Contents

Import Data

In [13]:
```python
# read task file to import data
import os

## path
notebook_path = os.path.abspath("Life_Science_Dev_Test.ipynb")
path=notebook_path.rsplit('/',1)[0]+'/life_science_resource_dev_task/'

## import instruction file
file = open(path+'life_science_resource_dev_task.txt','r+')
file_list = file.readlines()
```

Task 1: Build Protein Thesaurus

In [70]:
```python
# extract protein symbols
s_ind = [i for i,v in enumerate(file_list) if 'following 16 proteins' in v]
e_ind = [i for i,v in enumerate(file_list) if 'Please divide the proteins into specific families' in v]
gene_list = [i.replace('\n','') for i in file_list[s_ind[0]+2:e_ind[0]-1]]
```

In [71]:
```python
gene_list
```

Out[71]:
```
['ABCC8',
 'CACNA1A',
 'FRAP1',
 'INS',
 'INSR',
 'IRS1',
 'KCNJ11',
 'KRAS',
 'MAP2K1',
 'PIK3CA',
 'PPARG',
 'PTPN1',
 'RAF1',
 'RPS6KB1',
 'SLC2A2',
 'SOS1']
```

In [56]:
```python
# assign protein family from Uniprot
## Gene Ontology (GO) molecular function terms are used
protein_family = {
    'binding':['INS','INSR','IRS1','KCNJ11','PPARG'],
    'GTPase activity':['KRAS','SOS1'],
    'kinase activity':['FRAP1','MAP2K1','PIK3CA','RAF1','RPS6KB1'],
    'phosphatase activity':['PTPN1'],
    'transporter activity':['ABCC8','CACNA1A','SLC2A2']
}

# retrieve synonyms for genes from Entrez
gene_synonyms = {
    'ABCC8':['ABC36', 'HHF1', 'MRP8', 'PNDM3','TNDM2'],
    'CACNA1A':['APCA', 'CACNL1A4', 'DEE42', 'EIEE42','SCA6'],
    'FRAP1':['SKS', 'FRAP', 'FRAP2', 'RAFT1', 'RAPT1'],
    'INS':['IDDM', 'ILPR', 'IRDN', 'MODY10', 'PNDM4'],
    'INSR':['CD220', 'HHF5'],
    'IRS1':['HIRS-1'],
    'KCNJ11':['BIR', 'HHF2', 'IKATP', 'KIR6.2', 'MODY13', 'PHHI'],
    'KRAS':['C-K-RAS', 'CFC2', 'K-Ras', 'RALD', 'RASK2'],
    'MAP2K1':['CFC3', 'MAPKK1', 'MEK1', 'MEL', 'PRKMK1'],
    'PIK3CA':['CLAPO', 'MCM', 'PI3K', 'PI3K-alpha', 'p110-alpha'],
    'PPARG':['CIMT1', 'GLM1', 'NR1C3', 'PPARG1', 'PPARgamma'],
    'PTPN1':[' PTP1B'],
    'RAF1':['CMD1NN', 'CRAF', 'NS5', 'Raf-1', 'c-Raf'],
    'RPS6KB1':[' PS6K', 'S6K', 'S6K-beta-1', 'S6K1', 'STK14A'],
    'SLC2A2':['GLUT2'],
    'SOS1':['GF1', 'GINGF', 'HGF', 'NS4', 'SOS-1']
}
```

In [68]:
```python
# create protein thesaurus

protein_thes = ''
for gene in gene_synonyms:
    for fam in protein_family:
        if gene in protein_family[fam]:
            #print(fam.split(' ')[0]+'_'+gene)
            protein_thes = protein_thes+fam.split(' ')[0]+'_'+gene+'\n'
    #print('\t'+'PT '+gene)
    protein_thes = protein_thes+'\t'+'PT '+gene+'\n'
    for syn in gene_synonyms[gene]:
        #print('\t'+'SYN '+syn)
        protein_thes = protein_thes+'\t'+'SYN '+syn+'\n'

# write to file
with open(path+'Task1_Output.txt','w') as f:
    f.write(protein_thes)
```

