Self guided Tour

Reaxys Medicinal Chemistry

WHICH SUBSTANCES ARE THE MOST ACTIVE ON MY TARGET (HUMAN) OF INTEREST ?

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REAXYS®
Medicinal Chemistry

WHICH SUBSTANCES ARE THE MOST ACTIVE ON MY TARGET (HUMAN) OF INTEREST ?

1.1 Scenario (New Project)

New project focused on finding new AKT1 inhibitors with less affinity on AKT2 (minimizing adverse effect)

- Akt is associated with tumor cell survival, proliferation, and invasiveness.
- The activation of Akt is also one of the most frequent alterations observed in human cancer and tumor cells.
  - Akt1 has been implicated as a major factor in many types of cancer
  - Akt2 is an important signaling molecule in the Insulin signaling pathway
  - The role of Akt3 is less clear, though it appears to be predominantly expressed in the brain

Therefore, understanding Akt and its pathways is important for the creation of better therapies to treat cancer and tumor cells.

Search for active chemotype on AKT1?

1.2 Overview

Step no.	Steps and description	Action
1	Search Bioactivities	Ask Reaxys or Medicinal chemistry Query theme
2	Heatmap is displayed'	Click on Search Bioactivities
3	Filter by 'Target Species'	Filter by 'Target Species', select 'human', then click on 'Limit to'
4	Filter by 'pX'	Filter by 'pX(-log(Affinity), move the bar to ca > 9, then click on 'Limit to'
5	Display Structure in the Heatmap	Click on Structure
6	Select compounds in the Heatmap	Click on the row
7	Find Similar compounds	Will display similar compounds as well as pharmacology profile.

1.3 Step by step

There is two ways of Searching AKT 1 potent Inhibitors using "Ask Reaxys" or using the medicinal chemistry query theme. The two ways are providing the same results.
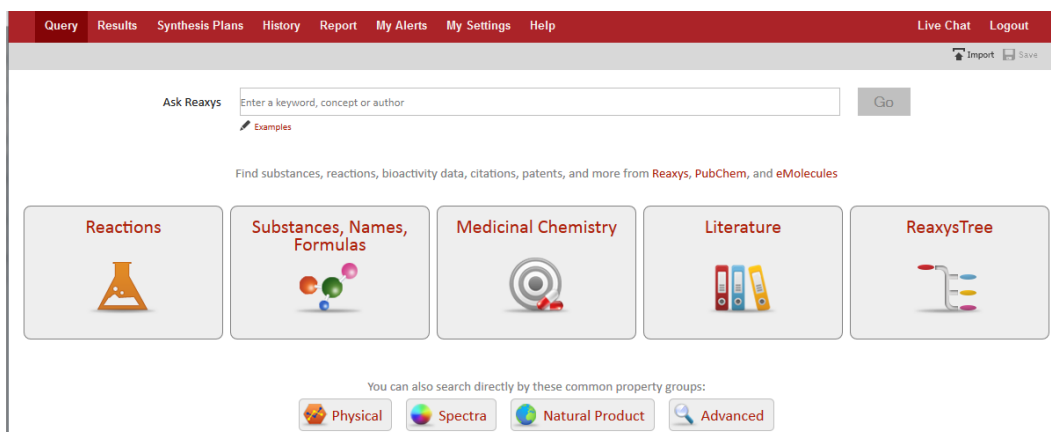
Step 1 : Search substances tested on AKT1

Using Ask reaxys

Ask Reaxys recognize the abbreviated terms as a target by using the target taxonomy (main terms as well as synonyms are searched) to retrieve substance tested on the corresponding target.

