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ACTIVITY 8

1. Use OMIM or Open Targets to investigate about Leprosy and Behcet's disease:
    - Summarize what is leprosy disease:

Leprosy is a chronic granulomatous infection caused by mycobacterium leprae. The granulomatous lesions are manifested in the skin, the mucous membranes, and the peripheral nerves. Two polar or principal types are lepromatous and tuberculoid.

- Summarize what is Behcet's disease:

A autoimmune disease of the cardiovascular system and is_a vasculitis that causes chronic inflammation in blood vessels throughout the body leading to ulcerations on the mouth and sometimes the genitals, notorious for causing hypopyon uveitis.

2. Use Open Targets to investigate about Thalidomide and answer the following questions:
    - Which are the targets of Thalidomide? (tip: query for "thalidomide" and find "Human targets" under the section "Mechanisms of Action")

CRBN : Substrate recognition component of a DCX E3 protein ligase complex that mediates the ubiquitination and subsequent proteasomal degradation of target proteins.

DDB1 : Protein, which is both involved in DNA repair and protein ubiquitination.

CUL4A : Core component of multiple cullin-RING-based E3 ubiquitin- protein ligase complexes which mediate the ubiquitination of target proteins.

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RBX1 : E3 ubiquitin ligase component of multiple cullin-RING-based E3 ubiquitin-protein ligase (CRLs) complexes which mediate the ubiquitination and subsequent proteasomal degradation of target proteins, including proteins involved in cell cycle progression

- In which kind of diseases has Thalidomide shown to be effective? (tip: query for “thalidomide” and find “Indication”under the section “Indications”)

Indication	Therapeutic Areas	Max Phase ↓
multiple myeloma	4 areas	Phase IV
immune system disease	immune system disease	Phase IV
colorectal neoplasm	2 areas	Phase III
diffuse large B-cell lymphoma	4 areas	Phase III
fallopian tube cancer	2 areas	Phase III
vascular malformation	3 areas	Phase III
peritoneum cancer	2 areas	Phase III
malignant epithelial tumor of ovary	3 areas	Phase III
extranodal nasal NK/T cell lymphoma	5 areas	Phase III
hepatocellular carcinoma	3 areas	Phase III

3. Use the Open Targets and HumanMine to investigate about the targets you identified in the previous question (tip: create a list with all the identified targets):
   CRBN, DDBI, CUL4A, RBX1
   - To which key therapeutic areas do these targets belong?
     genetic, familial or congenital disease, cancer or benign tumor, immune system disease, hematologic disease, gastrointestinal disease, reproductive system or breast disease, phenotype, cardiovascular disease, endocrine system disease, infectious disease, integumentary system disease
   - Which other drugs target the same genes (list just a few)?
     lenalidomide, pomalidomide, teclistamab, bortezomib
   - Do these genes interact physically? Do they interact genetically?
     They do interact physically

