Topic 8. Phenotypes and diseases

The drug discovery timeline. OMIM. Open Targets. InterMine.

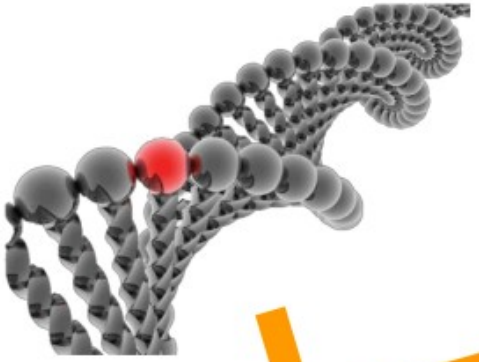
The Genotype to Phenotype challenge

Topic 5 – Genes & Genomes

Topic 6 – Functional genomics

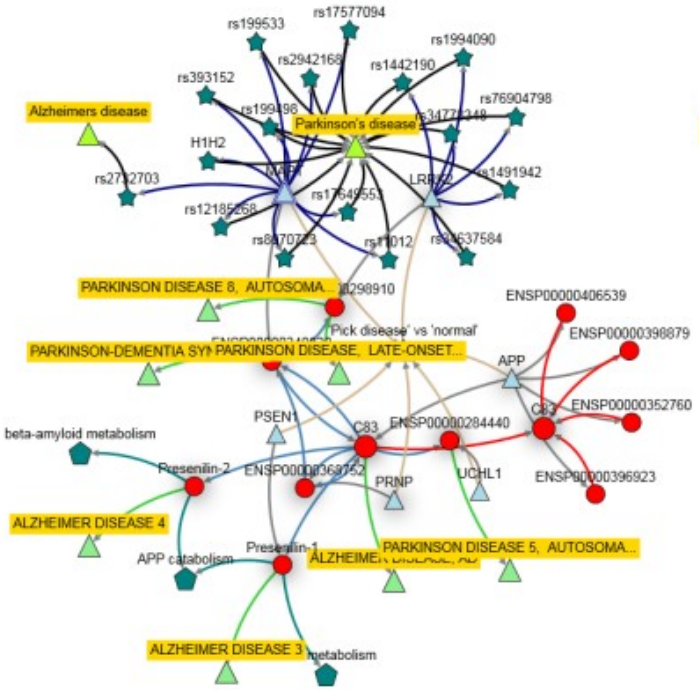
Topic 7 – Networks & Pathways

Topic 8 – Phenotypes & Diseases



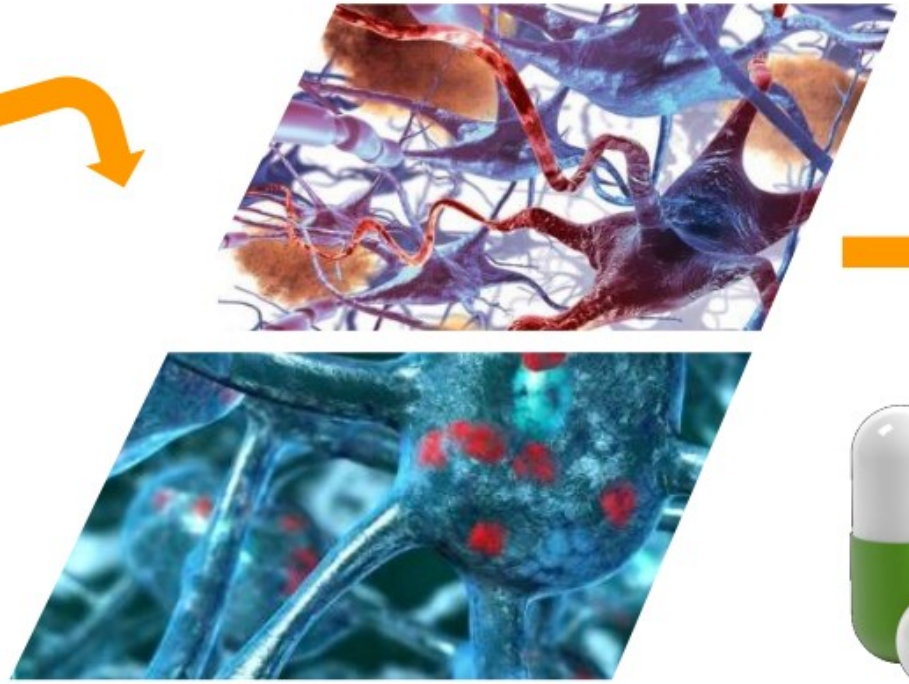
Genotype

GWAS, QTL



Biological Knowledge Discovery

Data selection, processing, transformation, integration, interpretation