In [65]:
```python
print(protein_thes)
```

```
transporter_ABCC8
        PT ABCC8
        SYN ABC36
        SYN HHF1
        SYN MRP8
        SYN PNDM3
        SYN TNDM2
transporter_CACNA1A
        PT CACNA1A
        SYN APCA
        SYN CACNL1A4
        SYN DEE42
        SYN EIEE42
        SYN SCA6
kinase_FRAP1
        PT FRAP1
        SYN SKS
        SYN FRAP
        SYN FRAP2
        SYN RAFT1
        SYN RAPT1
binding_INS
        PT INS
        SYN IDDM
        SYN ILPR
        SYN IRDN
        SYN MODY10
        SYN PNDM4
binding_INSR
        PT INSR
        SYN CD220
        SYN HHF5
binding_IRS1
        PT IRS1
        SYN HIRS-1
binding_KCNJ11
        PT KCNJ11
        SYN BIR
        SYN HHF2
        SYN IKATP
        SYN KIR6.2
        SYN MODY13
        SYN PHHI
GTPase_KRAS
        PT KRAS
        SYN C-K-RAS
        SYN CFC2
        SYN K-Ras
        SYN RALD
        SYN RASK2
kinase_MAP2K1
        PT MAP2K1
        SYN CFC3
        SYN MAPKK1
        SYN MEK1
        SYN MEL
        SYN PRKMK1
kinase_PIK3CA
        PT PIK3CA
        SYN CLAPO
        SYN MCM
        SYN PI3K
        SYN PI3K-alpha
        SYN p110-alpha
binding_PPARG
        PT PPARG
        SYN CIMT1
        SYN GLM1
        SYN NR1C3
        SYN PPARG1
        SYN PPARgamma
phosphatase_PTPN1
        PT PTPN1
        SYN  PTP1B
kinase_RAF1
        PT RAF1
        SYN CMD1NN
        SYN CRAF
        SYN NS5
        SYN Raf-1
        SYN c-Raf
kinase_RPS6KB1
        PT RPS6KB1
        SYN  PS6K
        SYN S6K
        SYN S6K-beta-1
        SYN S6K1
        SYN STK14A
transporter_SLC2A2
        PT SLC2A2
        SYN GLUT2
GTPase_SOS1
        PT SOS1
        SYN GF1
        SYN GINGF
        SYN HGF
        SYN NS4
        SYN SOS-1
```