Using the Medicinal chemistry Query theme

On target Name click on "look up" to Access the Target Taxonomy

A new popup displays the Target Taxonomy then Search for 'AKT1' in .
Preferred term "Cyclooxygenase 2" is selected because Cox-2 was found as synonym (to display synonyms move the mouse pointer on the node name.)
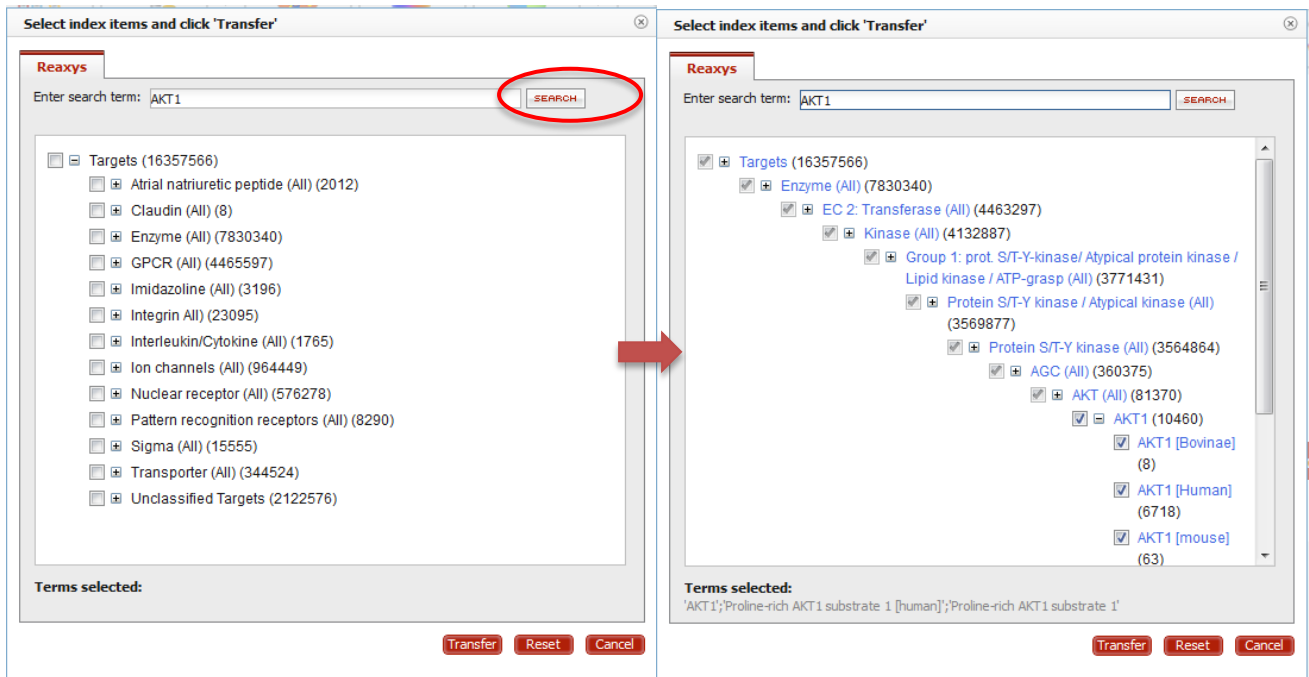