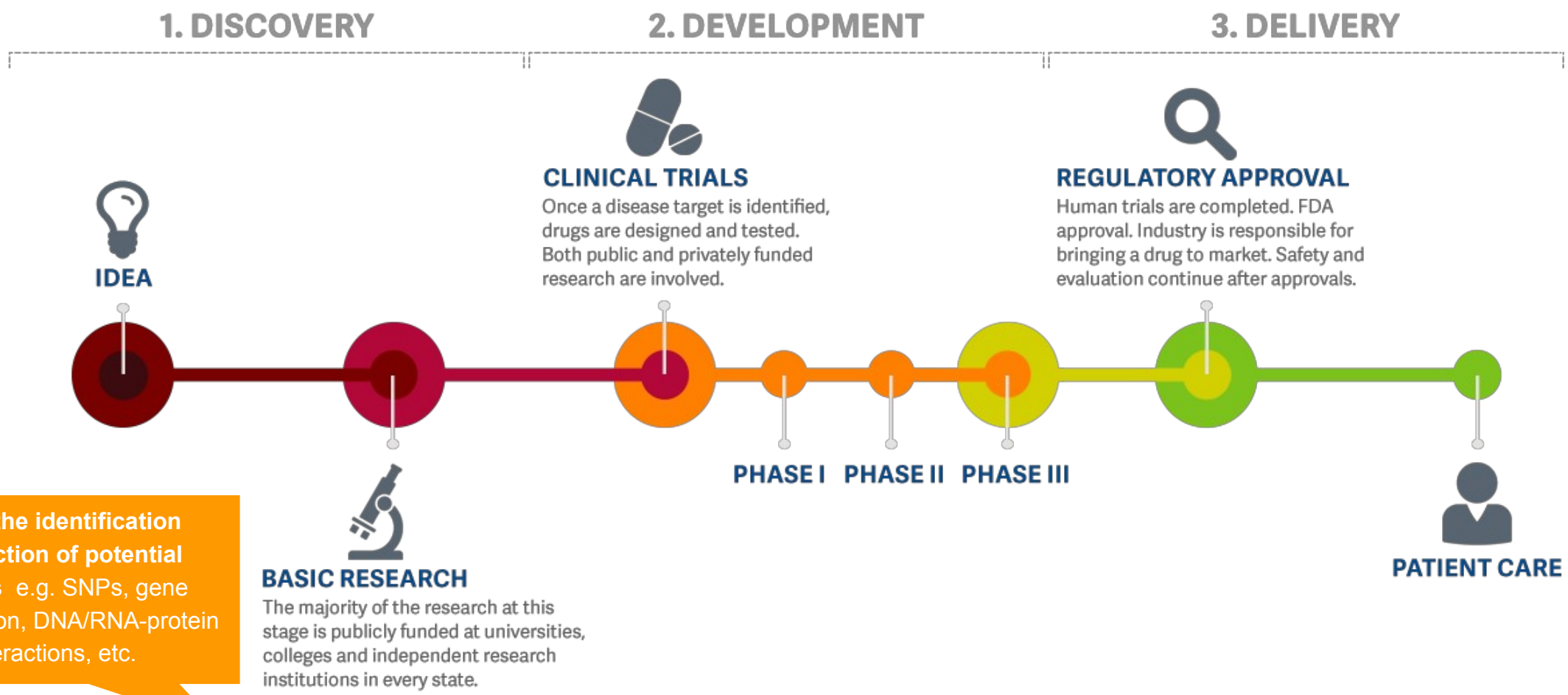
Phenotype

Alzheimer, Parkinson

Drugs

Precision medicine

Drug discovery timeline



Improve the identification and selection of potential targets e.g. SNPs, gene expression, DNA/RNA-protein interactions, etc.

Characterization of the disease process and identification of drug targets

Less than 10% of candidate targets turn out to be valid

De novo drug discovery and development is a 10-17 year process

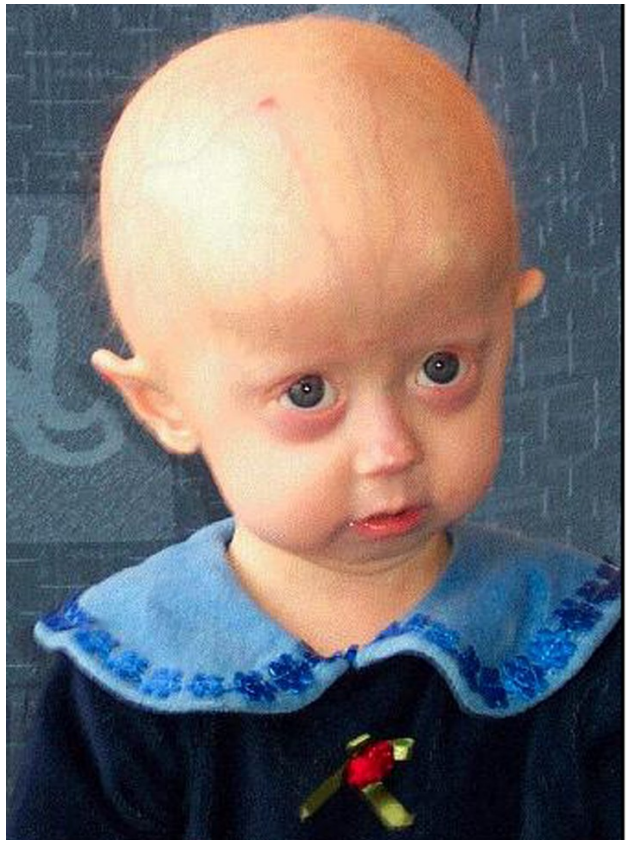
Where to start?

