

WTAC Computational Systems Biology for Complex Human Disease 21-26 of April 2024

Instructor: Anna Niarakis

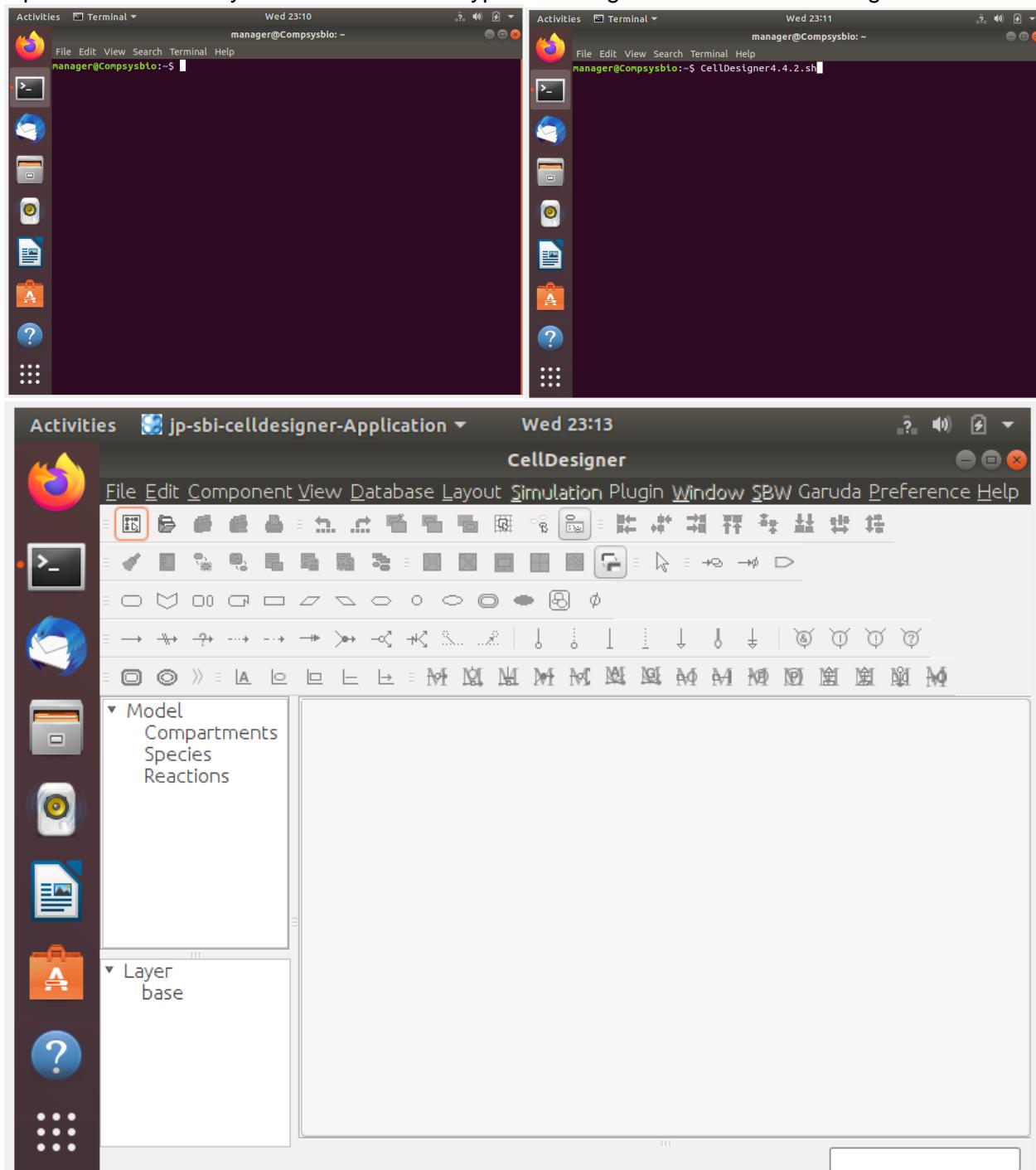
Hands-on session with CellDesigner

In this session, we will see examples of CellDesigner diagram functionalities. We will also open and observe a file containing a graphical model of apoptosis.

The functionalities we will see are summarised below:

Open a new model	Create a reaction	Add anchor point	Add catalytic reaction	Set active state
Change color	Include compartment	Add residue to protein	Change position of residue	Create complex
Include genes and RNAs	Connect to databases	Choose layout		

Open the terminal in your VM session and type CellDesigner4.4.2.sh or CellDesigner



You will see in your screen the general view as discussed in the demo:

General view

TREE AREA

displays all the list of the components in a tree structure.

DRAW AREA

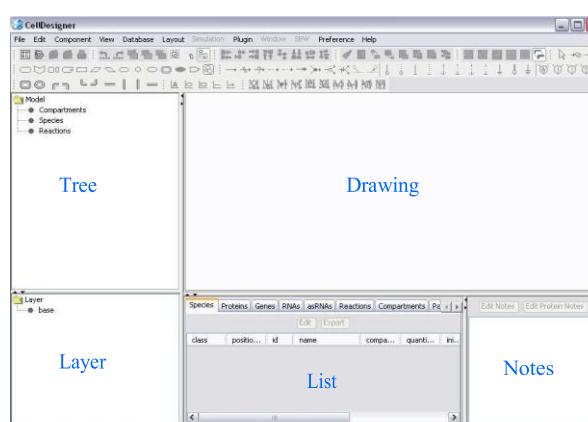
is the area where the model is built from the tool bar items.

LIST AREA

displays and edits the list of the components of the model (species, proteins, genes, RNAs, etc.)

NOTES AREA

displays and edits the notes of each component (reactions, protein, complex, etc.)



The screenshot shows the CellDesigner interface with the following layout:

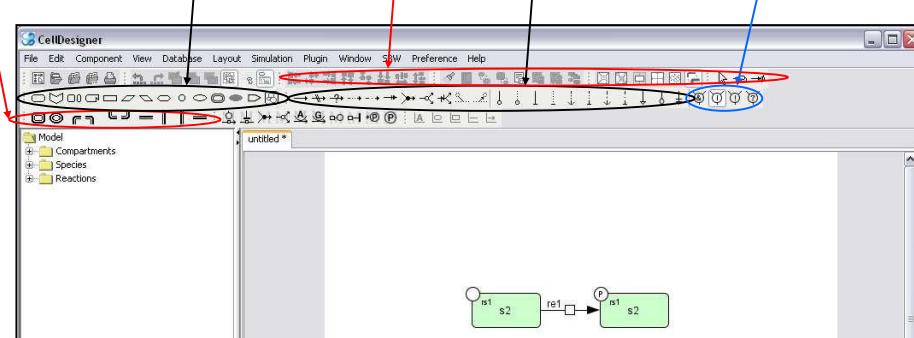
- Tree:** A panel on the left showing a hierarchical tree structure of model components: Model > Compartments > Species > Reactions.
- Drawing:** The main workspace where models are built using tools from the toolbar.
- Layer:** A panel showing the current layer structure, which is currently set to "base".
- Notes:** A panel for managing component notes, with tabs for Species, Proteins, Genes, RNAs, siRNAs, Reactions, Compartments, and Parameters.

Take some time to explore the menu. Check the glyphs, the arcs and the macros. Highlighted below the Compartment menu, the chemical species menu, the visualization menu, the reaction menu and the Boolean gates menu.



The menu

Compartment menu
Chemical species menu
Visualization menu
Reaction menu
Boolean logic menu



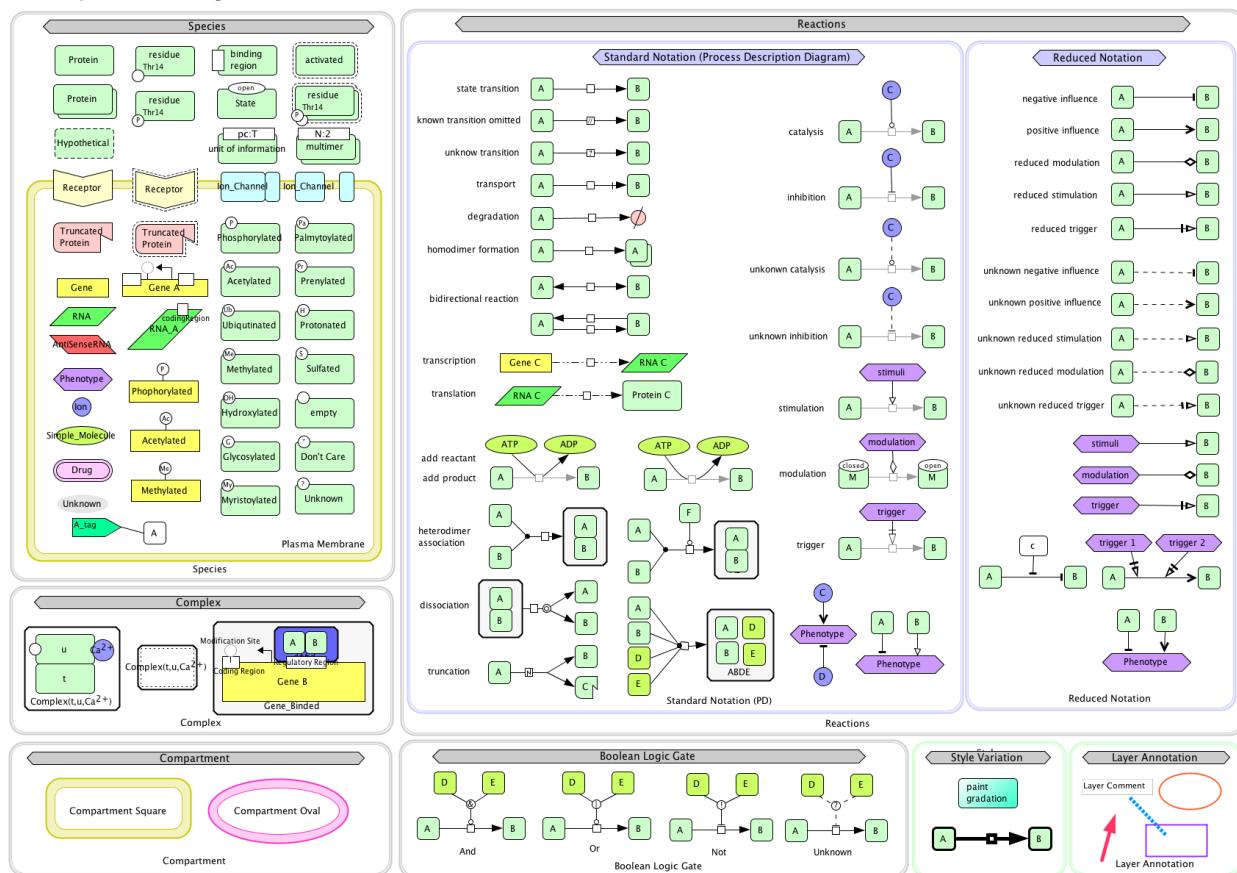
The screenshot shows the CellDesigner interface with the following menu bar:

- File
- Edit
- Component
- View
- Database
- Layout
- Simulation
- Plugin
- Window
- Help

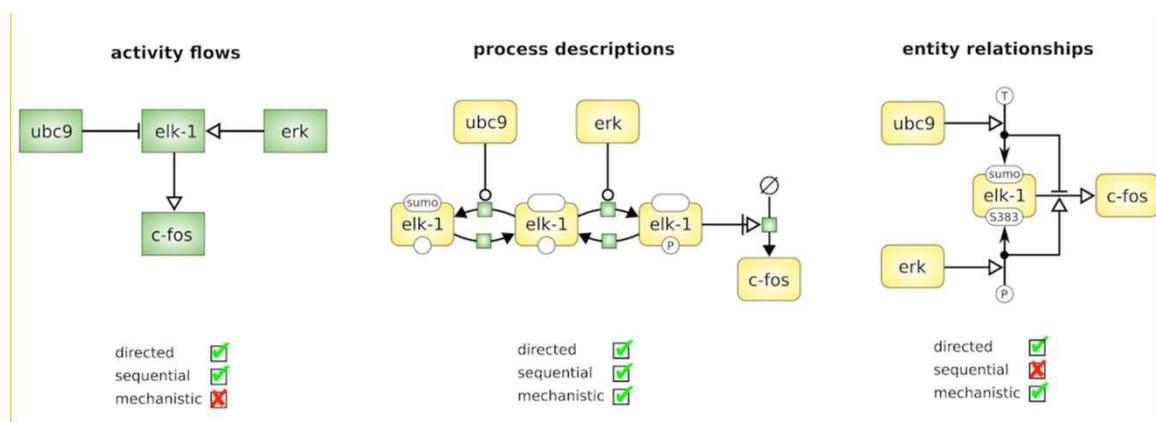
Below the menu bar, specific menus are highlighted with red arrows:

- Compartment menu (highlighted in red)
- Chemical species menu (highlighted in red)
- Visualization menu (highlighted in red)
- Reaction menu (highlighted in red)
- Boolean logic menu (highlighted in blue)

Here is a summary of all schemas that can be used to create your diagram:
The software suite can accommodate different SBGN schemes such as Process Description or Activity Flow diagrams.