The search is done by substring in the target name as well as in the synonyms consequently some targets may be not always relevant. To unselect these unwanted targets uncheck the corresponding node and then click on "transfer".
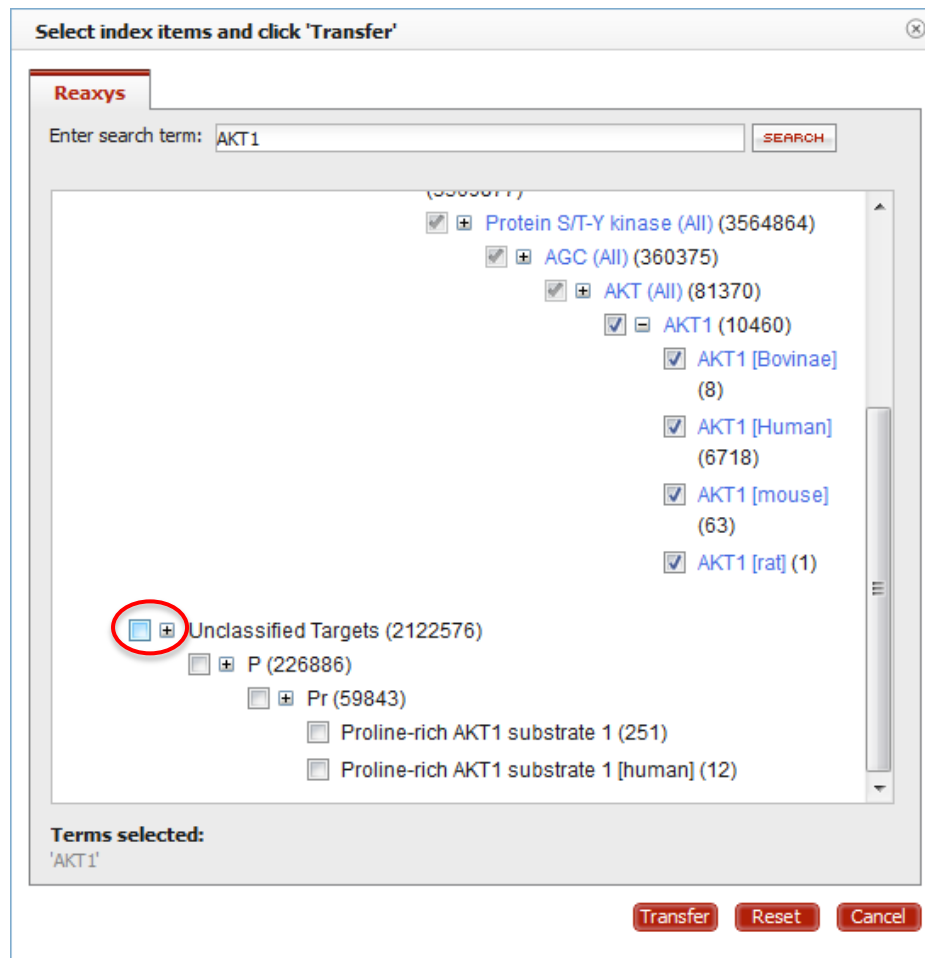
Step 2 : A full heatmap will appear with compounds tested on AKT1
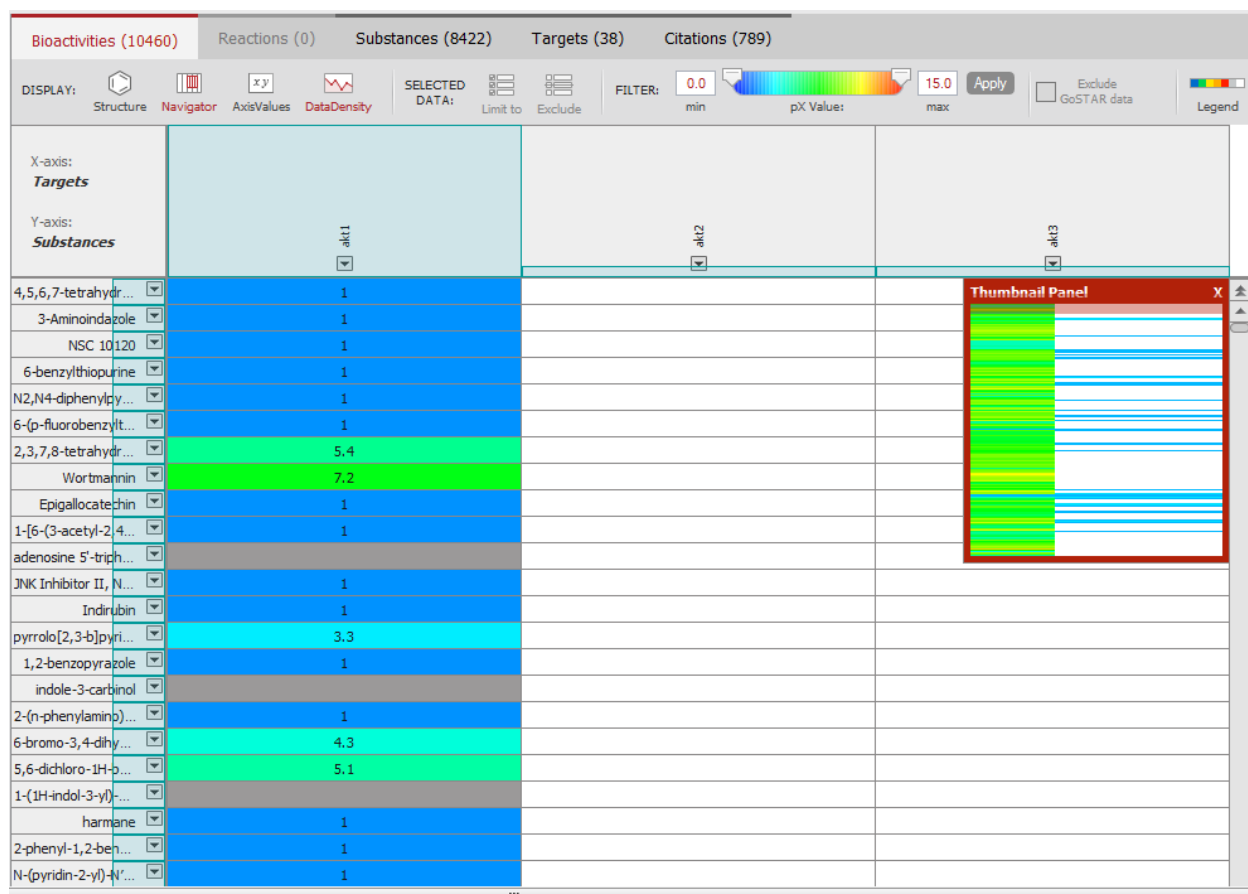
Step 3 : Filter by Target Species