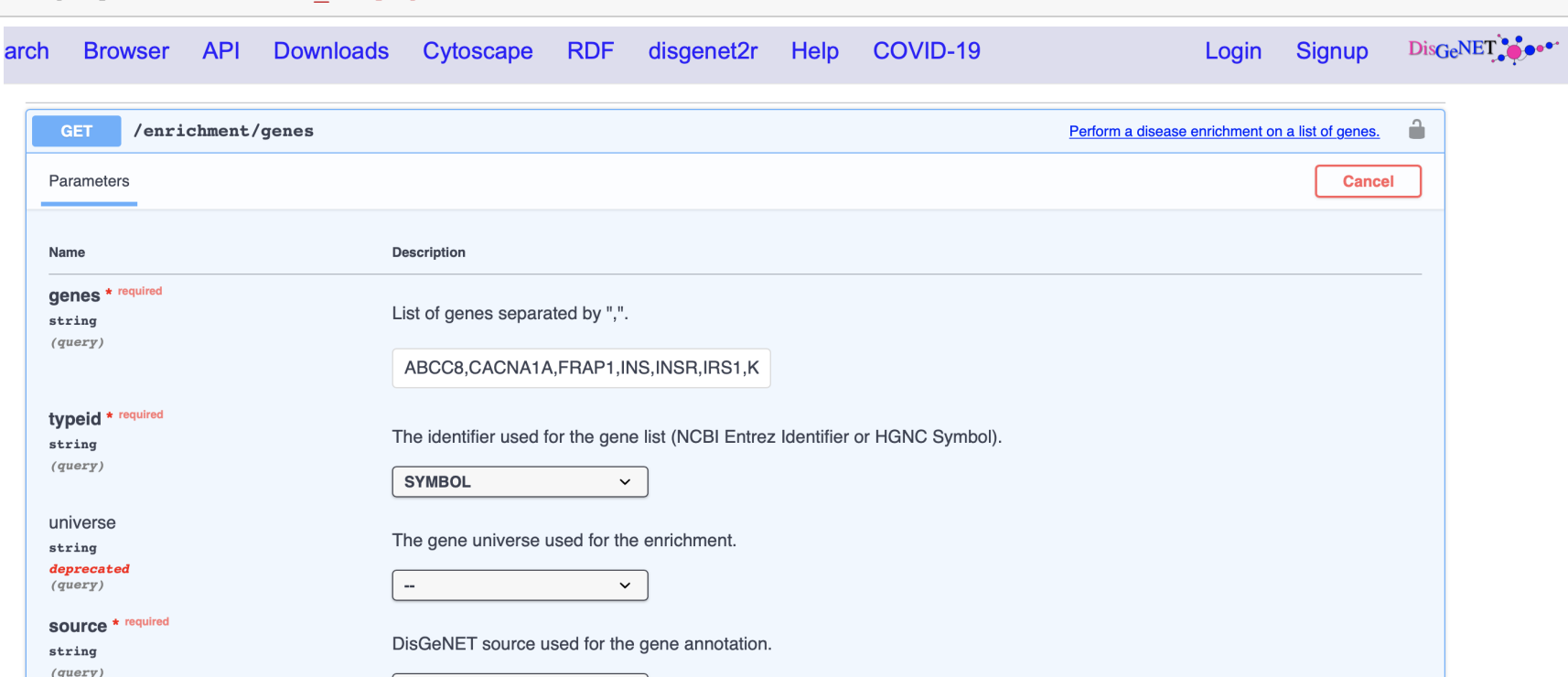
Associated isease

A disese enrichment analysis was performed on DisGeNET using the browser API service

In [81]:
```python
from IPython.display import Image

Image(path+'DisGeNET_ss.png')
```

Out[81]:



In [84]:
```python
# analyse results
import json

## read file
with open(path+'DisGeNET.json') as f:
    disease_enr = json.load(f)

## find enriched disease
disease_pvals = [(res['adjusted_pvalue'],res['disease_name']) for res in disease_enr['results']]
disease_pvals.sort()
top10diseases = [i[1] for i in disease_pvals[0:10]]
```