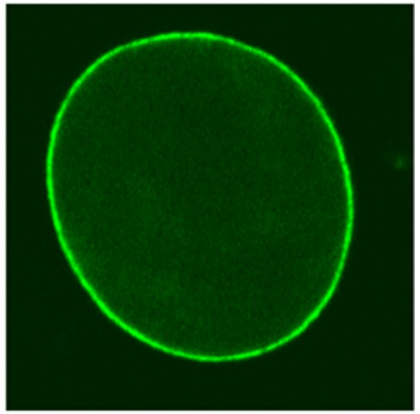
We are looking for better understanding of Hutchinson-Gilford progeria syndrome

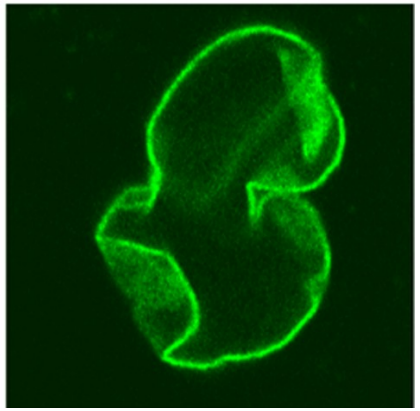
Yes, and ultimately, interested in identifying drug targets for this extremely rare disease

Where could we start finding more about this disease and possible targets?

Where to start?







Google

Hutchinson-Gilford progeria

Totes Imatges Vídeos Maps Més Configuració Eines

Aproximadament 132.000 resultats (0,66 segons)

Consell: Cerca només resultats en **català**. Podeu especificar l'idioma de la cerca a Preferències

Articles acadèmics per Hutchinson-Gilford progeria

Lamin a truncation in **Hutchinson-Gilford progeria** - De Sandre-Giovannoli - Citat per 972
... in lamin A cause **Hutchinson–Gilford progeria** ... - Eriksson - Citat per 1499
... in nuclear architecture in **Hutchinson–Gilford progeria** ... - Goldman - Citat per 758

Hutchinson-Gilford progeria syndrome - Genetics Home Reference

https://ghr.nlm.nih.gov/.../hutchinson-gilford-progeria-syndr... ▾ Tradueix aquesta pàgina

Hutchinson-Gilford progeria syndrome is a genetic condition characterized by the dramatic, rapid appearance of aging beginning in childhood. Affected children ...

Progeria - Wikipedia

https://en.wikipedia.org/wiki/Progeria ▾ Tradueix aquesta pàgina

Progeria is an extremely rare genetic disorder in which symptoms resembling aspects of aging ... The condition was later named **Hutchinson–Gilford progeria** syndrome. The word progeria comes from the Greek words "pro" (πρό), meaning ...

Sam Berns · Hallermann–Streiff syndrome · Progeria Research Foundation

Where to start?

NCBI Resources How To Sign in to NCBI

PubMed.gov
US National Library of Medicine
National Institutes of Health

PubMed | Hutchinson-Gilford progeria | Search

Create RSS Create alert Advanced Help

Article types
Clinical Trial
Review
Customize ...

Text availability
Abstract
Free full text
Full text

PubMed Commons
Reader comments
Trending articles

Publication dates
5 years
10 years
Custom range...