On the left had side click on "Target species" select human and click on "Limit to"

A new heat map will appear with the AKT1 target

Step 4 : Retrieve Active compounds by filtering by pX value >9 (Bioactivities Ki, IC50, Kd, etc…<1nM)

Move the cursor to the right without releasing the mouse button and click on "Apply"
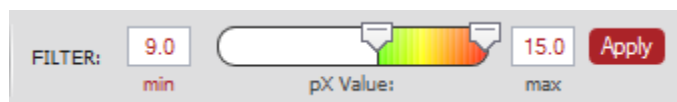
Heatmap will appear with the most active compounds on AKT1

Click on the AKT1 arrow ▼ and select "sort descending on this column" See Below.
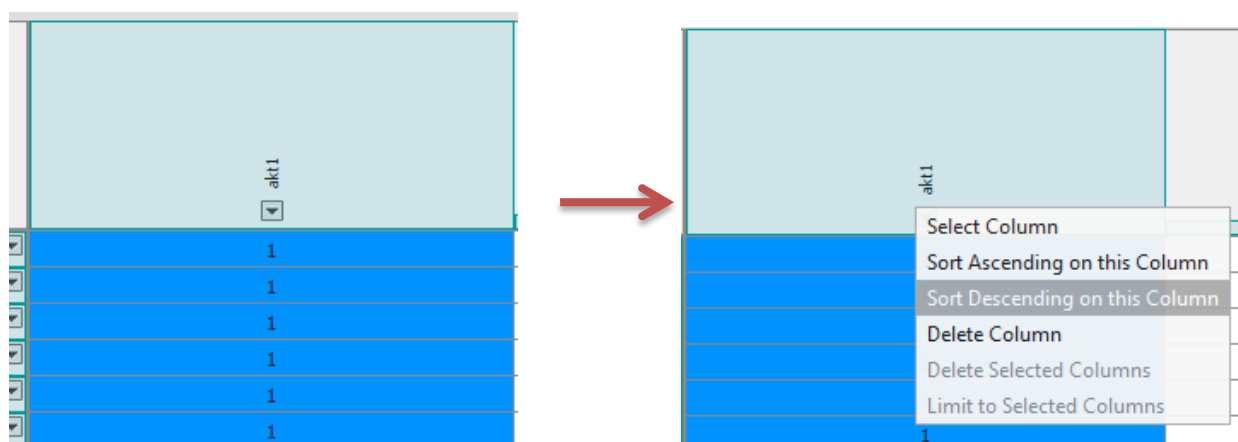
The most active compound will be on the top of the Heatmap
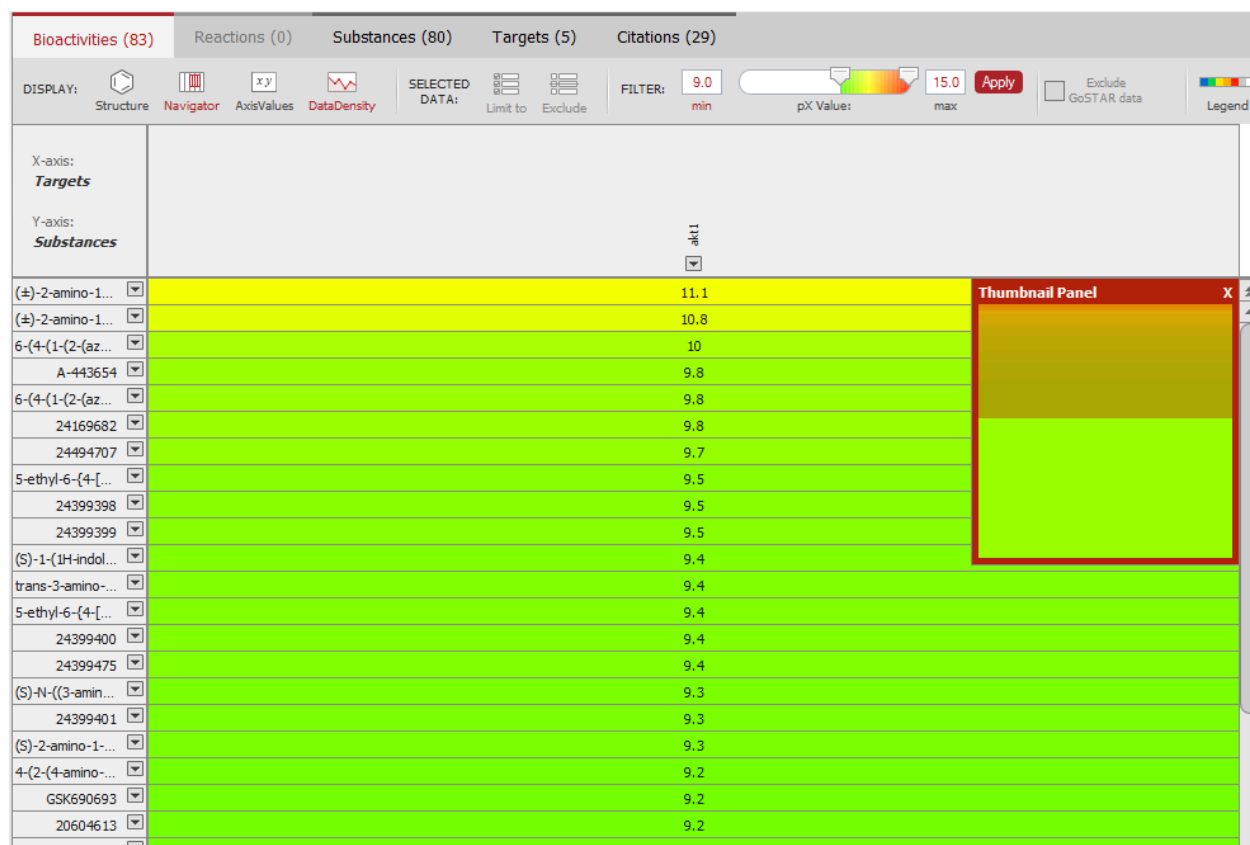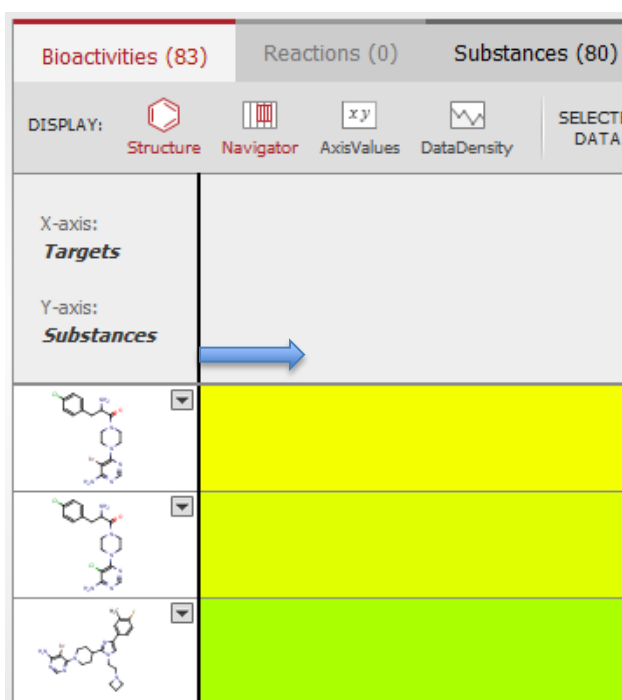