In [83]:
```python
top10diseases
```

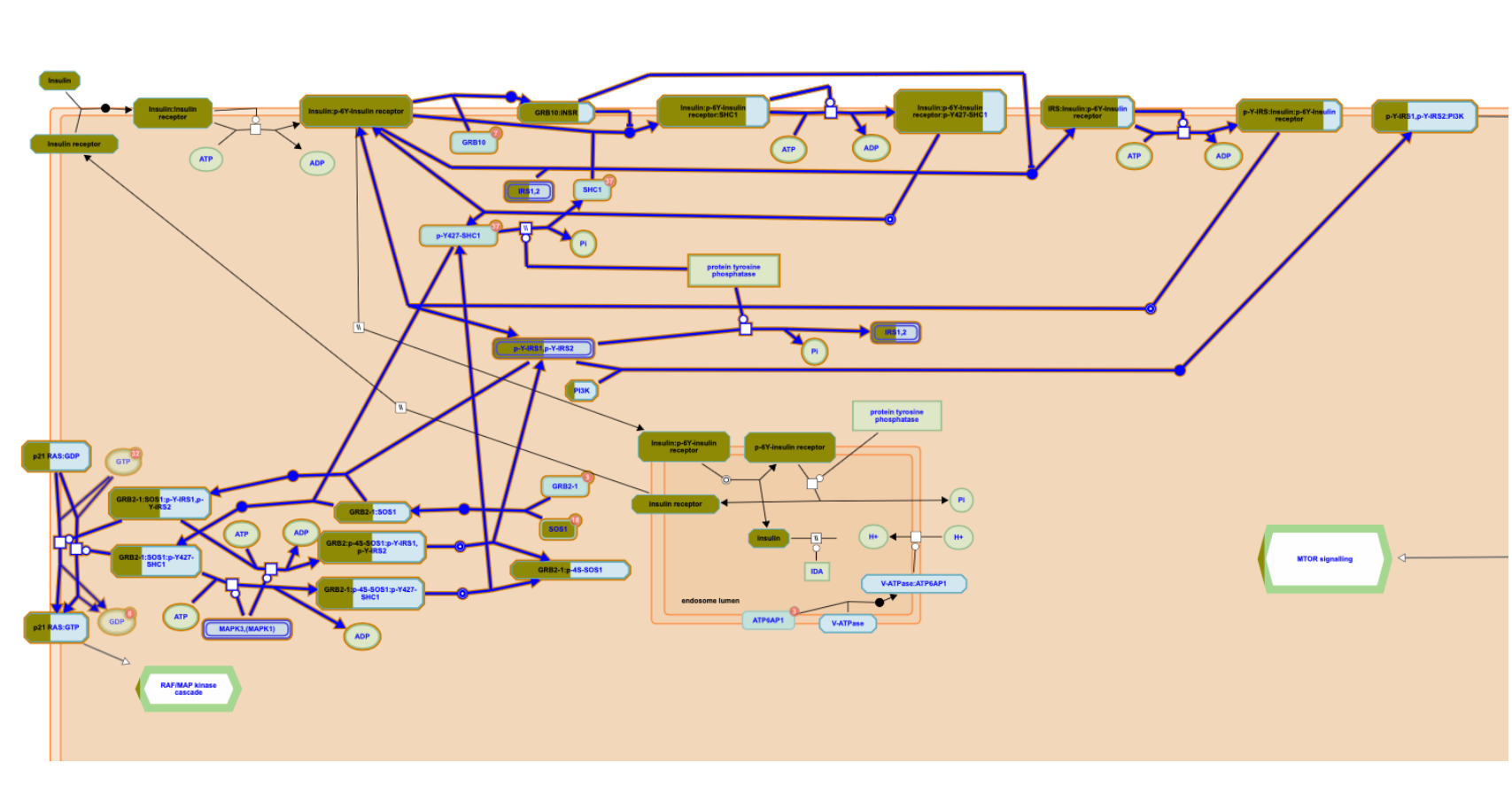
Out[83]:
```
['Decreased waist to hip ratio',
 'Insulin Resistance',
 'LEOPARD Syndrome',
 'Impaired glucose tolerance',
 'Hypertrophic obstructive cardiomyopathy',
 'Gestational Diabetes',
 'Insulin Sensitivity',
 'Fetal Growth Retardation',
 'Diabetes Mellitus',
 'Hyperglycemia']
```

Disease Mechanism

A pathway enrichment analysis was performed in Reactome and the most significantly matched pathway was the insulin receptor signaling pathway.

In [82]:
```python
Image(path+'Reactome_ss.png')
```

Out[82]:



Task 2: Build Protein/Gene Interactions

In [2]:
```python
# extract protein symbols
s_ind = [i for i,v in enumerate(file_list) if 'a list of entities of interest' in v]
e_ind = [i for i,v in enumerate(file_list) if 'You are given 200 scientific' in v]
entity_list = [i.replace('\n','') for i in file_list[s_ind[0]+2:e_ind[0]-1]]
```

In [72]:
```python
entity_list
```

Out[72]:
```
['c-fos',
 'c-jun',
 'IFN-gamma',
 'IL-2',
 'IL-6',
 'Interferon gamma',
 'kappa B-3',
 'ISG',
 'LTB4',
 'M-CSF',
 'Nef',
 'NF-kappa B',
 'PKC',
 'PMA']
```

In [3]:
```python
# extract ontology
s_ind = [i for i,v in enumerate(file_list) if 'RELATIONAL ONTOLOGY' in v]
e_ind = [i for i,v in enumerate(file_list) if 'NOTES' in v]
RELN_list = [i.replace('\n','') for i in file_list[s_ind[0]+2:e_ind[0]-1]]

# create dictionary
inds = []
for i,v in enumerate(RELN_list):
    if v!='' and '\t' not in v:
        inds.append(i)

RELN_dict = {}
for i,v in enumerate(inds):
    if i+1!=len(inds):
        RELN_dict[RELN_list[v]] = [j.replace('\t','') for j in RELN_list[v+1:inds[i+1]-1]]
    else:
        RELN_dict[RELN_list[v]] = [j.replace('\t','') for j in RELN_list[v+1:len(RELN_list)-1]]
del RELN_dict['GG_gene_gene'] # remove gene-gene relation
```