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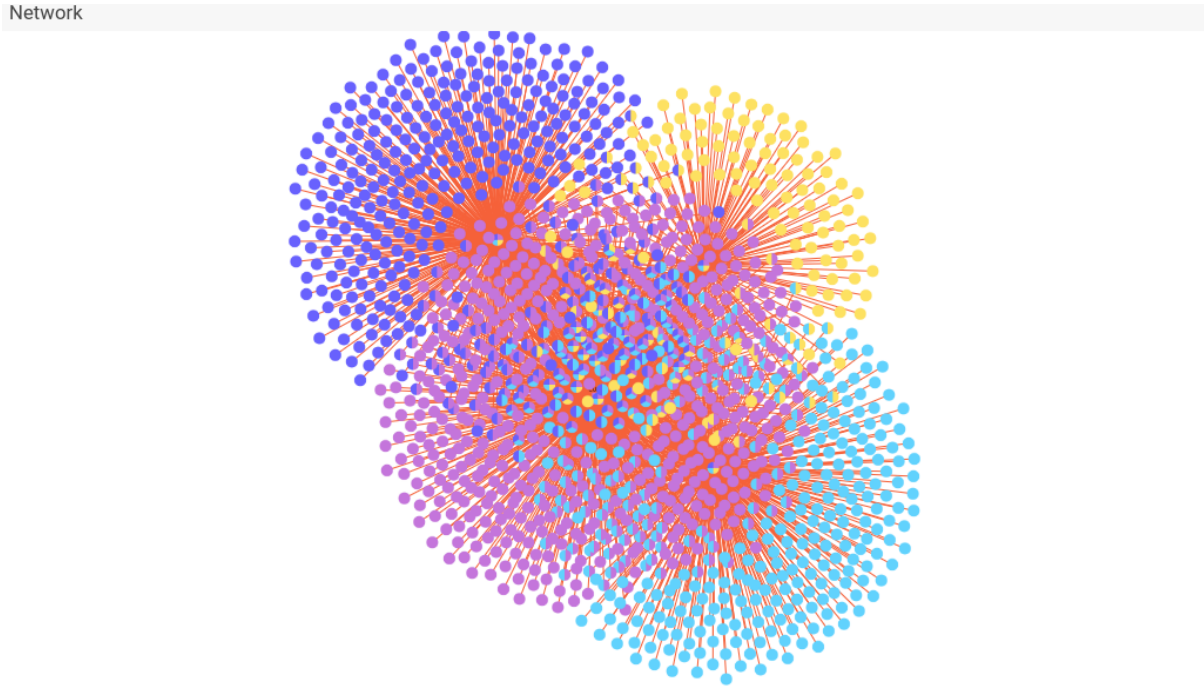
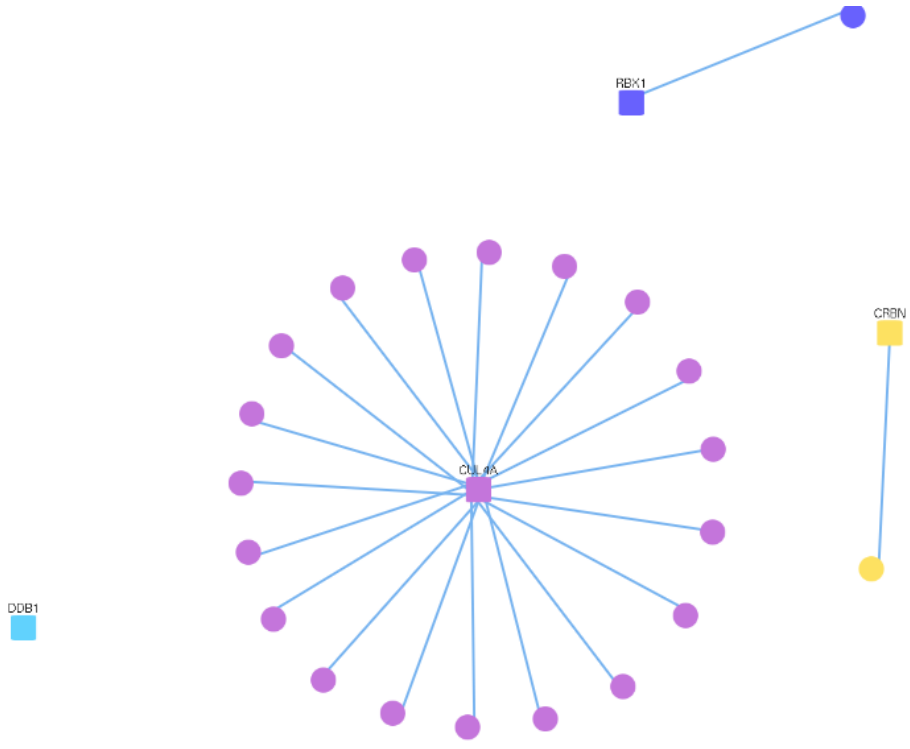


They don’t interact genetically



- Are all these genes located in the same chromosome?
  No, they are located in Chr1, Chr3, Chr5 and other chromosomes.
- Are there Gene Ontology terms enriched in this list of target genes?

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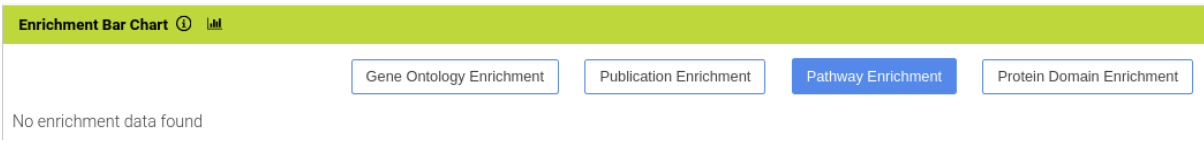
They are enriched

- Are there pathways enriched in this list of target genes?



There are no enriched pathways

4. Finally, focus on the gene CUL4A and use HumanMine to investigate about this gene:

- Is the gene differentially expressed under any condition?

Yes under Huntington disease or a multiple myeloma there is a downregulation.
In healthy individuals there is a downregulation of the gene in the brain caudate nucleus.

Atlas Expression T Statistic	Atlas Expression Type	Atlas Expression Condition	Atlas Expression Expression	Atlas Expression P Value
-20.4	disease_state	Huntingtons disease	DOWN	0
-19.5	disease_state	multiple myeloma	DOWN	0
-15.9	disease_state	multiple myeloma	DOWN	0
-14.8	organism_part	brain caudate nucleus	DOWN	0
-11.9	disease_state	bipolar disorder	DOWN	1.4114754059871501e-30

Upregulation when an individual has cervical carcinoma, and with healthy individuals it is upregulated in organism parts like skeletal muscle and cervix.

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18.6	organism_part	skeletal muscle	UP	0
17.6	organism_part	cervix	UP	0
17.1	disease_state	cervical carcinoma	UP	0
12.6	organism_part	skeletal muscle	UP	3.8551503546018125e-34

- Do fruitflies have this gene in their genomes? What is its name?
  Yes, CUL4.