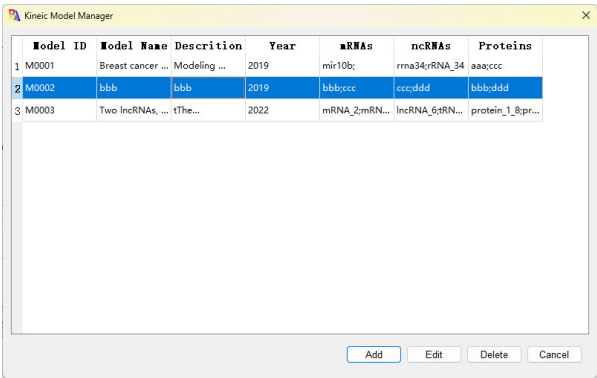


Figure 33: Select database model.

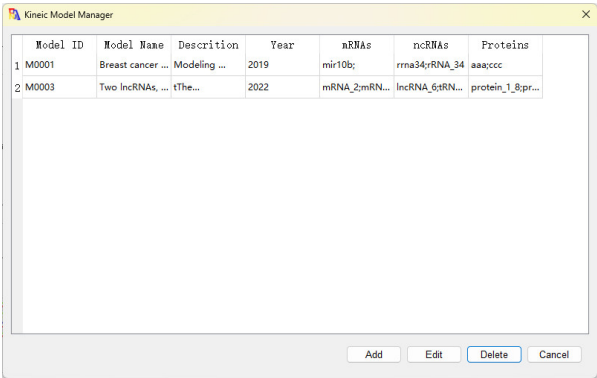


Figure 34: Delete database model.

3.2 Kinetic Model Viewer

Click the kinetic model viewer button to enter the dynamic model database viewing page, where the brief information of the model in the database will be printed.

You can enter the target dynamic model data you want to query in the search bar below, and then click search to find the target dynamic model, or click the target dynamic model you want to view the detailed information in this page to enter the detailed data page of the target model.

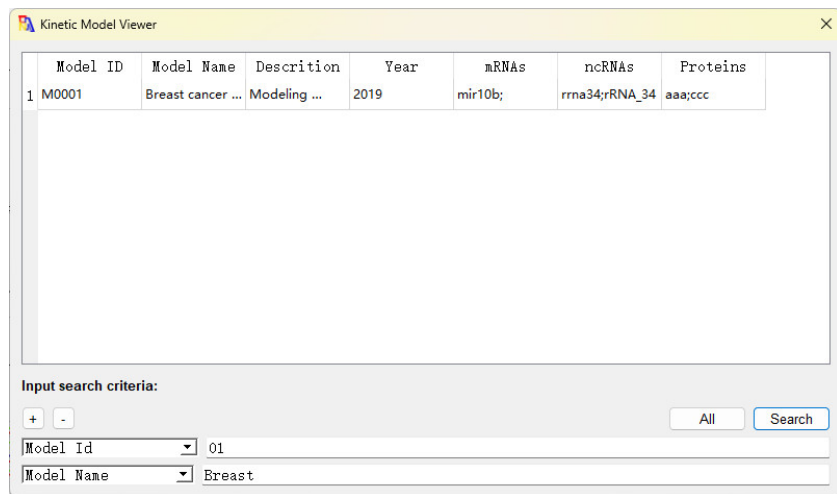


Figure 35: Search database model.