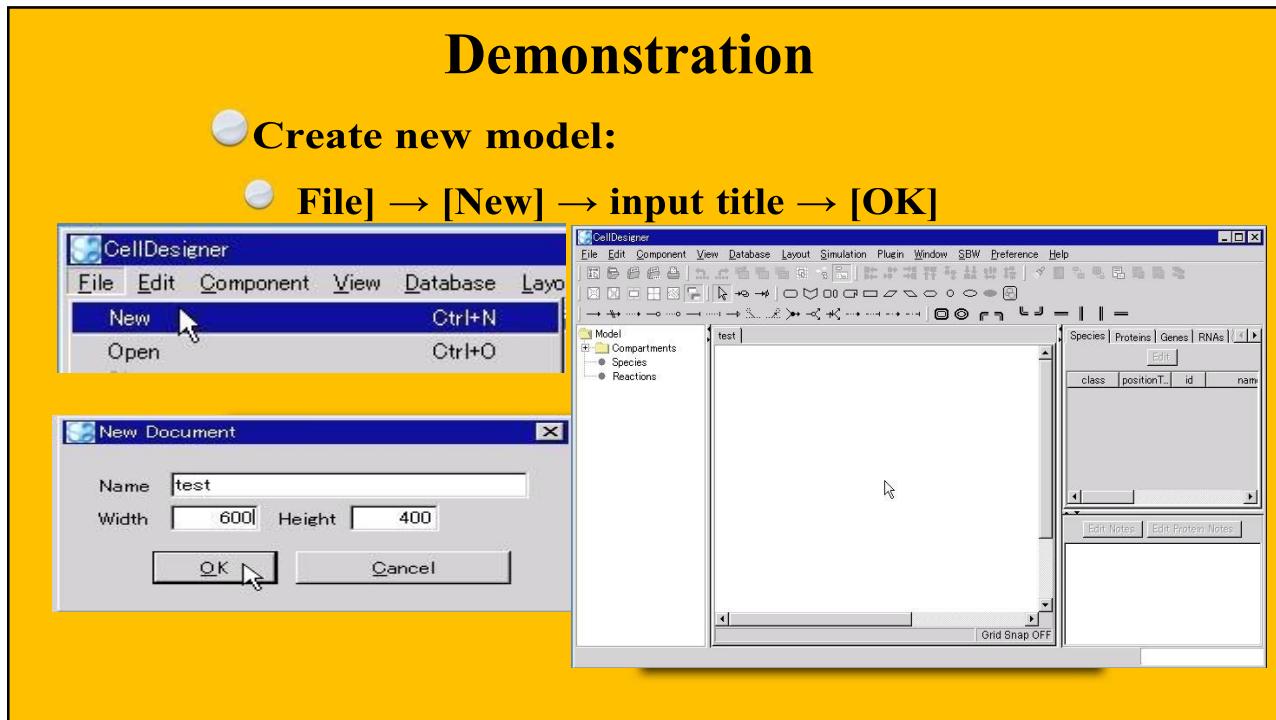


Can you make some comments about the reduced notation scheme? Here are the three different languages of SBGN to help you understand better.

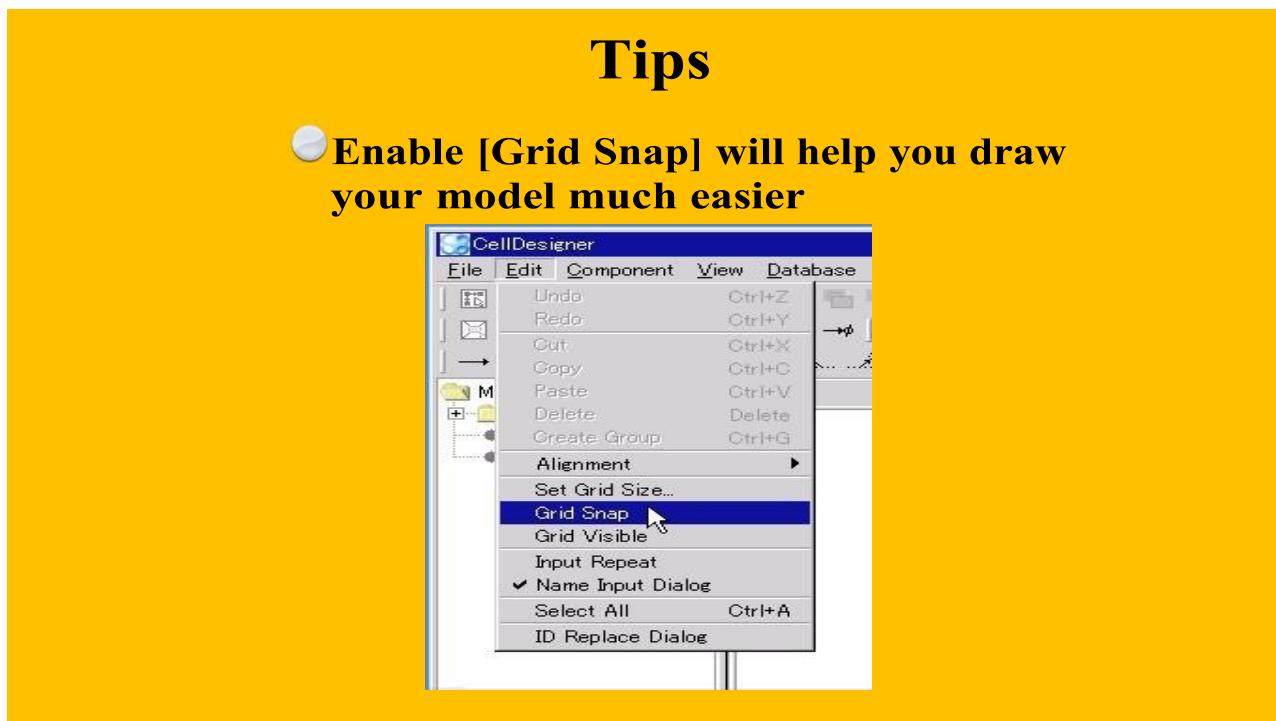


Let's start creating a diagram!

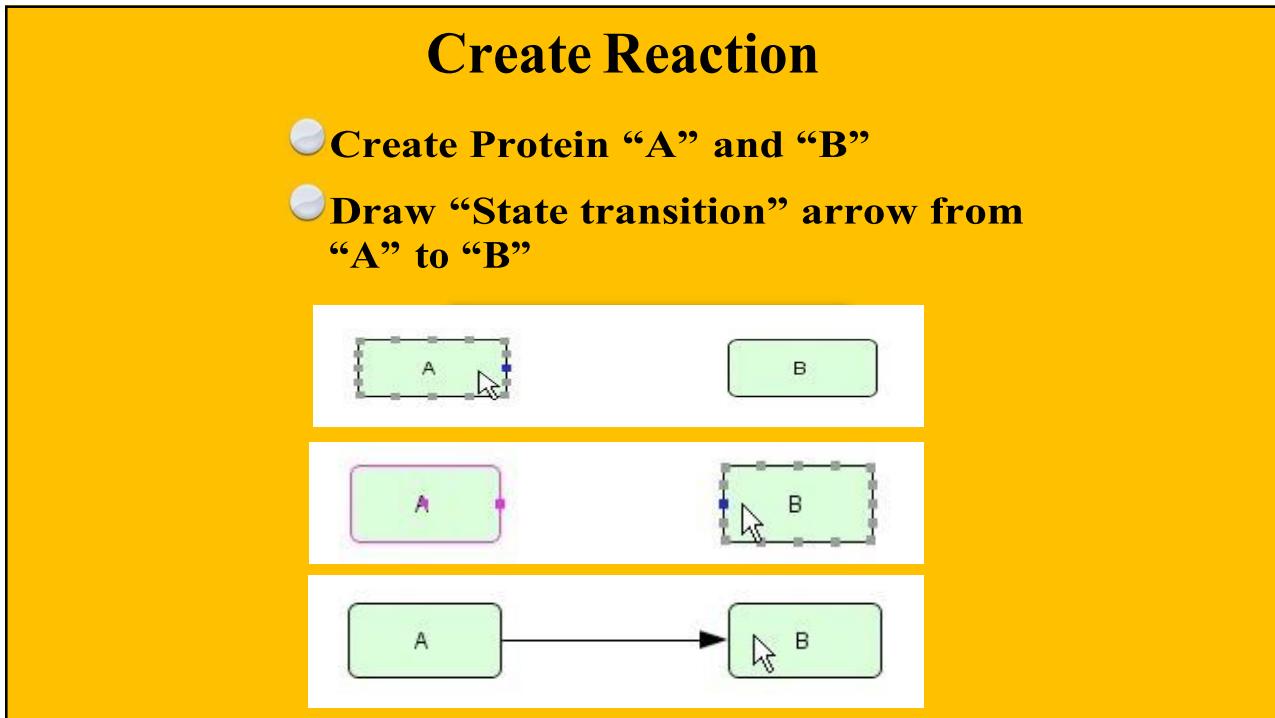
Click on File, then New, then write the title: test and click OK. We will use the default size settings.



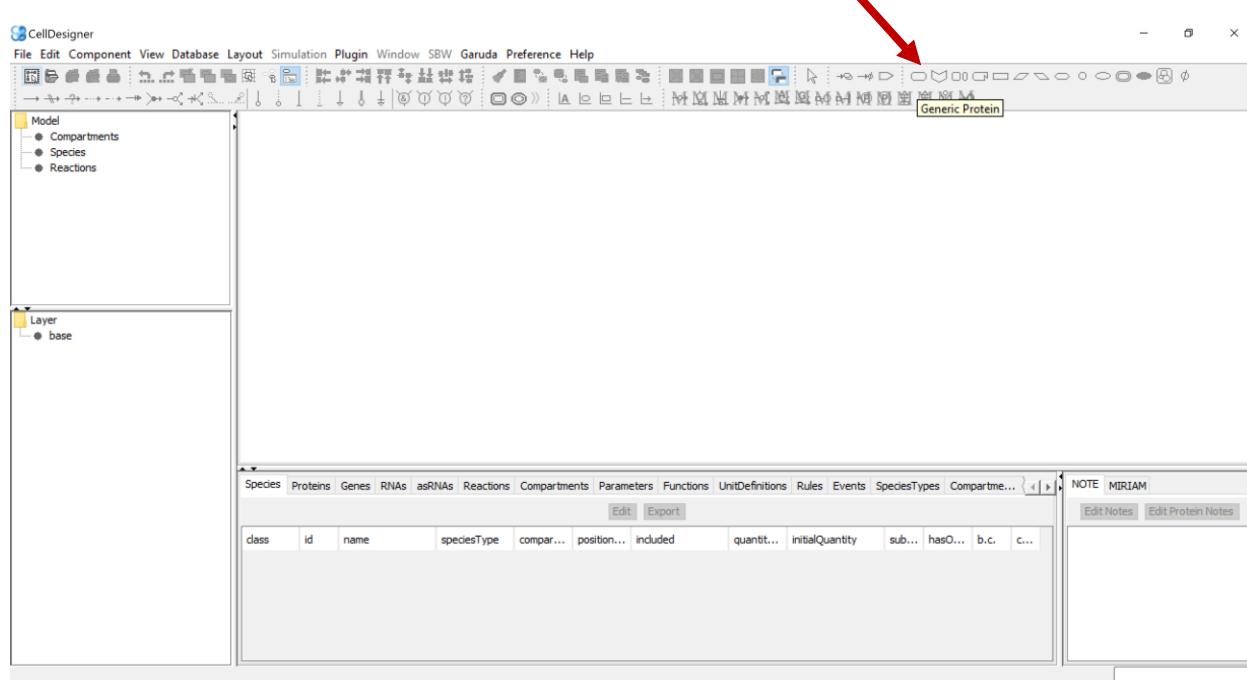
We will also enable the grid to help us draw more aligned diagrams. To do so, we will click on Edit in the Menu bar and then on Grid Snap as seen in the screenshot below:



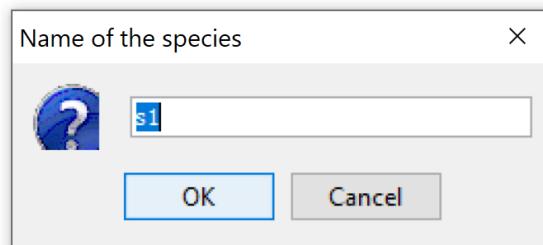
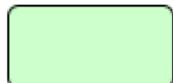
Now we are ready to create our first reaction!



