Step-by-Step Guide:

1. Install a suitable version of Python 3.x for your machine/OS from

https://www.python.org/downloads/

Note: If you are using Windows, please check that you dowload the appropriate version for your processor. AMD and Intel processors each have their own version of Python. You can check your system information by right clicking on "Computer" in the Start Menu and selecting "Properties".

Note 2: Make sure the networkx folder is located in the same directory as the script, otherwise the script will not run. (Networkx is a Python module for constructing graphs, which are used to trace the relationships among the proteins in the script)

2. Find IDs for proteins of interest. The script will recognize KEGG ID, NCBI-GeneID, NCBI-GI, or Unitprot ID.

```
Example: BRAF (KEGG ID = hsa:673), RAC1 (KEGG ID = hsa:5879)
Note: KEGG ID is constructed from NCBI-GeneID by adding a 3 or 4 character organism code to the gene number. [i.e. BRAF (NCBI-GeneID = 673), BRAF (KEGG ID= hsa:673]
```

3. Input IDs into script when prompted.

Example:

```
Please enter gene ID [KEGG-ID, NCBI-GENEID, or UNIPROT] : 673
Please enter gene ID [KEGG-ID, NCBI-GENEID, or UNIPROT] : 5879
```

Note: The script will attempt to validate the input ID. If you receive an error, double check that you input the ID correctly and using a supported format.

4. The script will begin to fetch and analyze data.

Example:

```
Building data requests for hsa:673
Building data requests for hsa:5879
Fetching data for hsa:673
Analyzing data for hsa:673
Fetching data for hsa:5879
Analyzing data for hsa:5879
Finding points of crosstalk
Links:1757
```

Note: This is the most time consuming part of the script. Expect for it to take about 5 minutes.

5. The script will output the data as a .csv file with the name "crosstalk.csv" in the directory where the script is located.

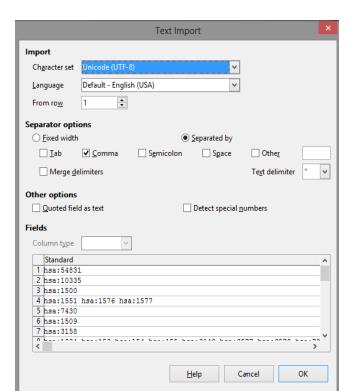
Example:

鷆 networkx	3/24/2014 11:55 AM	File folder	
■ crosstalk.csv	5/1/2014 12:44 AM	OpenOffice.org 1	1,291 KB
README.txt	3/24/2014 12:29 PM	TXT File	3 KB
spider map memory.pv	5/1/2014 12:52 AM	PY File	22 KB

Note: Be sure to change the name of the output file from "crosstalk.csv" to prevent your results

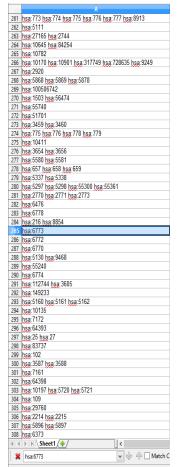
from being overwritten by a subsequent run of the script!

6. Open "crosstalk.csv" with spreadsheet program. Be sure to select commas as a delimiter. **Example**:



7. The first column is a list of all the linking proteins. Search for your protein(s) of interest KEGG ID within this column.

Example:



Note: It may be easier to search the column by copying it to a new spreadsheet.

7. If you wish to know more about the proteins/activities of the links, the columns after A show each step in the link. The tracing from the first input protein to the linking protein are first, followed by the tracing from the second input protein to the linking protein. Both tracings are preceded by a blank column. The cells are formatted as follows: protein1 –activity--> protein2 in pathwayX

Example:

A	B C D	
1172 hsa:54361	hsa:673activation> hsa:5604 hsa:5605 in hsa05218 hsa:5604 hsa:5605activation> hsa:5594 hsa:5595 in hsa05218	
1173 hsa:4087 hsa:4088	hsa:673activation> hsa:5604 hsa:5605 in hsa05218 hsa:5604 hsa:5605activation> hsa:5594 hsa:5595 in hsa05218	
1174 hsa:70	hsa:673activation> hsa:5604 hsa:5605 in hsa05218 hsa:5604 hsa:5605activation> hsa:5594 hsa:5595 in hsa05218	hsa:5594 hsa:5595indirect effect> hsa:367 in hsa09 hsa:367compound> hsa:5566 hsa:5567 hsa:5568 hsa:5613 in l
1175 hsa:5009	hsa:673activation> hsa:5604 hsa:5605 in hsa05218 hsa:5604 hsa:5605activation> hsa:5594 hsa:5595 in hsa05218	hsa:5594 hsa:5595indirect effect> hsa:367 in hsa09 hsa:367compound> hsa:5566 hsa:5567 hsa:5568 hsa:5613 in l
1176 hsa:3932	hsa:673phosphorylation> hsa:5604 in hsa04010 hsa:5604activation> hsa:5599 hsa:5601 hsa:5602 in hsa05212	hsa:5599 hsa:5601 hsa:5602binding/association> b hsa:1398 hsa:1399activation> hsa:2889 in hsa05211
1177 hsa: 100137049 hsa: 123745 hsa: 255189 hsa	hsa:673phosphorylation> hsa:5604 in hsa04010 hsa:5604inhibition> hsa:572 in hsa04510	hsa:572inhibition> hsa:836 in hsa05161 hsa:836activation> hsa:1630 in hsa05200
1178 hsa:3931	hsa:673activation> hsa:5604 hsa:5605 in hsa05218 hsa:5604 hsa:5605activation> hsa:5594 hsa:5595 in hsa05218	hsa:5594 hsa:5595activation> hsa:7157 in hsa049 ₱ hsa:7157expression> hsa:5728 in hsa04115
1179 hsa:3937	hsa:673activation> hsa:5604 hsa:5605 in hsa05218 hsa:5604 hsa:5605activation> hsa:5594 hsa:5595 in hsa05218	hsa:5594 hsa:5595activation> hsa:7068 in hsa049 ≯hsa:7068activation> hsa:23533 hsa:5290 hsa:5291 hsa:5293 h:
1180 hsa:9588	hsa:673activation> hsa:5604 hsa:5605 in hsa05218 hsa:5604 hsa:5605activation> hsa:5594 hsa:5595 in hsa05218	hsa:5594 hsa:5595indirect effect> hsa:3458 in hsa0 hsa:3458expression> hsa:169355 hsa:3620 in hsa05143
1181 hsa:3938	hsa:673activation> hsa:5604 hsa:5605 in hsa05218 hsa:5604 hsa:5605activation> hsa:5594 hsa:5595 in hsa05218	hsa:5594 hsa:5595activation> hsa:7068 in hsa049 ₱ hsa:7068expression> hsa:3091 in hsa04919
1182 hsa:3939	hsa:673activation> hsa:5604 hsa:5605 in hsa05218 hsa:5604 hsa:5605activation> hsa:5594 hsa:5595 in hsa05218	hsa:5594 hsa:5595activation> hsa:7068 in hsa0491 hsa:7068expression> hsa:3091 in hsa04919
1183 hsa:10663 hsa:10803 hsa:1230 hsa:1232 hg	hsa:673phosphorylation> hsa:5604 in hsa04010 hsa:5604inhibition> hsa:572 in hsa04510	hsa:572inhibition> hsa:836 in hsa05161 hsa:836activation> hsa:4214 in hsa04010
1184 hsa:5236 hsa:55276	hsa:673activation> hsa:5604 hsa:5605 in hsa05218 hsa:5604 hsa:5605activation> hsa:5594 hsa:5595 in hsa05218	
1185 hsa: 158835 hsa: 8694	hsa:673activation> hsa:5604 hsa:5605 in hsa05218 hsa:5604 hsa:5605activation> hsa:5594 hsa:5595 in hsa05218	hsa:5594 hsa:5595indirect effect> hsa:3458 in hsa0 hsa:3458expression> hsa:169355 hsa:3620 in hsa05143
1186 hsa:25898	hsa:673activation> hsa:5604 hsa:5605 in hsa05218 hsa:5604 hsa:5605activation> hsa:5594 hsa:5595 in hsa05218	hsa:5594 hsa:5595activation> hsa:7157 in hsa049 hsa:7157expression> hsa:25898 in hsa04115
1187 hsa:8793	hsa:673activation> hsa:5604 hsa:5605 in hsa05218 hsa:5604 hsa:5605activation> hsa:5594 hsa:5595 in hsa05218	hsa:5594 hsa:5595inhibition> hsa:100132074 hsa:2 hsa:100132074 hsa:2308 hsa:2309 hsa:4303expression> hsa:8
1188 hsa:8792	hsa:673activation> hsa:5604 hsa:5605 in hsa05218 hsa:5604 hsa:5605activation> hsa:5594 hsa:5595 in hsa05218	hsa:5594 hsa:5595 -inhibition> hsa:100132074 hsa:2 hsa:100132074 hsa:2308 hsa:2309 hsa:4303expression> hsa:{
1189 hsa:10020	hsa:673activation> hsa:5604 hsa:5605 in hsa05218 hsa:5604 hsa:5605activation> hsa:5594 hsa:5595 in hsa05218	hsa:5594 hsa:5595activation> hsa:7068 in hsa049⊅ hsa:7068expression> hsa:3091 in hsa04919
1190 hsa:7082	hsa:673activation> hsa:5604 hsa:5605 in hsa05218 hsa:5604 hsa:5605activation> hsa:5594 hsa:5595 in hsa05218	hsa:5594 hsa:5595inhibition> hsa:2697 hsa:57369 -hsa:2697 hsa:57369binding/association> hsa:7082 in hsa04540
1191 hsa:8795	hsa:673activation> hsa:5604 hsa:5605 in hsa05218 hsa:5604 hsa:5605activation> hsa:5594 hsa:5595 in hsa05218	hsa:5594 hsa:5595activation> hsa:7157 in hsa049 ₱ hsa:7157expression> hsa:8795 in hsa04115
1192 hsa:8794	hsa;673activation> hsa;5604 hsa;5605 in hsa05218 hsa;5604 hsa;5605activation> hsa;5594 hsa;5595 in hsa05218	
1193 hsa:8411	hsa:673activation> hsa:5604 hsa:5605 in hsa05218 hsa:5604 hsa:5605activation> hsa:5594 hsa:5595 in hsa05218	
1194 hsa:6775	hsa:673activation> hsa:5604 hsa:5605 in hsa05218 hsa:5604 hsa:5605activation> hsa:5594 hsa:5595 in hsa05218	
1195 hsa:6774	hsa:673activation> hsa:5604 hsa:5605 in hsa05218 hsa:5604 hsa:5605activation> hsa:5594 hsa:5595 in hsa05218	
1196 hsa:6773	hsa:673activation> hsa:5604 hsa:5605 in hsa05218 hsa:5604 hsa:5605activation> hsa:5594 hsa:5595 in hsa05218	hsa:5594 hsa:5595activation> hsa:6772 in hsa049 ₱hsa:6772expression> hsa:4615 in hsa05161