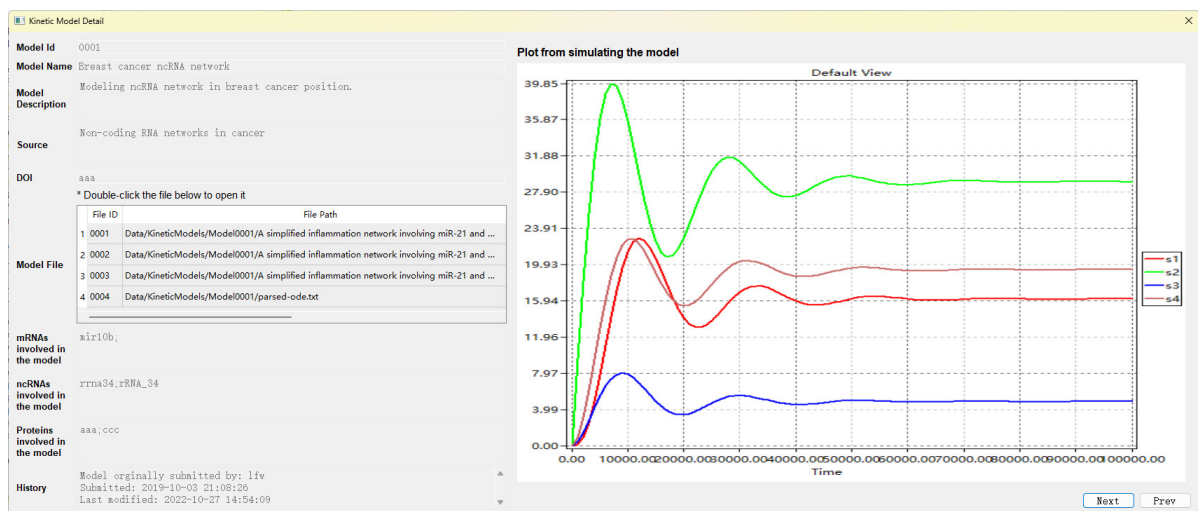


Figure 36: View model information.

4 Examples

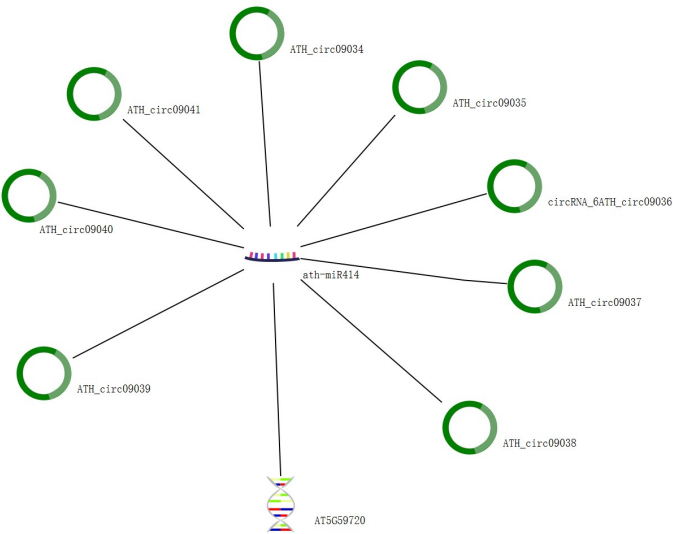


Figure 37: Arabidopsis thaliana.