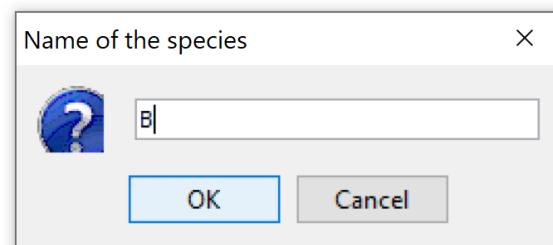
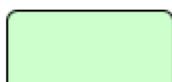
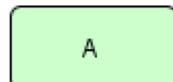
Choose from the glyph menu a generic protein :



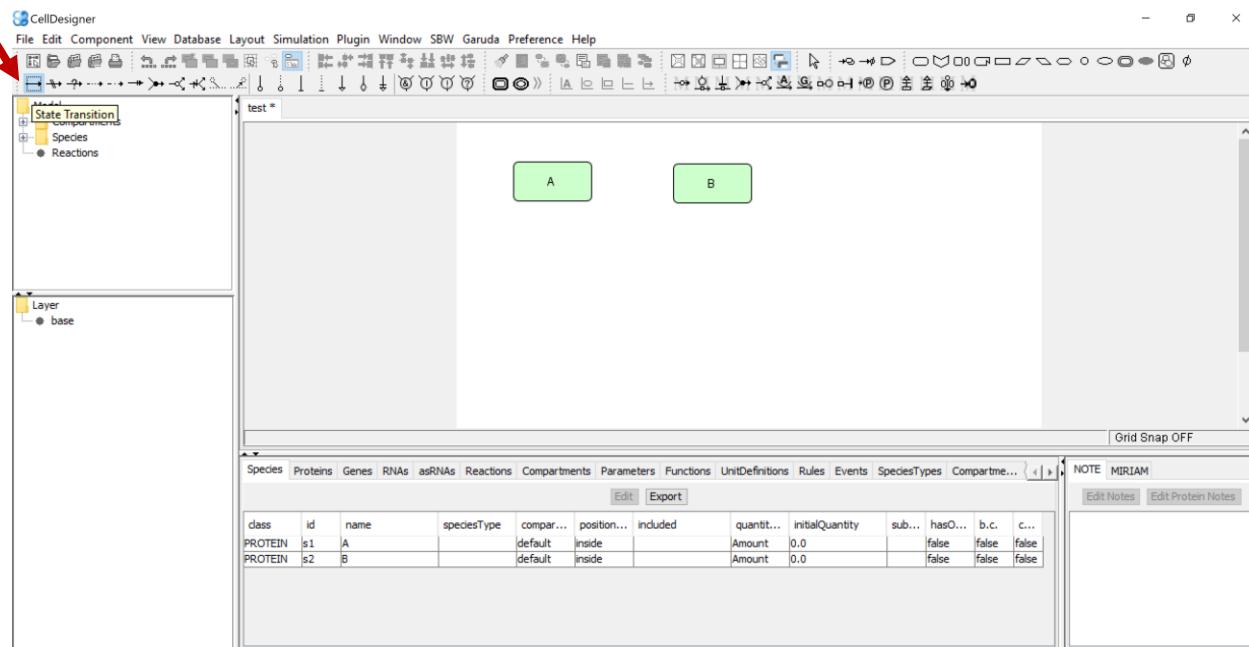
and then click on the window of the drawing space. Name the protein A.



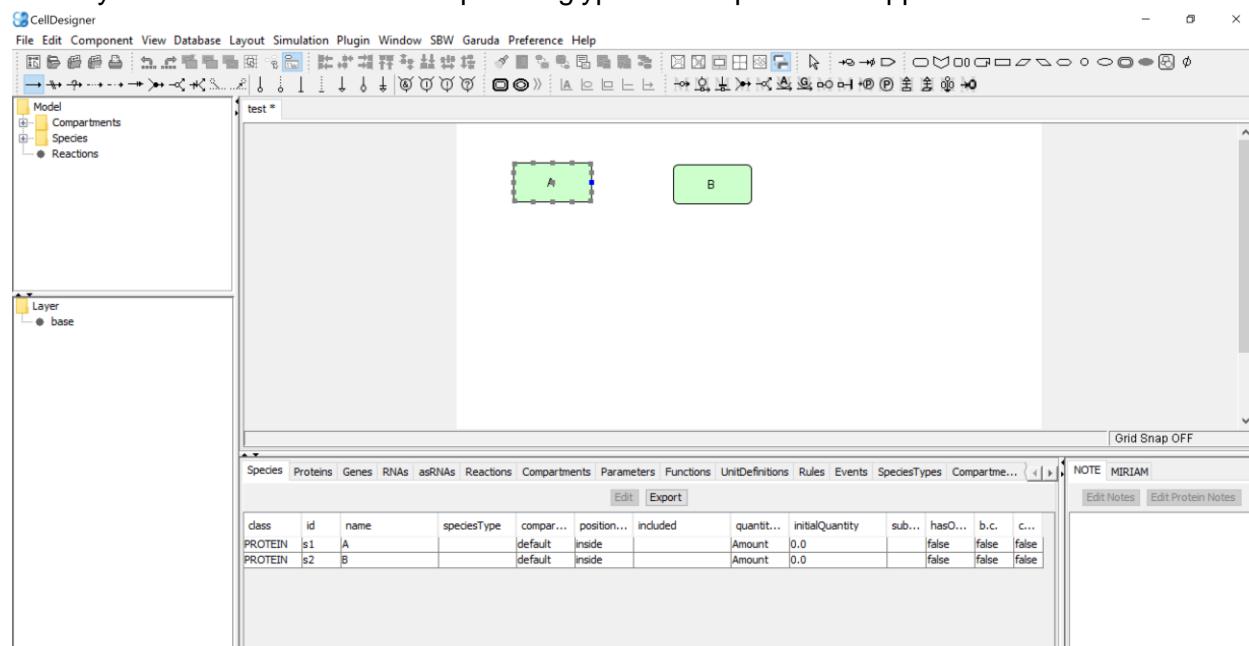
Repeat and name the protein B:



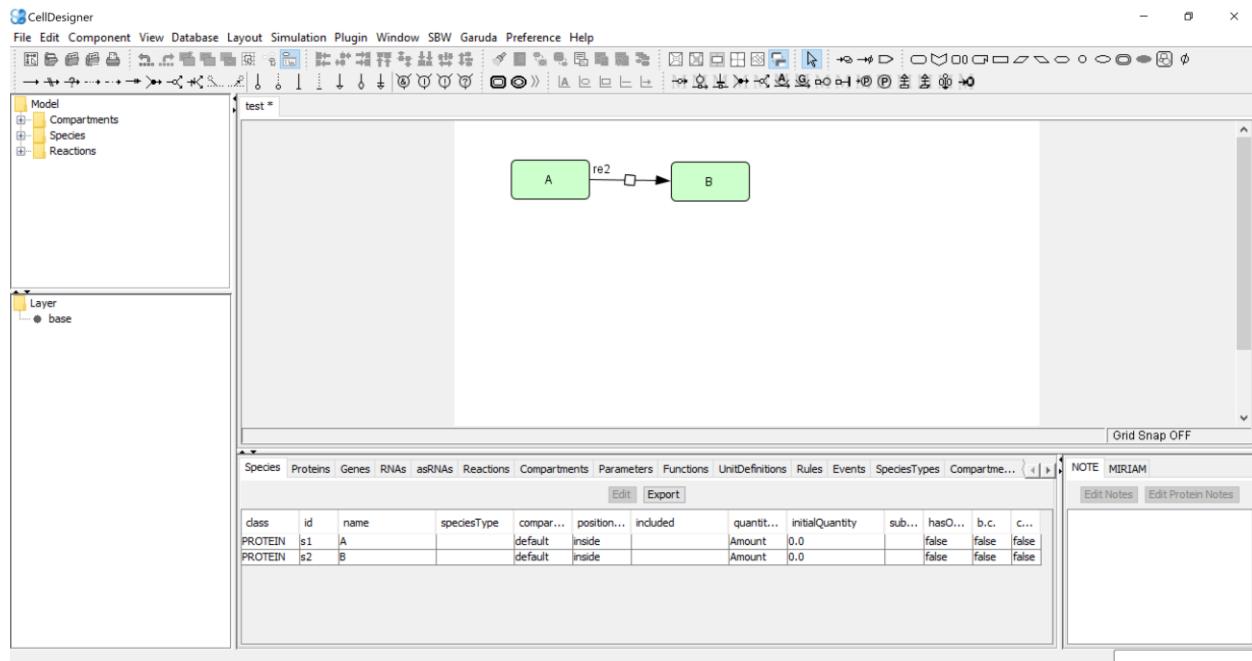
Then click on the state transition arrow



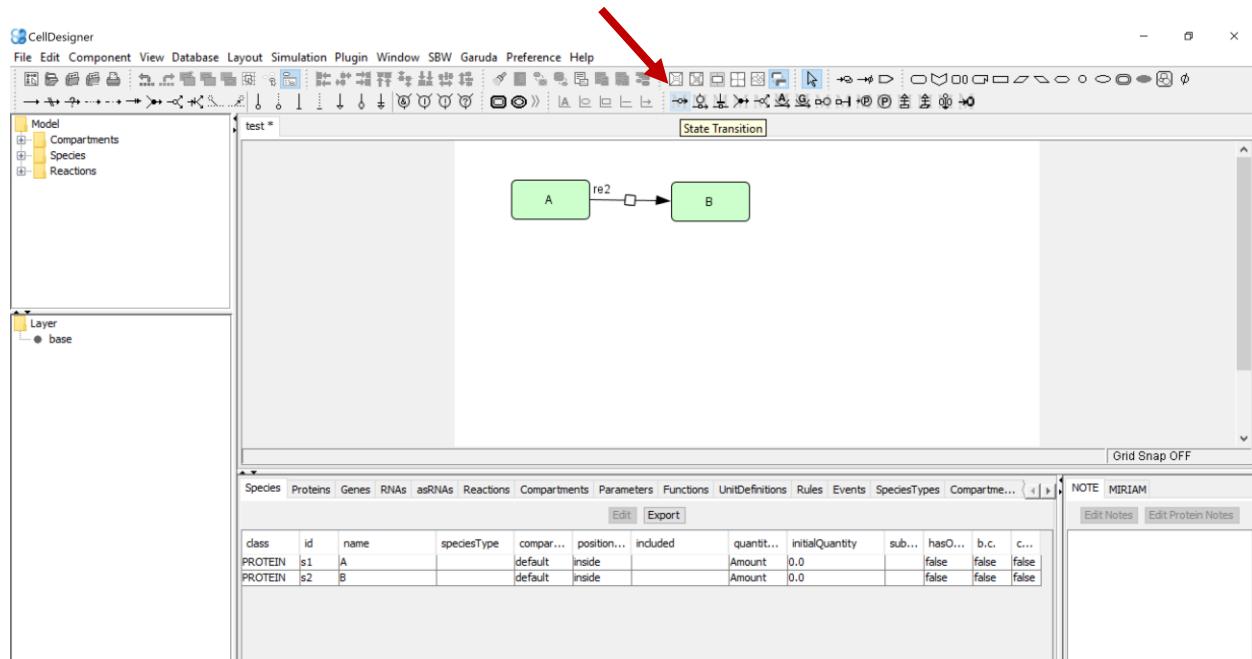
When you move the cursor on the protein glyph anchor points will appear.