Step 5 : Hide data density and then click on structure to display the Chemical structure in the Heatmap
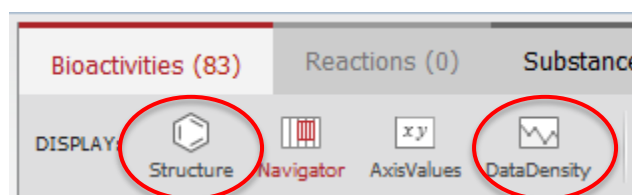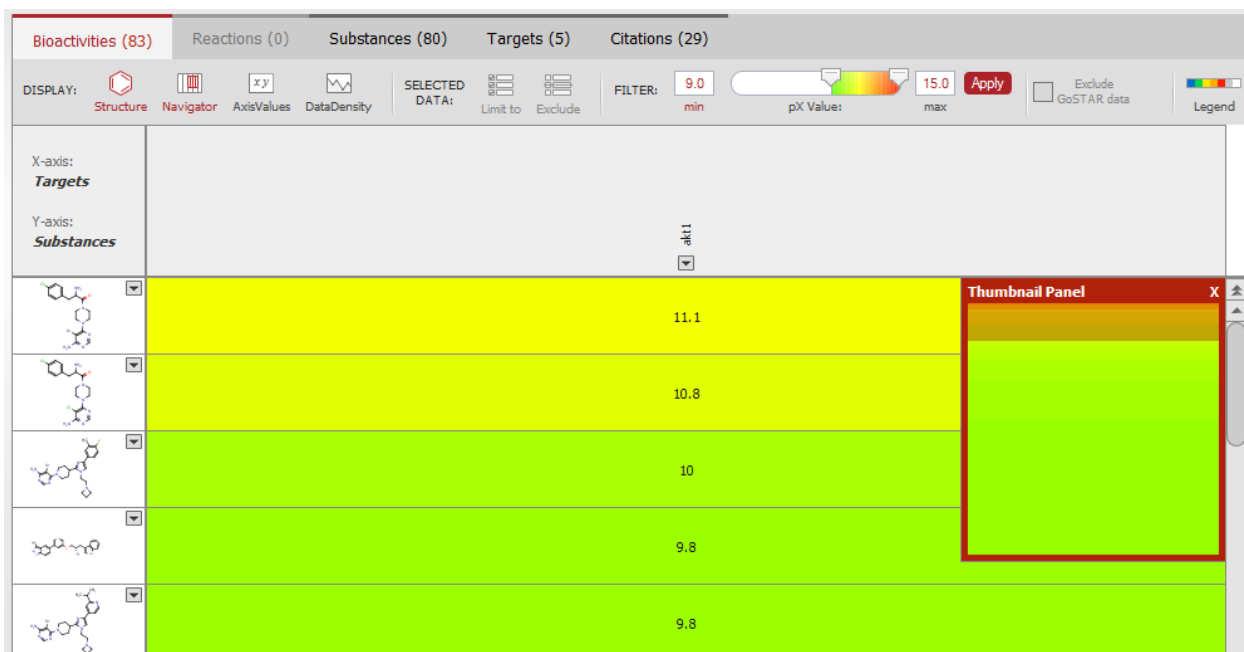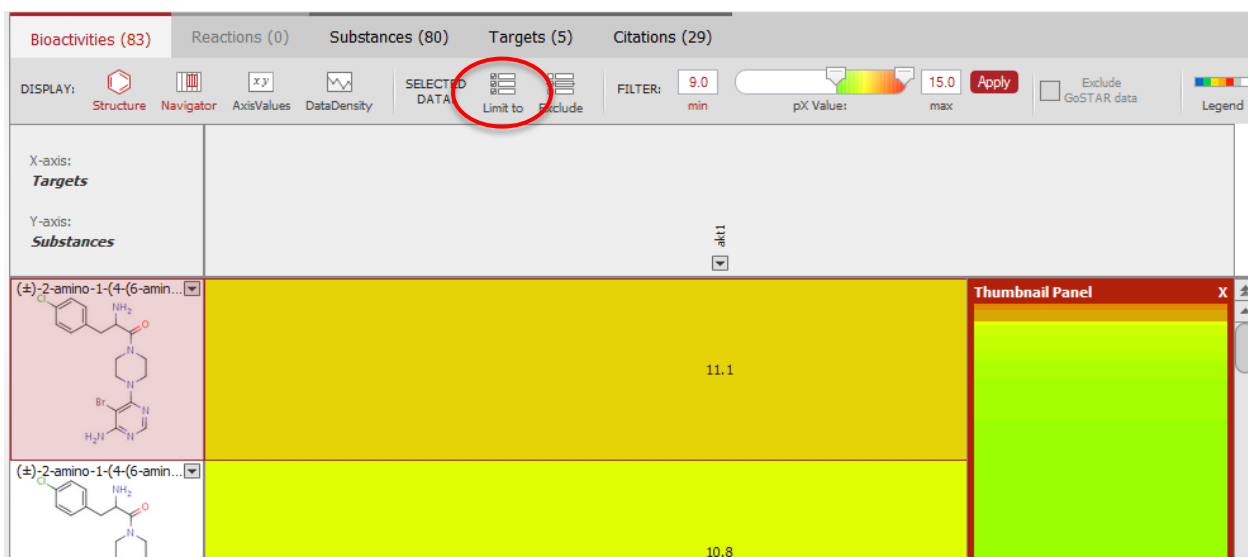
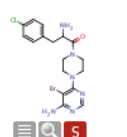If chemical structures