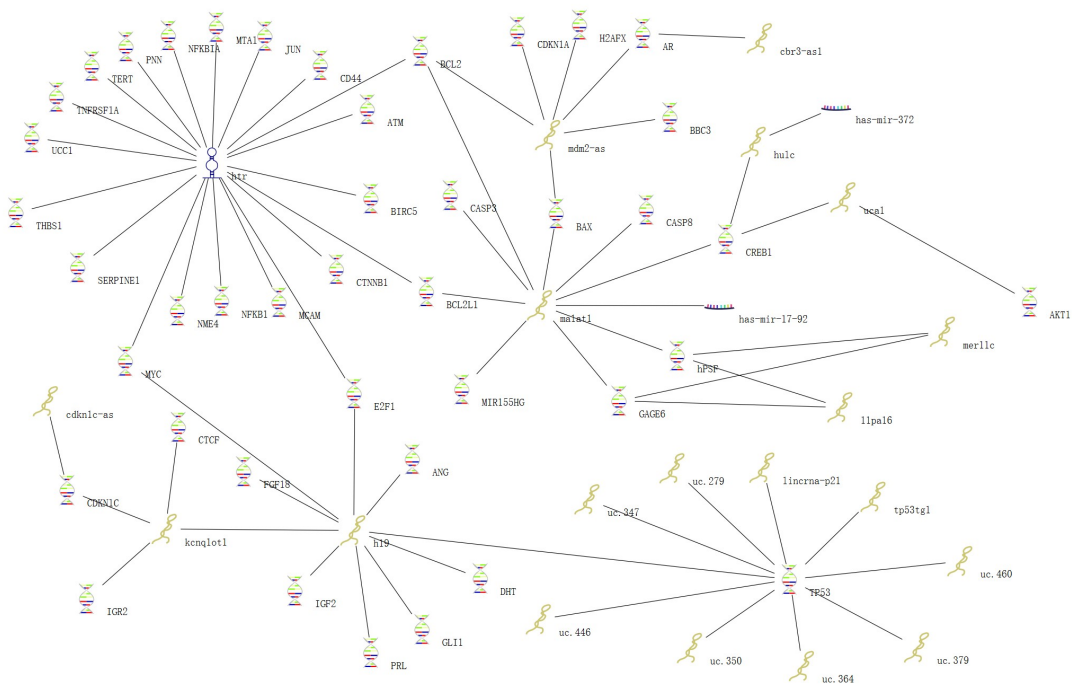


Figure 38: Human.

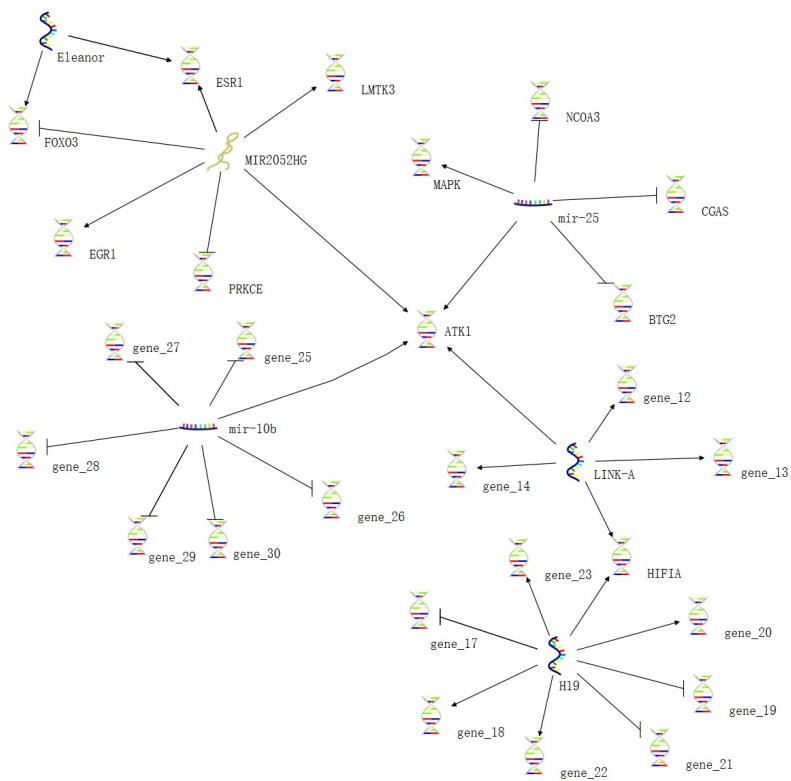


Figure 39: Breast cancer.

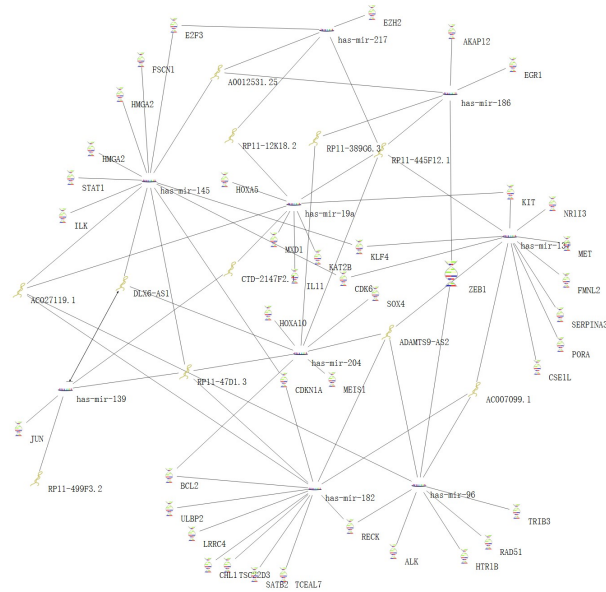


Figure 40: Cerna.