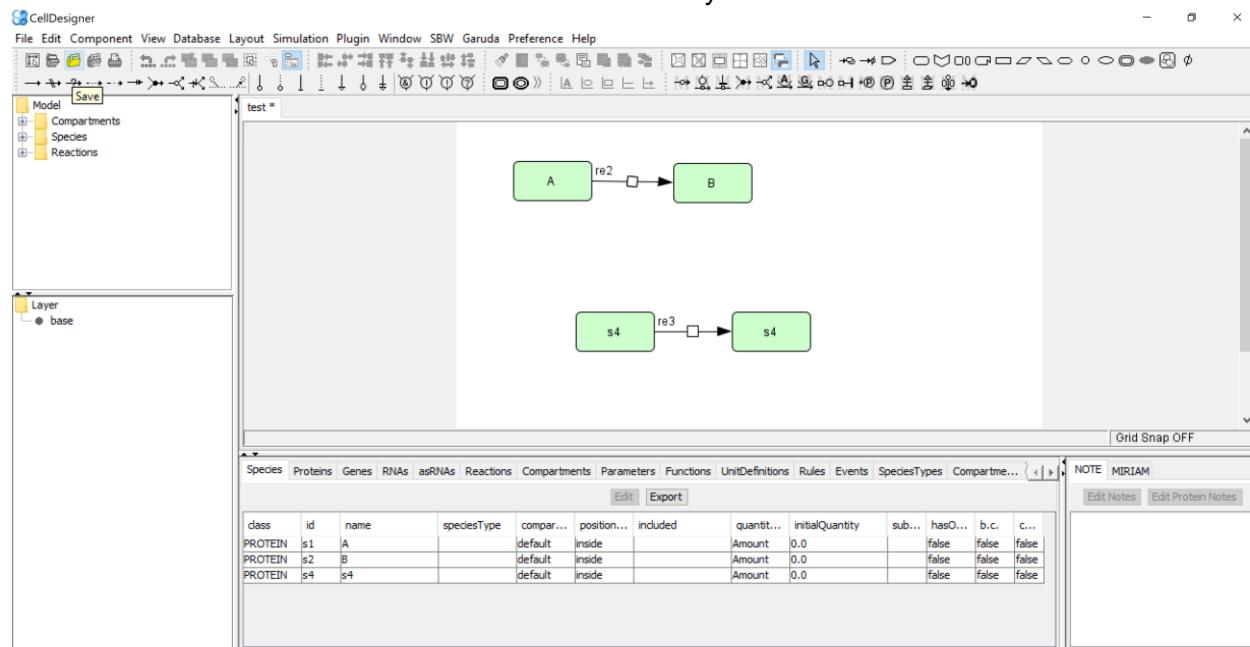
Choose the middle on the right on protein A, click and then choose the middle on the left of protein B and click again to have your arrow drawn.



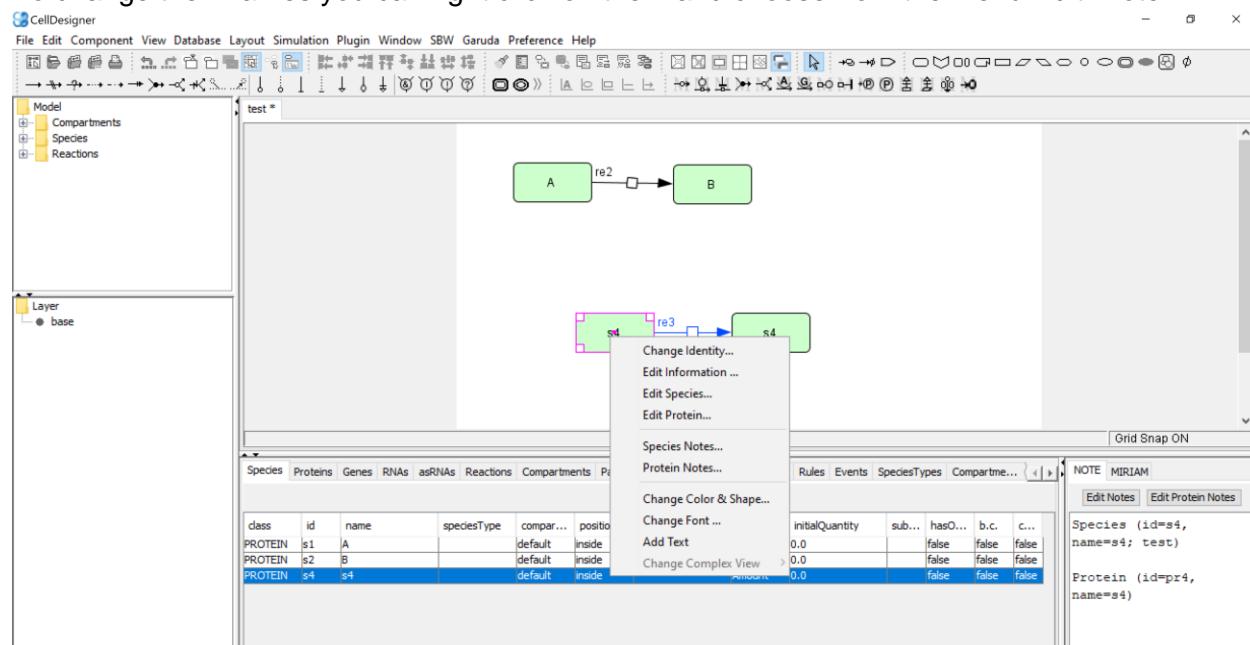
Notice that you can use macros to draw this reaction automatically. Choose the state transition from the macros menu and then click on the drawing space just below the reaction you created:



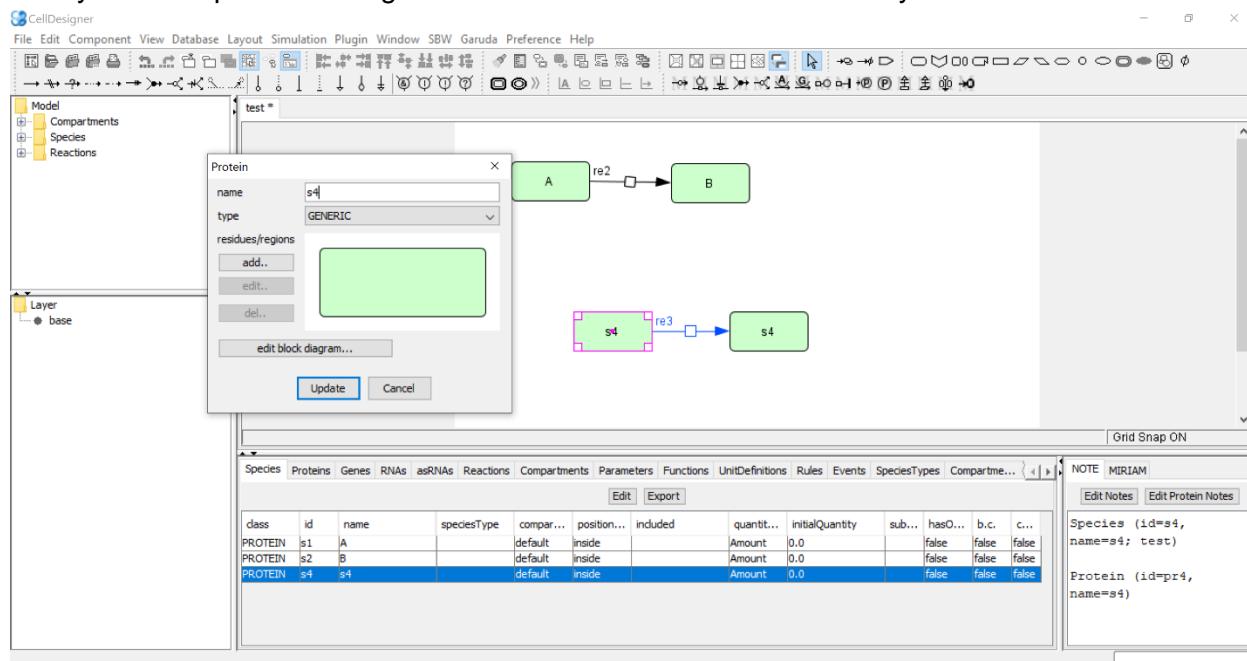
A state transition reaction is now created automatically:



To change their names you can right click on them and choose from the menu Edit Protein



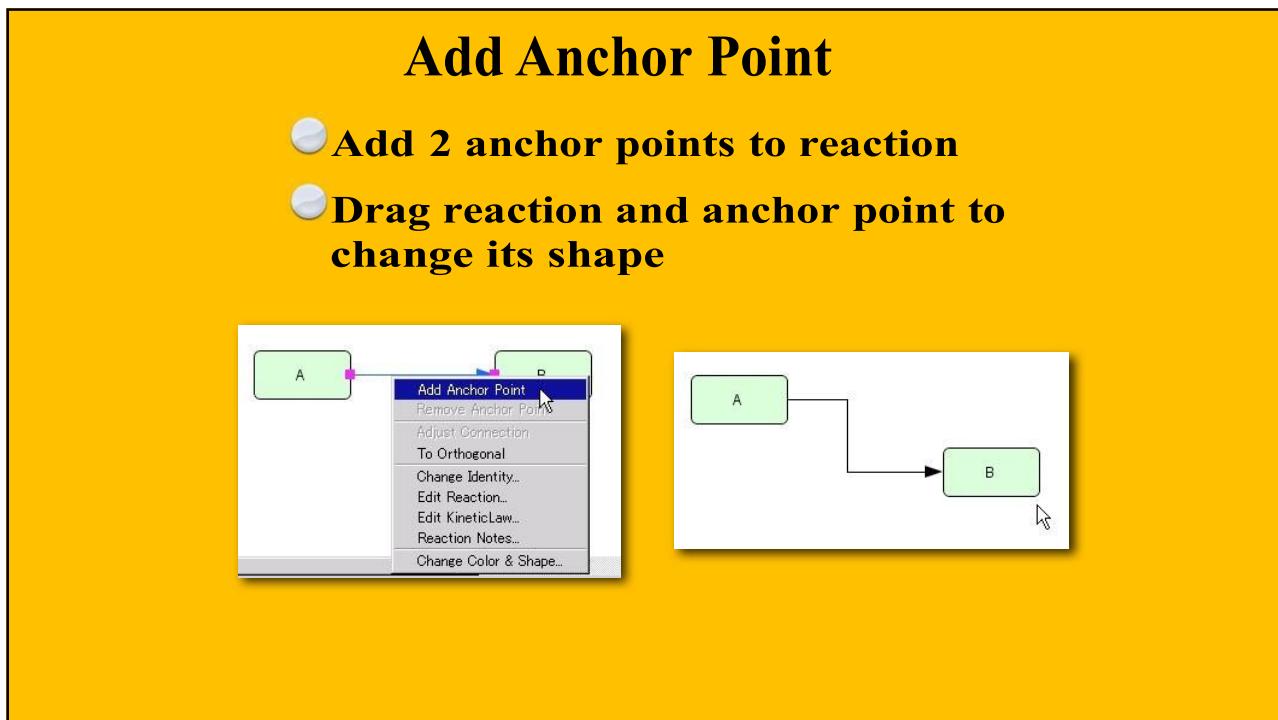
Now you can replace the s4 generic name with C or whatever name you want. You can name it