are too small grab the column line and move it to the right to resize it.
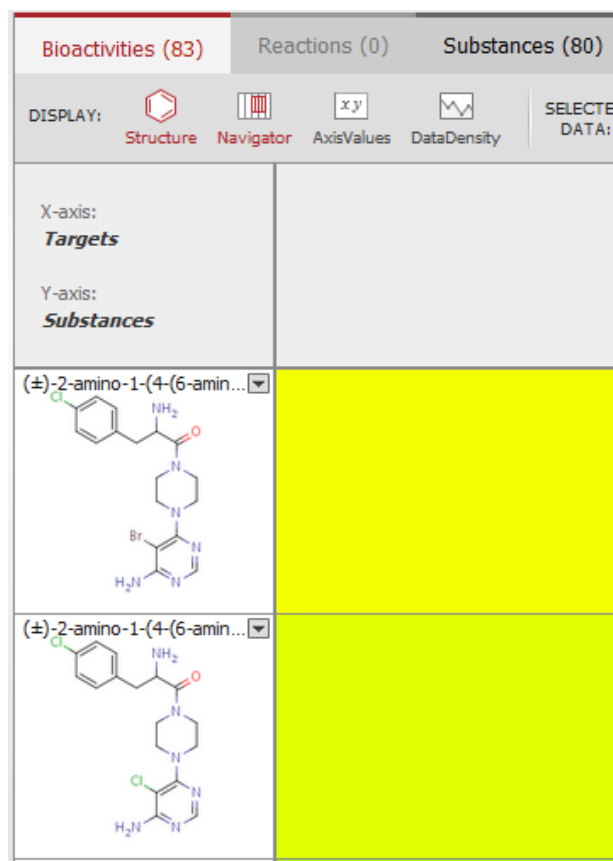
Step 6 : Then select the compound by clicking on the row header (Chemical structure) and limit to
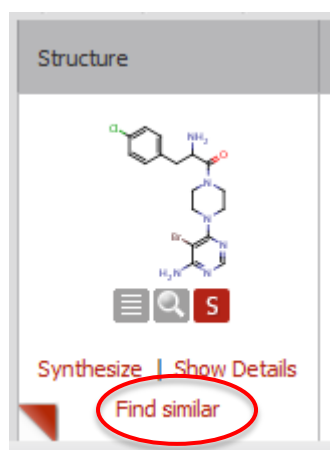
Cick on the substance tab