In [73]:
```python
RELN_dict
```

Out[73]:
```
{'GG_inhibit': ['PT inhibit',
  'SYN inhibits',
  'SYN inhibited',
  'SYN suppresses',
  'SYN suppressed',
  'SYN blocks',
  'SYN blocked',
  'SYN down-regulates',
  'SYN down-regulated'],
 'GG_increase': ['PT increase',
  'SYN increases',
  'SYN increased',
  'SYN exacerbates',
  'SYN exacerbated',
  'SYN activates',
  'SYN activated'],
 'GG_affect': ['PT affect',
  'SYN affects',
  'SYN affected',
  'SYN modulates',
  'SYN modulated',
  'SYN mediates',
  'SYN mediated']}
```

In [5]:
```python
# parse abstract xml
import xml.etree.ElementTree as ET

tree = ET.parse(path+'200abstracts.xml')
root = tree.getroot()
```

In [75]:
```python
# search abstract for relations

output = []
p = 0
for art in range(len(root)):
    p+=1
    #print(f"Abstract Number: {p}/{len(root)}")
    abstract = root[art][2].text
    sentences = abstract.split('. ')
    for line in sentences:
        for i1,entity1 in enumerate(entity_list):
            for entity2 in entity_list[i1+1:len(entity_list)-1]:
                for ont in RELN_dict:
                    c = 0
                    for term in RELN_dict[ont]:
                        if all([i in line for i in [entity1,entity2,term.split(' ')[1]]]):
                            #print(f"RELN: {term.split(' ')[1]}, Entity1: {entity1}, Entity2: {entity
2}")

                            c+=1
                    if c>0:
                        reln = RELN_dict[ont][0].split(' ')[1]
                        output.append([reln,entity1,entity2,line])
```

In [12]:
```python
# write output to folder
import pandas as pd

output_data = pd.DataFrame(output,columns=['Relation','Entity_1','Entity_2','Reference_Sentences'])
output_data.to_csv(path+'Task2_Output.csv',index=False,header=True)
```

In [41]:
```python
output_data
```

Out[41]:

	Relation	Entity_1	Entity_2	Reference_Sentences
0	increase	c-fos	c-jun	Okadaic acid treatment was found to dramatical...
1	increase	c-jun	M-CSF	Treatment of these cells with 10(3) units/ml h...
2	increase	c-jun	M-CSF	Nuclear run-on assays and mRNA stability studi...
3	increase	c-fos	M-CSF	We further demonstrate that M-CSF increases c-...
4	increase	M-CSF	PKC	We show that M-CSF activates and translocates PKC
5	affect	NF-kappa B	PKC	Thus, TNF alpha-induced NF-kappa B activation ...
6	increase	NF-kappa B	PKC	Furthermore, we found that cytoplasmic acidifi...
7	affect	NF-kappa B	PKC	Furthermore, we found that cytoplasmic acidifi...
8	inhibit	c-fos	c-jun	The present work demonstrates that the glucoco...
9	increase	c-fos	c-jun	The present work demonstrates that the glucoco...
10	inhibit	c-fos	c-jun	Nuclear run-on assays demonstrate that: (1) in...
11	inhibit	IL-2	NF-kappa B	We propose that KBF1 is a competitive inhibito...
12	increase	c-fos	c-jun	The increase in AP-1-binding activity was acco...
13	increase	c-fos	LTB4	LTB4 increased the expression of the c-fos gen...
14	affect	c-fos	c-jun	Stability of the c-fos and c-jun mRNA was not ...
15	affect	c-fos	LTB4	Stability of the c-fos and c-jun mRNA was not ...
16	affect	c-jun	LTB4	Stability of the c-fos and c-jun mRNA was not ...
17	increase	c-fos	c-jun	Nuclear transcription studies in vitro showed ...
18	increase	c-fos	LTB4	Nuclear transcription studies in vitro showed ...
19	increase	c-jun	LTB4	Nuclear transcription studies in vitro showed ...
20	increase	c-fos	c-jun	Interferon gamma activated strongly c-fos and ...
21	increase	c-fos	Interferon gamma	Interferon gamma activated strongly c-fos and ...
22	increase	c-jun	Interferon gamma	Interferon gamma activated strongly c-fos and ...
23	increase	c-fos	IL-2	A number of genes known to be induced followin...
24	increase	c-fos	NF-kappa B	A number of genes known to be induced followin...
25	increase	IL-2	NF-kappa B	A number of genes known to be induced followin...
26	increase	IFN-gamma	ISG	Although IFN-gamma alone does not induce ISG e...
27	increase	IFN-gamma	ISG	However, the increase in ISGF3 activity ultima...
28	inhibit	c-fos	c-jun	Staurosporine, a nonspecific inhibitor of PKC,...
29	inhibit	c-fos	PKC	Staurosporine, a nonspecific inhibitor of PKC,...
30	inhibit	c-jun	PKC	Staurosporine, a nonspecific inhibitor of PKC,...
31	inhibit	NF-kappa B	PKC	In contrast to the transient NF-kappa B activa...
32	inhibit	Nef	NF-kappa B	We report here that the HIV-1-encoded Nef prot...
33	inhibit	Nef	NF-kappa B	Additionally, Nef inhibits the induction of HI...
34	inhibit	Nef	NF-kappa B	Further evidence suggests that Nef inhibits NF...
35	affect	IL-6	LTB4	We furthermore demonstrate that this process i...
36	increase	IL-2	NF-kappa B	Similarly, IL-2 activates NF-kappa B in the hu...
37	increase	IL-2	NF-kappa B	Enhanced NF-kappa B binding activity is follow...
38	affect	IL-2	NF-kappa B	Enhanced NF-kappa B binding activity is follow...
39	increase	c-fos	c-jun	The expression of c-fos, c-jun and jun B proto...
40	increase	c-fos	c-jun	These results suggest that the decreased IL-2 ...
41	increase	c-fos	IL-2	These results suggest that the decreased IL-2 ...
42	increase	c-jun	IL-2	These results suggest that the decreased IL-2 ...
43	inhibit	kappa B-3	NF-kappa B	To investigate the molecular basis for the cri...
44	affect	kappa B-3	NF-kappa B	To investigate the molecular basis for the cri...
45	inhibit	kappa B-3	NF-kappa B	Results from in vivo expression studies perfor...
46	affect	kappa B-3	NF-kappa B	Results from in vivo expression studies perfor...
47	inhibit	kappa B-3	NF-kappa B	Together, these findings suggest that the nucl...

In [69]:
```python
output_data.describe()
```

Out[69]:

	Relation	Entity_1	Entity_2	Reference_Sentences
count	48	48	48	48
unique	3	9	8	31
top	increase	c-fos	NF-kappa B	Nuclear transcription studies in vitro showed ...
freq	26	20	14	3

Conclusion

- The protein thesaurus was built for the 16 input genes. The input genes fall under five major class of protein families including binding, kinases, phosphatases, GPIases and transporters.
- The family mapping and synonym identification were performed manually using UniProt and Entrez respectively. An improvement on this would be to use APIs to automate this process for scaling purposes and to reduce errors.
- A disease enrichment analysis was performed with DisGeNET and the top hits point to insulin-related diseases such as diabetes and insulin resistance.
- A pathway enrichment analysis was performed with Reactome and the most significantly over-represented pathway was the insulin receptor signaling pathway. This result corroborates with the DisGeNET analysis. Reactome shows how the input gene list overlaps with the reactions in the pathway thereby shedding insight into the potential disease mechanism.
- The protein/gene interactions were generated from the input list and orthologes. More than half of the retrieved relations are of the protein/protein type.
- An improvement on task 2 would be to use more synonym terms and regular expressions to capture all the different versions of protein/gene names and their relations.