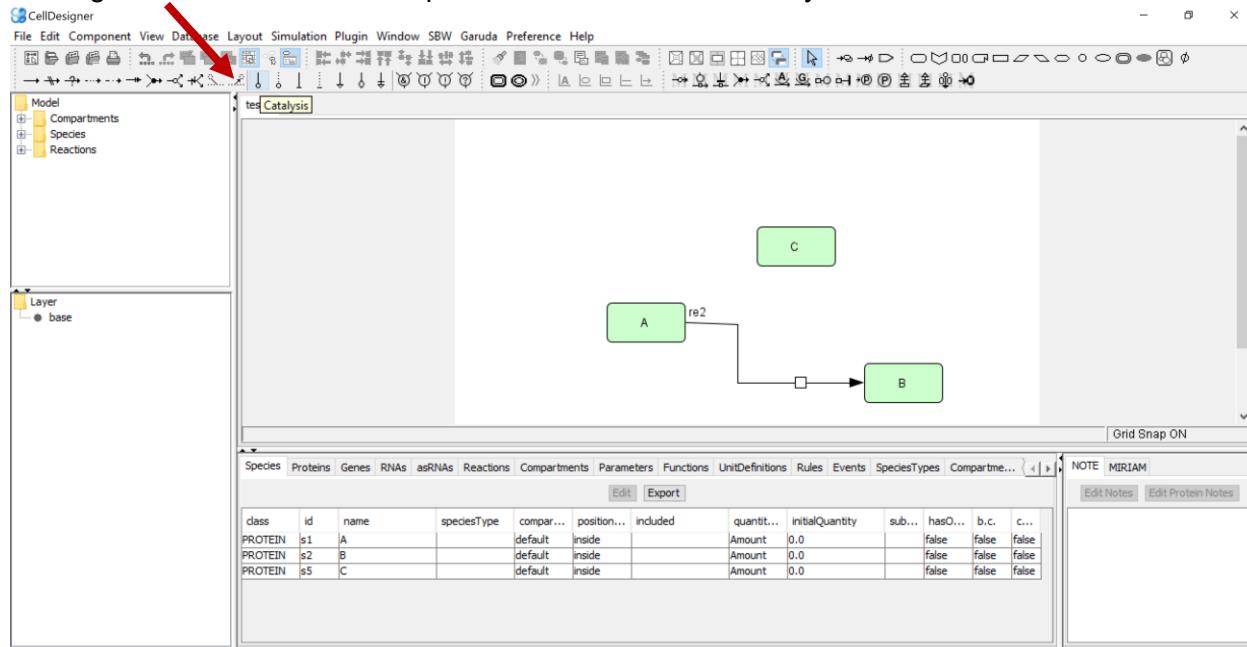
IL6.

What do you observe?

We can also add anchor points:

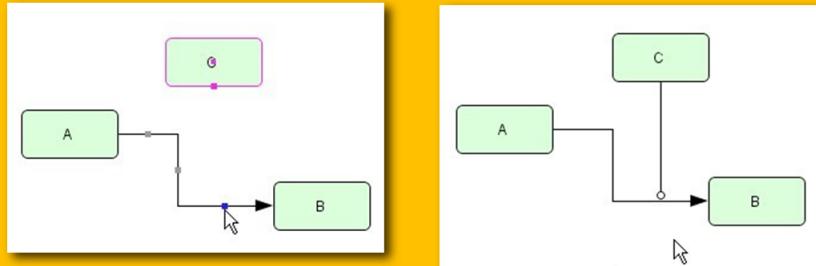


Now let us try to add a protein that has a positive effect (catalyzes) the reaction we created previously. We would need to select a generic protein, click on the drawing space, and then change its name. The next step would be to select the catalysis arrow and add it:



Add Catalysis reaction

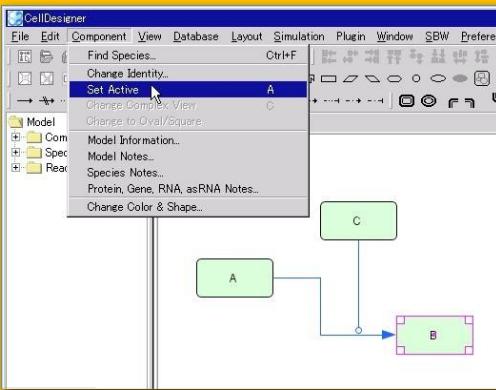
- ➊ Add Protein “C”
- ➋ Add Catalysis reaction from “C” to the reaction

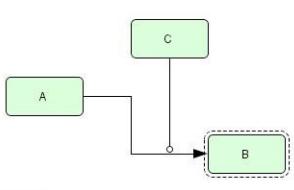


In CellDesigner you can use dots to indicate an active state, however, this notation is not used in SBGN language

Set Active state

- Select Protein “B”
- [Component] → [SetActive]





```
graph LR; A[A] --> B[B]
```

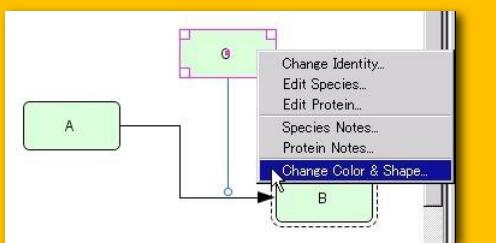


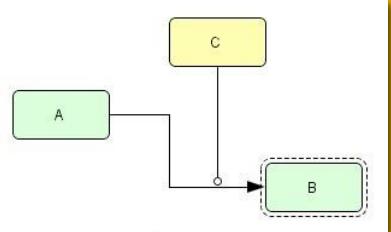
```
graph LR; A[A] --> B[B]
```

You can also change the color by right clicking on the element.

Change Color

- Right click on Protein “C”
- Select [Change Color & Shape...]





```
graph LR; A[A] --> B[B]
```

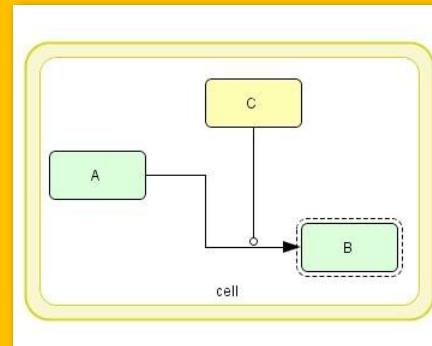


```
graph LR; A[A] --> B[B]
```

Adding compartments is also important:

Compartment

- ➊ Click [Compartment] icon 
- ➋ Drag mouse cursor to specify its area
- ➌ Input name of compartment

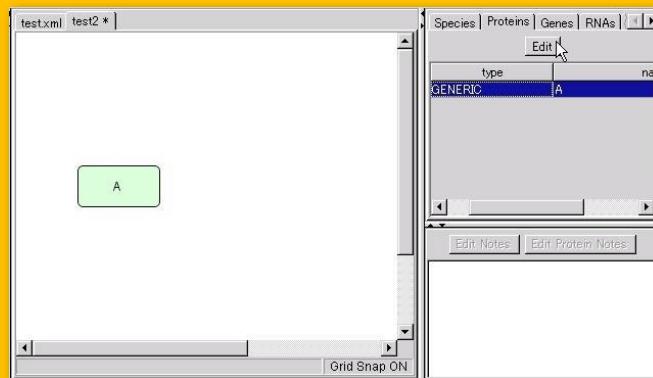


Practice makes perfect !

The following exercises in pages 15 – 18 are for practice at home – let's go to page 19 and connect to databases!

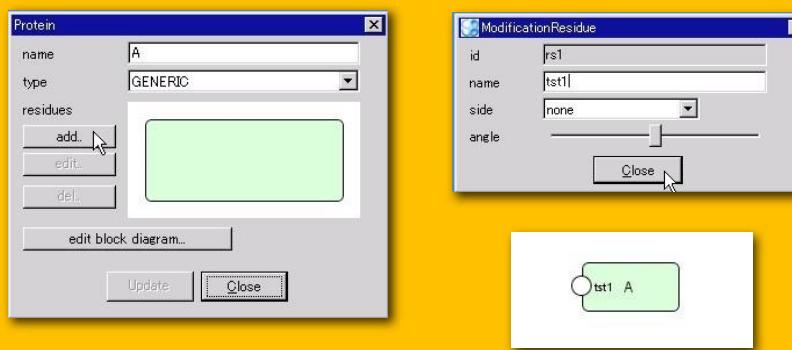
Add Residue to Protein

- Create new model (test2)
- Create Protein “A”
- Select Protein “A” in [Proteins] Tab
- Click [Edit] button



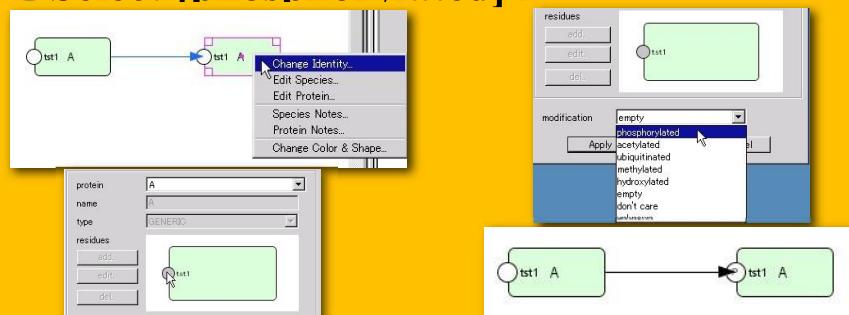
Add Residue to Protein

- Click [add] button on [Protein] dialog
- Input name for the residue (tst1)
- Click [Close] button
- Click [Update] Button



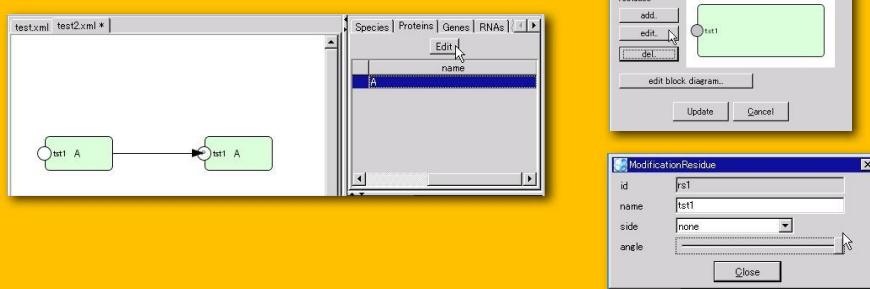
Add Residue to Protein

- ➊ Copy & Paste Protein “A” and then draw “State Transition” arrow
- ➋ Right Click on “A” (right side) and select [Change Identity..]
- ➌ Click residue “tst1” in Dialog
- ➍ Select [phosphorylated] in modification



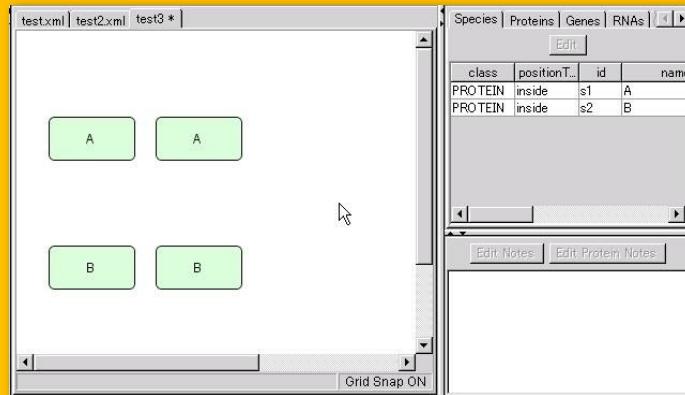
Change position of Residue

- ➊ Select Protein “A” in [Proteins] Tab
- ➋ Click [Edit] button
- ➌ Click residue “tst1” in Dialog
- ➍ Click [edit] button
- ➎ Drag [angle] sidebar