Step 7: Is there known similar compounds and what are their pharmacology profiles?

Use the find similar function to do so. Similar compounds will be retrieved

Find Similar Compounds...

Click on one of the hyperlinks below for getting similar compounds according to the selected scope:

Query Structure	Position/Stereo Isomers ❓	Near ❓	Medium ❓	Wide ❓	Widest ❓
	1	6	22	103	318

Cancel

Medium category was used

Substances are ranked by decreasing similarity (Based on tanimoto metric)
Clicking on the Bioactivities tab will display the phamacology profile of similar substances.

X-axis: **Targets** / Y-axis: **Substances**	akt	akt1	melanocortin 1 r...	melanocortin 3 r...	melanocortin 4 r...	melanocortin 5 r...
	(gray)					
		7.3				
			1	1	1	1
			5	5.3	5.6	5.4
			(gray)	(gray)	(gray)	(gray)
				5	5	
	(gray)					
			1	1	1	1
		8.7				
		10.8				
		11.1				
		9.3				
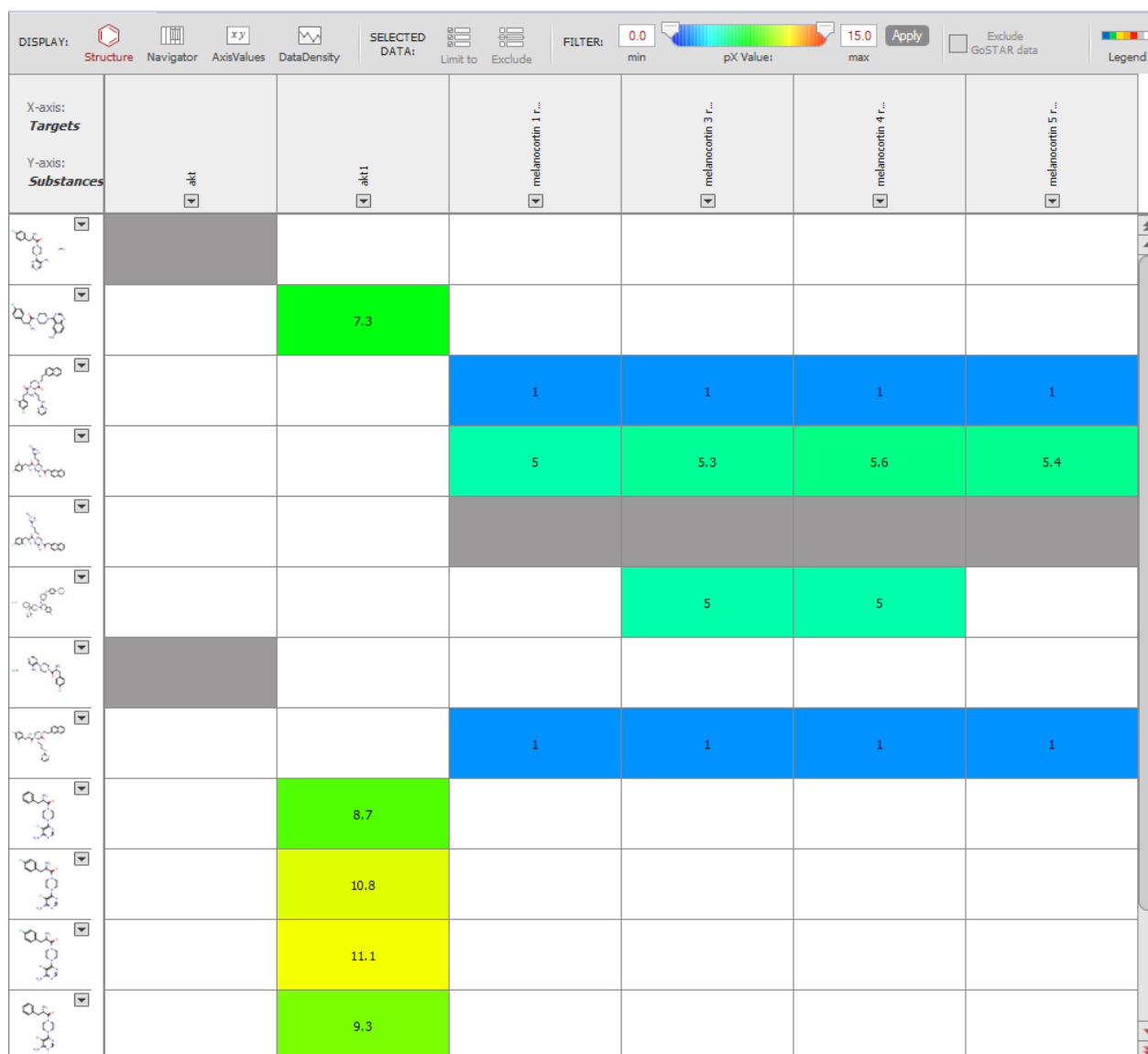
For more information please Contact