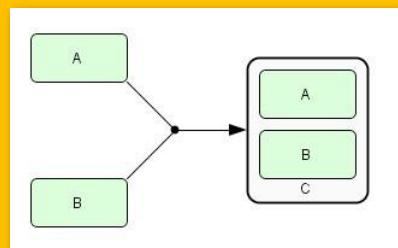
Complex

- Create new model (test3)
- Create Proteins “A” and “B”
- Copy & Paste both “A” and “B”



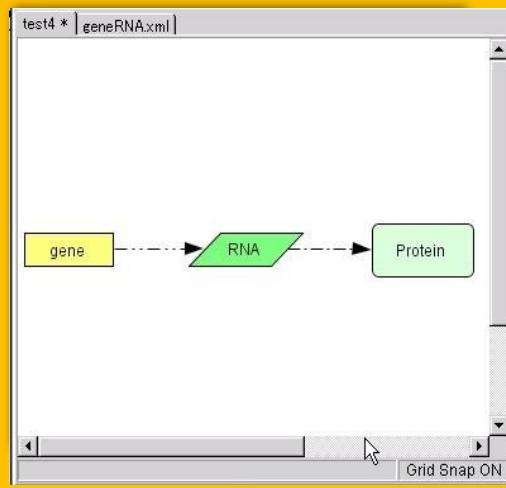
Complex

- Click [Complex] icon and create complex “C”
- 
- Drag Protein “A” and “B” into complex C
 - Draw “Association” arrow

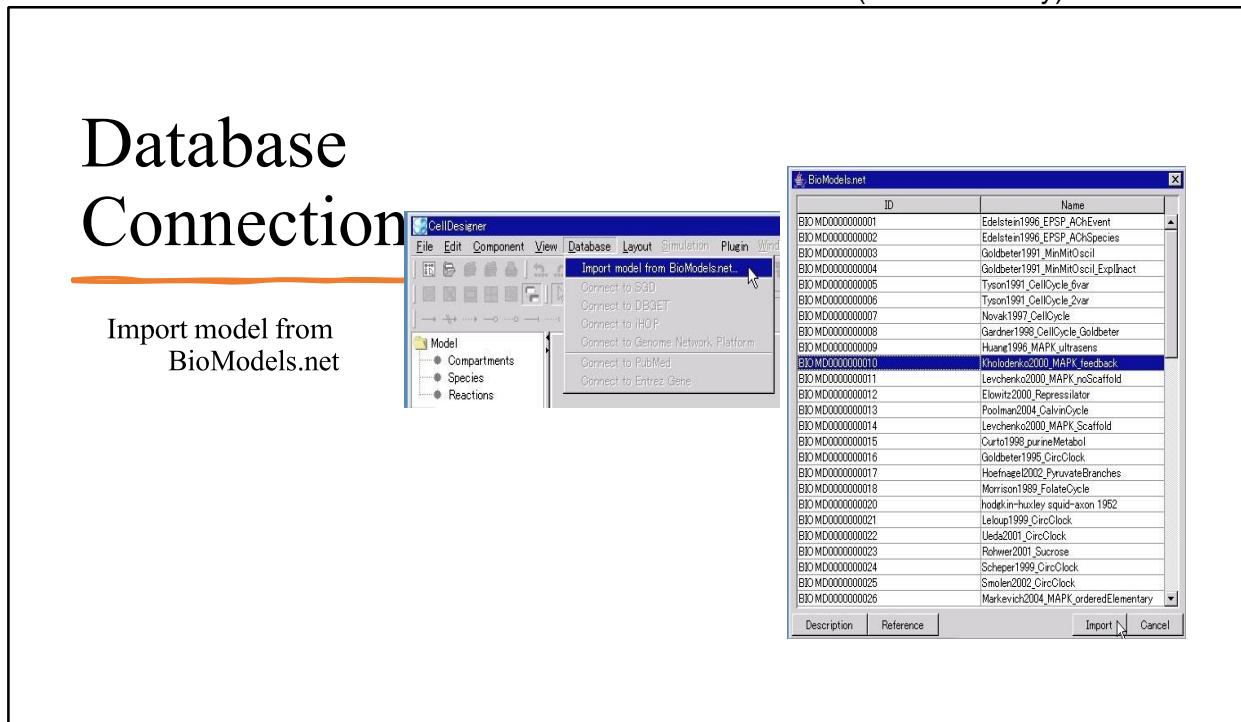


Gene & RNA

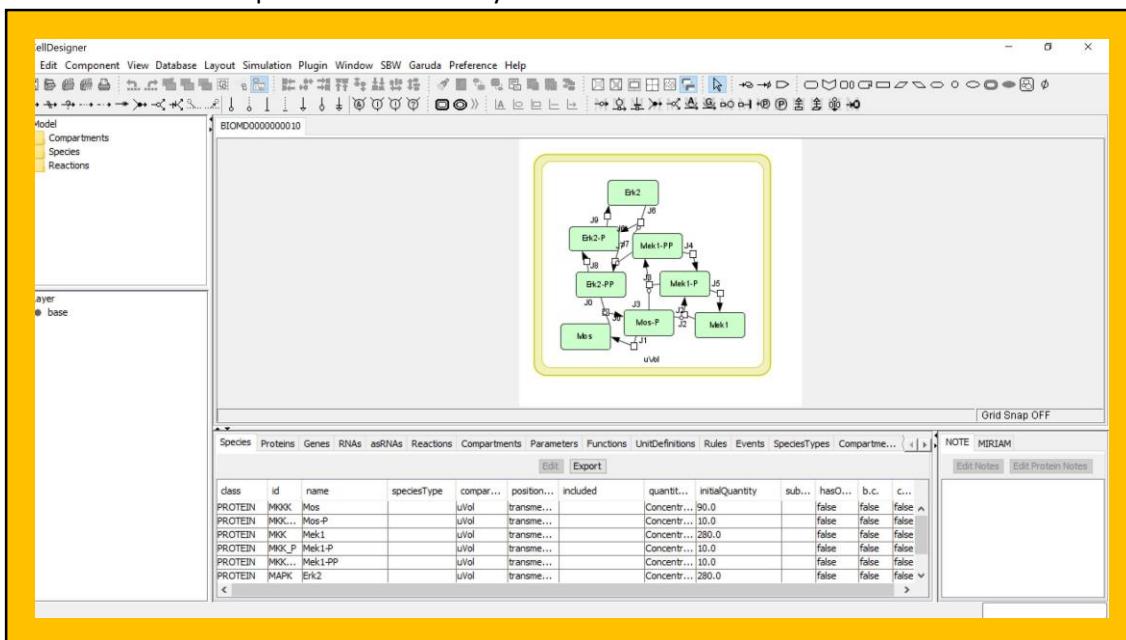
- Create new model (test4)
- Create gene, RNA and Protein
- Draw “Transcription” and “Translation”



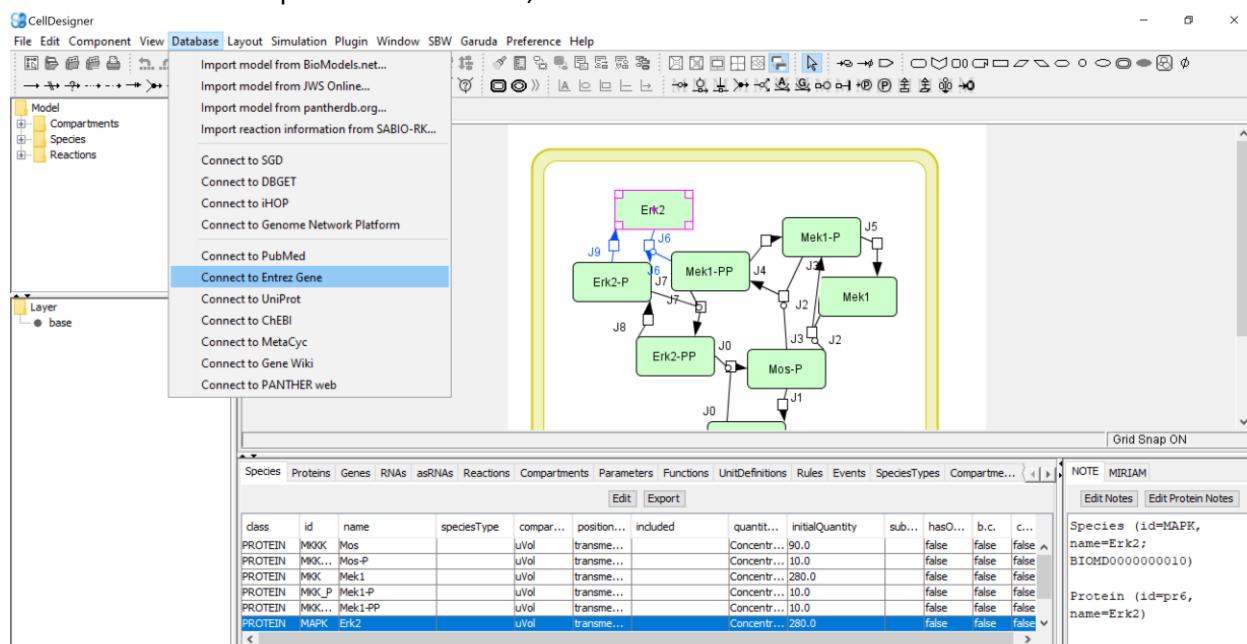
Welcome! Let's see how we can import a model from a database! Start from a clean slate! Create a new model (File, New etc). Then click on the Database tab of the Menu and select a model from BioModels. Here we have selected the MAPK model of Kholodenko (Ultrasensitivity).



The model is then imported automatically! Take some time to observe it!



Now click on the ERk2 protein of the model, then click on Databases and select Connect to Entrez Gene



CellDesigner

File Edit Component View Database Layout Simulation Plugin Window SBW Garuda Preference Help

Import model from BioModels.net...
Import model from JWS Online...
Import model from pantherdb.org...
Import reaction information from SABIO-RK...

Connect to SGD
Connect to DBGET
Connect to iHOP
Connect to Genome Network Platform

Connect to PubMed
Connect to Entrez Gene (highlighted)
Connect to UniProt
Connect to ChEBI
Connect to MetaCyc
Connect to Gene Wiki
Connect to PANTHER web

Layer
base

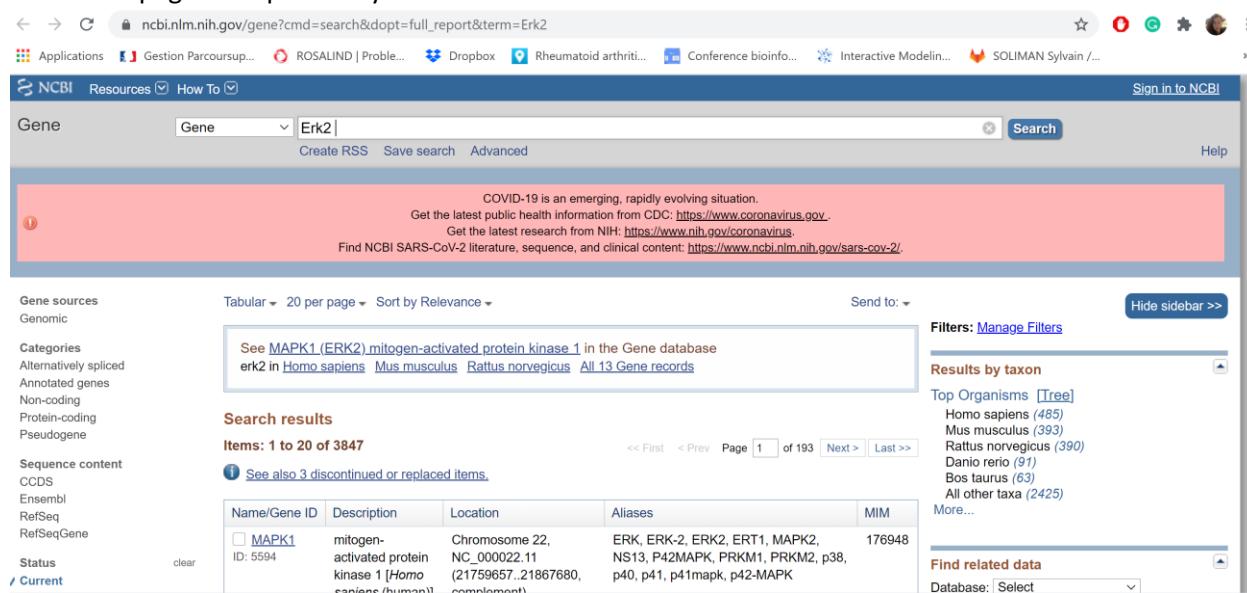
Species Proteins Genes RNAs asRNAs Reactions Compartments Parameters Functions UnitDefinitions Rules Events SpeciesTypes Compartme... [Edit](#) [Export](#)

class	id	name	speciesType	compar...	position...	included	quantit...	initialQuantity	sub...	hasO...	b.c.	c...
PROTEIN	M9KK	Mos		uVol	transme...		Concentr...	90.0		false	false	▲
PROTEIN	M9KK...	Mos-P		uVol	transme...		Concentr...	10.0		false	false	▲
PROTEIN	MKK	Mek1		uVol	transme...		Concentr...	280.0		false	false	▲
PROTEIN	MKK_P	Mek1-P		uVol	transme...		Concentr...	10.0		false	false	▲
PROTEIN	M9KK...	Mek1-PP		uVol	transme...		Concentr...	10.0		false	false	▲
PROTEIN	MAPK	Erk2		uVol	transme...		Concentr...	280.0		false	false	▼

NOTE MIRIAM
Edit Notes Edit Protein Notes

Species (id=MAPK, name=Erk2; BIOMD0000000010)
Protein (id=pr6, name=Erk2)

A browser page will open and you will be transferred to the Entrez Gene database site:



ncbi.nlm.nih.gov/gene/?cmd=search&dopt=full_report&term=Erk2

Applications Gestion Parcoursup... ROSALIND | Proble... Dropbox Rheumatoid arthriti... Conference bioinfo... Interactive Modelin... SOLIMAN Sylvain / ...

NCBI Resources How To

Gene Gene Search

Gene sources Genomic

Categories Alternatively spliced Annotated genes Non-coding Protein-coding Pseudogene

Sequence content CCDS Ensembl RefSeq RefSeqGene

Status Current clear

Tabular 20 per page Sort by Relevance Send to: Hide sidebar >>

See MAPK1(ERK2) mitogen-activated protein kinase 1 in the Gene database
erk2 in Homo sapiens Mus musculus Rattus norvegicus All 13 Gene records

Search results Items: 1 to 20 of 3847 << First < Prev Page 1 of 193 Next > Last >>

See also 3 discontinued or replaced items.

Name/Gene ID	Description	Location	Aliases	MIM
<input type="checkbox"/> MAPK1 ID: 5594	mitogen-activated protein kinase 1 [Homo sapiens (human)]	Chromosome 22, NC_000022.11 (21759657..21867680, complement)	ERK, ERK-2, ERK2, ERT1, MAPK2, NS13, P42MAPK, PRKM1, PRKM2, p38, p40, p41, p41mapk, p42-MAPK	176948

Filters: Manage Filters

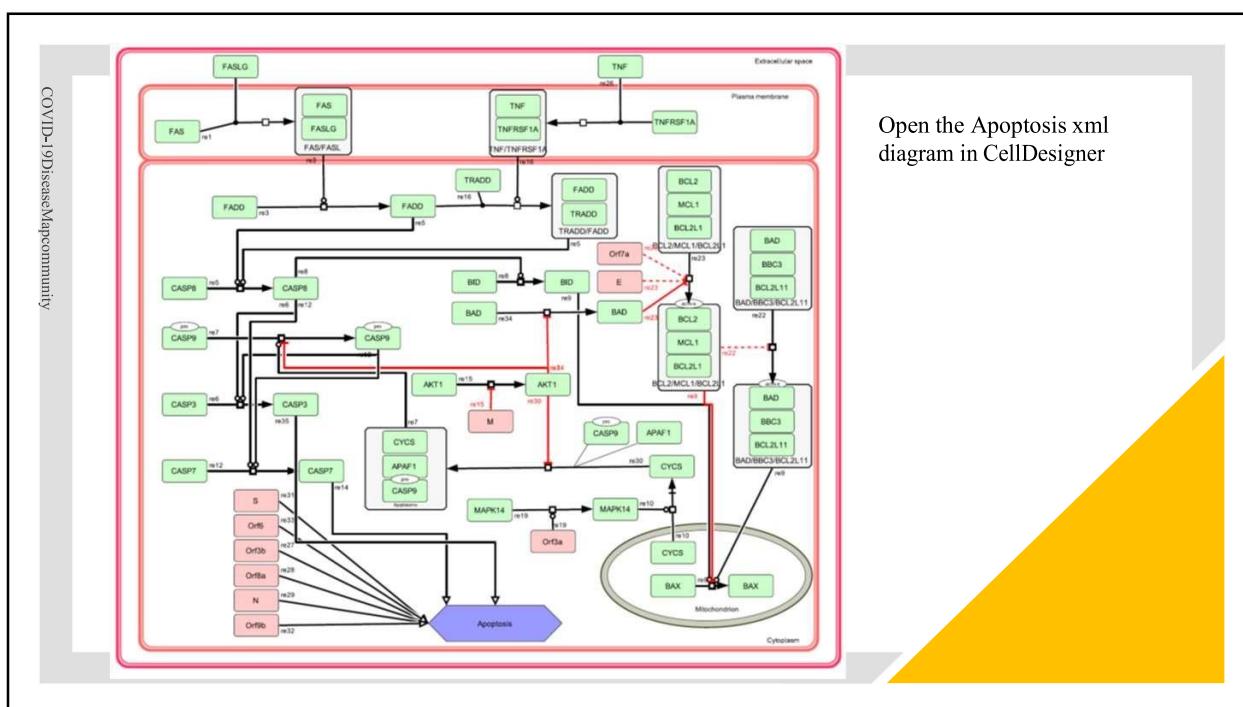
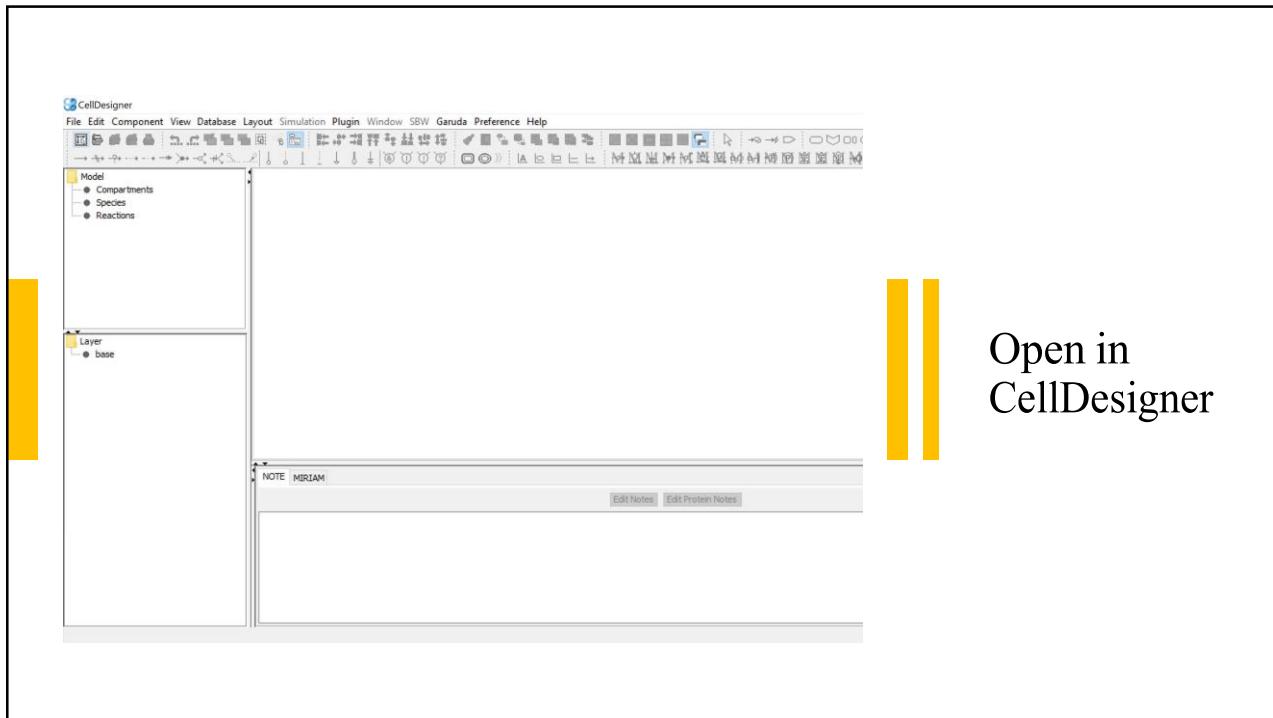
Results by taxon

Top Organisms [Tree](#)
Homo sapiens (485)
Mus musculus (393)
Rattus norvegicus (390)
Danio rerio (91)
Bos taurus (63)
All other taxa (2425)
More...

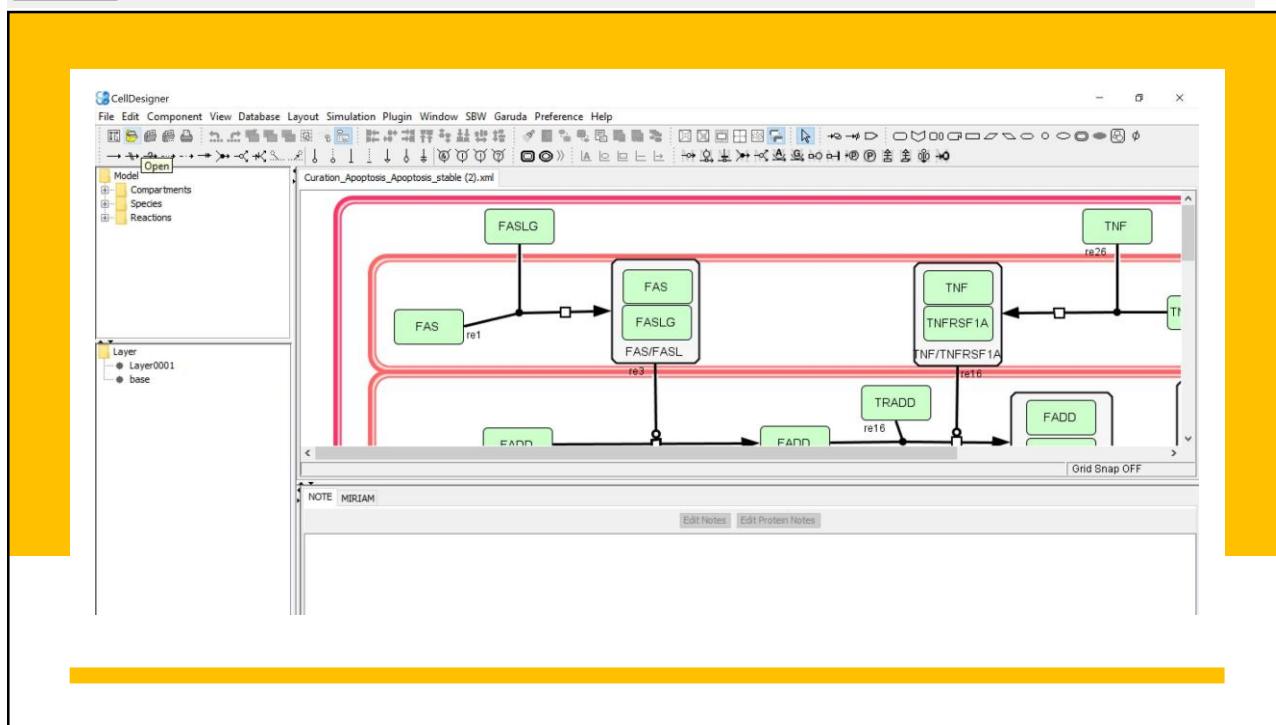
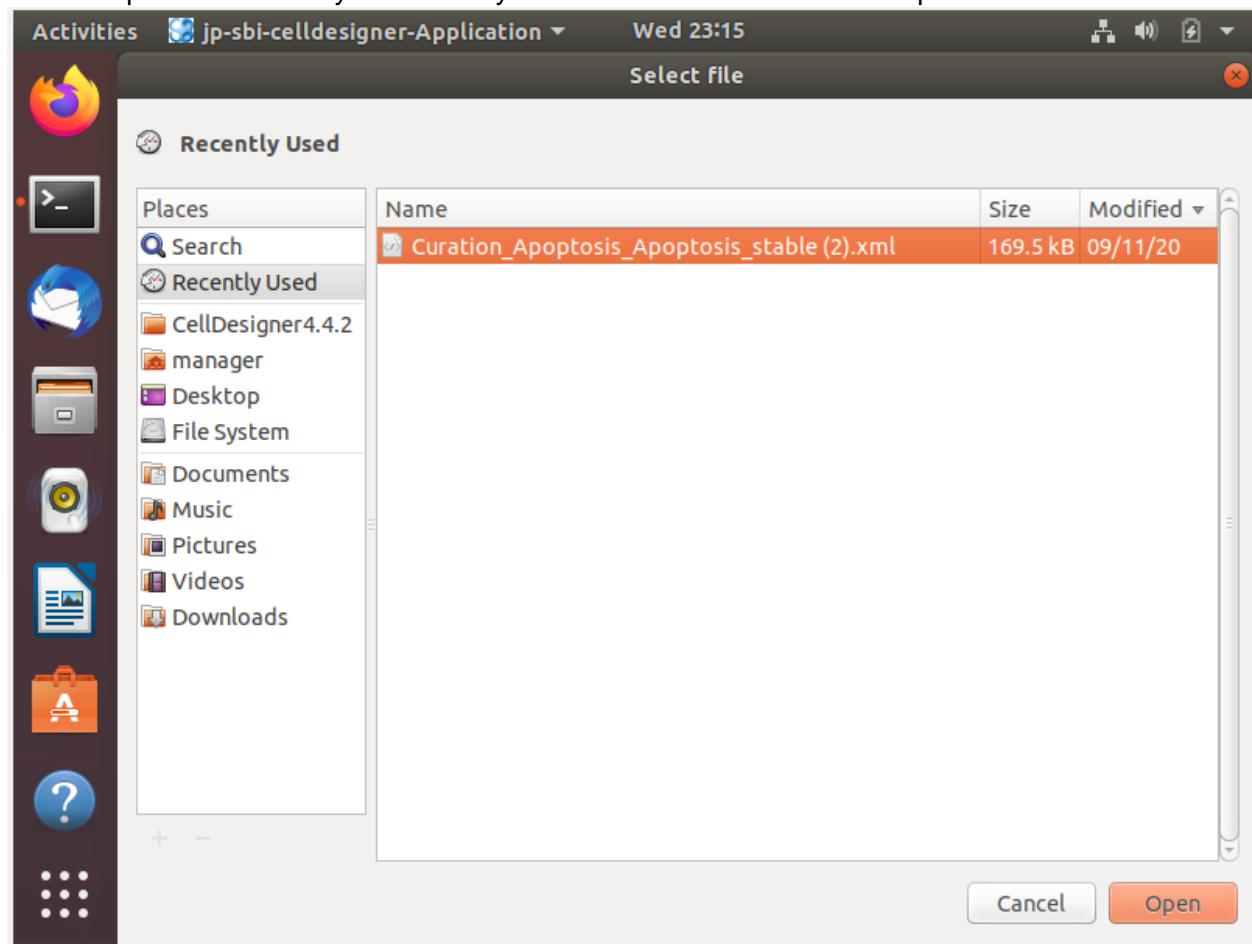
Find related data

Database: Select

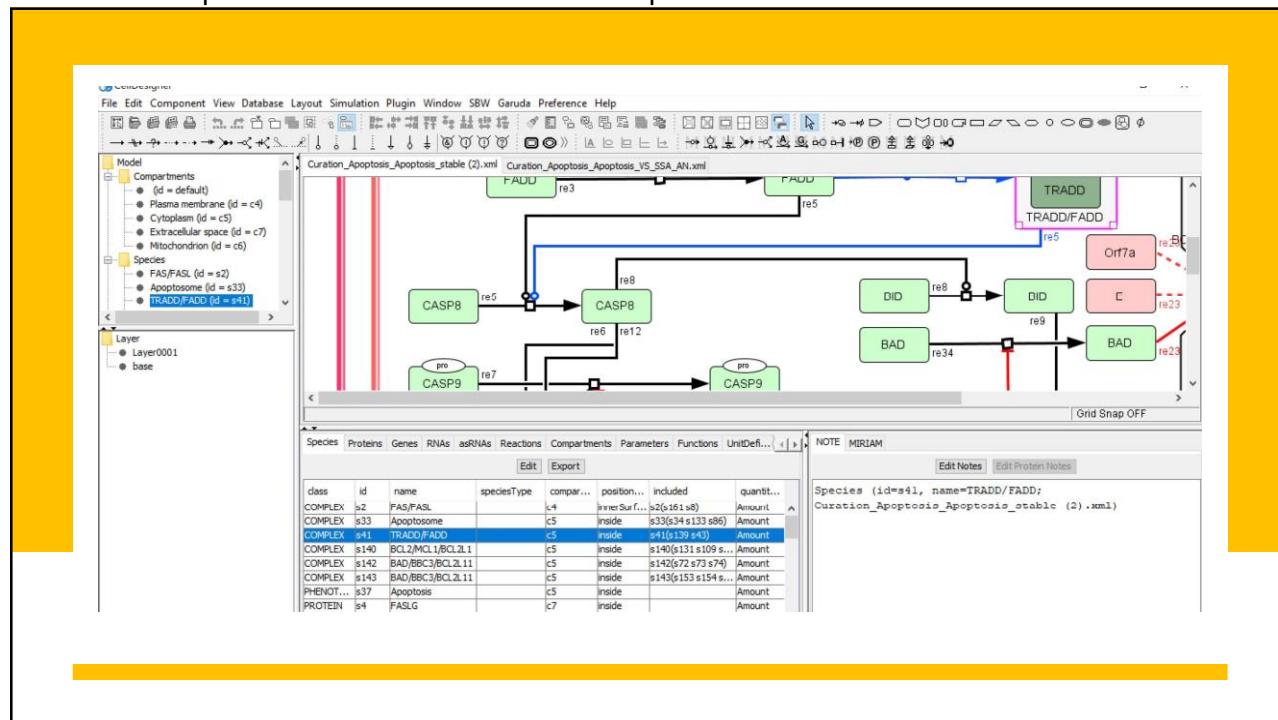
Bonus! Open in CellDesigner the xml file of the Apoptosis module form the COVID19 Disease Map repository. Take some time to observe the layout, the compartments, the species, the annotations. Click on elements and then connect to Entrez Gene or Pubmed to find relevant information!



File-> Open and search your directory to find the file! Here is an example:

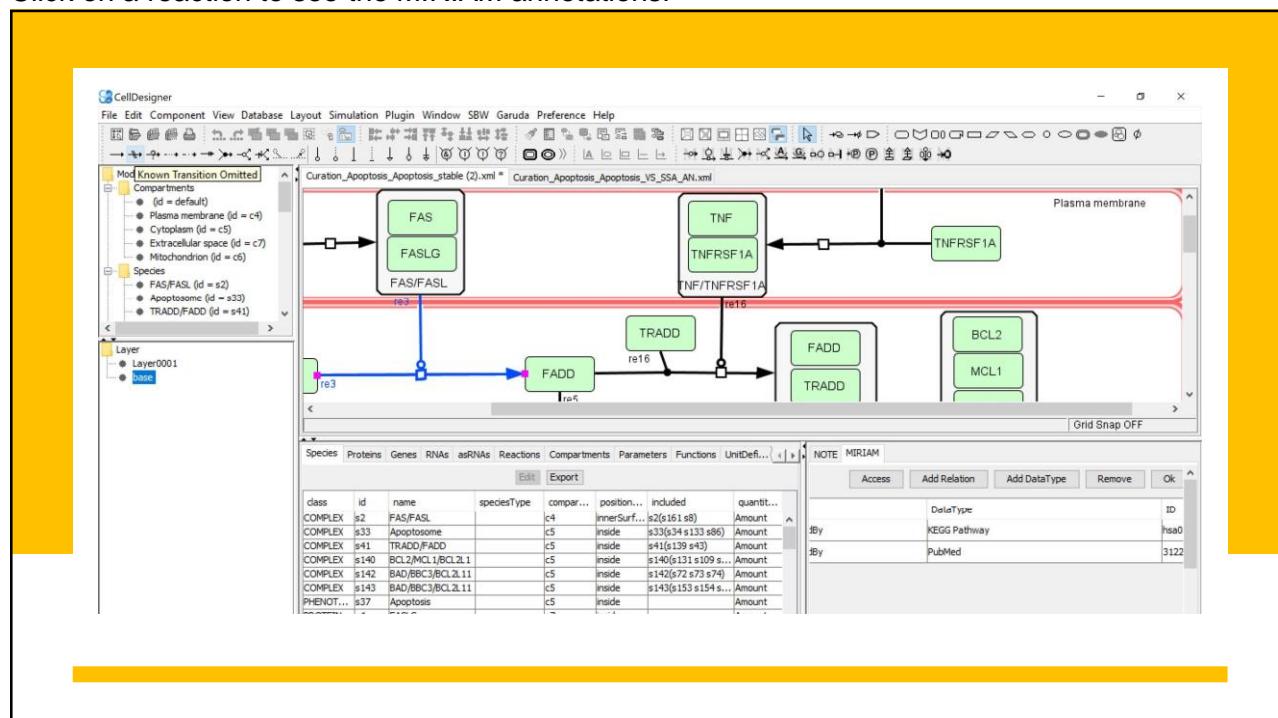


Click on a complex to see the information in the species tab



class	id	name	speciesType	compart...	position...	included	quantit...
COMPLEX	s2	FAS/FASL		c4	innerSurf...	s2(0 16 1 8)	Amount
COMPLEX	s33	Apoptosome		c5	inside	s33(5 34 5 133 8 6)	Amount
COMPLEX	s41	TRADD/FADD		c5	inside	s41(5 139 4 3)	Amount
COMPLEX	s140	BCL2/MCL1/BCL2L1		c5	inside	s140(5 131 5 109 ...)	Amount
COMPLEX	s142	BAD/BBC3/BCL2L11		c5	inside	s142(5 72 5 73 5 74)	Amount
COMPLEX	s143	BAD/BBC3/BCL2L11		c5	inside	s143(5 153 5 154 ...)	Amount
PHENOT...	s37	Apoptosis		c5	inside	s143(5 153 5 154 ...)	Amount
PROTEIN	s4	FASLG		c7	inside		Amount

Click on a reaction to see the MIRIAM annotations!



class	id	name	speciesType	compar...	position...	included	quantit...
COMPLEX	s2	FAS/FASL		c4	innerSurf...	s2(0 16 1 8)	Amount
COMPLEX	s33	Apoptosome		c5	inside	s33(5 34 5 133 8 6)	Amount
COMPLEX	s41	TRADD/FADD		c5	inside	s41(5 139 4 3)	Amount
COMPLEX	s140	BCL2/MCL1/BCL2L1		c5	inside	s140(5 131 5 109 ...)	Amount
COMPLEX	s142	BAD/BBC3/BCL2L11		c5	inside	s142(5 72 5 73 5 74)	Amount
COMPLEX	s143	BAD/BBC3/BCL2L11		c5	inside	s143(5 153 5 154 ...)	Amount
PHENOT...	s37	Apoptosis		c5	inside	s143(5 153 5 154 ...)	Amount