Species
Humans
Other Animals

Clear all

Show additional filters

Format: Summary Sort by: Most Recent Per page: 20 Send to

Filters: Manage Filters

Best matches for Hutchinson-Gilford progeria:

Hutchinson-Gilford progeria syndrome.
Ullrich NJ et al. Handb Clin Neurol. (2015)

Epigenetic involvement in **Hutchinson-Gilford progeria** syndrome: a mini-review.
Arancio W et al. Gerontology. (2014)

Hutchinson-Gilford progeria syndrome through the lens of transcription.
Prokocimer M et al. Aging Cell. (2013)

Switch to our new best match sort order

Search results

Items: 1 to 20 of 610

<< First < Prev Page 1 of 31 Next > Last >>

1. The Potential of iPSCs for the Treatment of Premature Aging Disorders.
Compagnucci C, Bertini E.
Int J Mol Sci. 2017 Nov 7;18(11). pii: E2350. doi: 10.3390/ijms18112350. Review.
PMID: 29112121 Free Article
Similar articles

2. Protein sequestration at the nuclear periphery as a potential regulatory mechanism in premature aging.
Serebryannyy L, Misteli T.
J Cell Biol. 2017 Oct 19. pii: jcb.201706061. doi: 10.1083/jcb.201706061. [Epub ahead of print] Review.
PMID: 29051264

Results by year

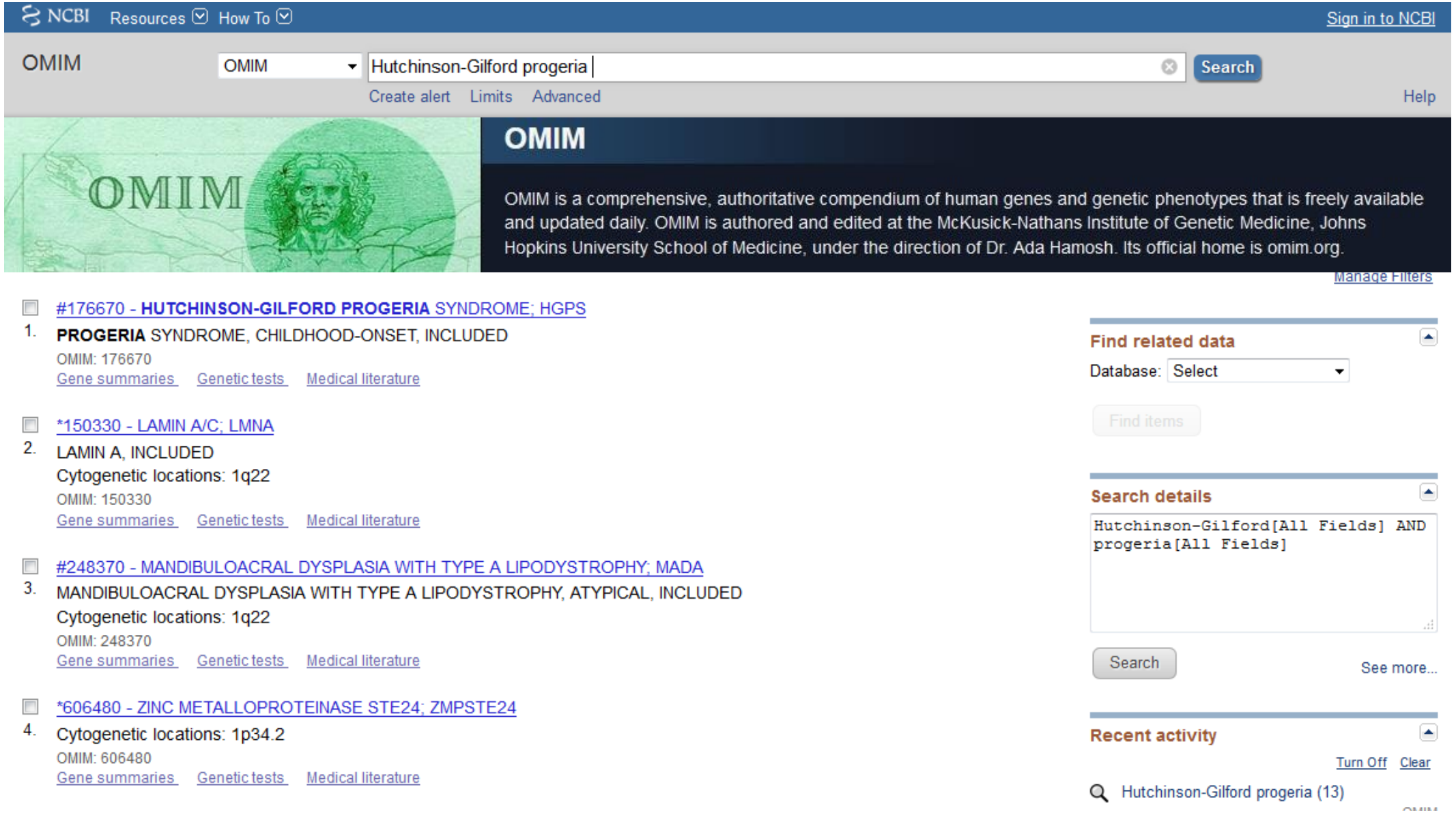
Download CSV

Related searches

hutchinson-gilford progeria syndrome

PMC Images search for *Hutchinson-Gilford progeria*

Where to start?



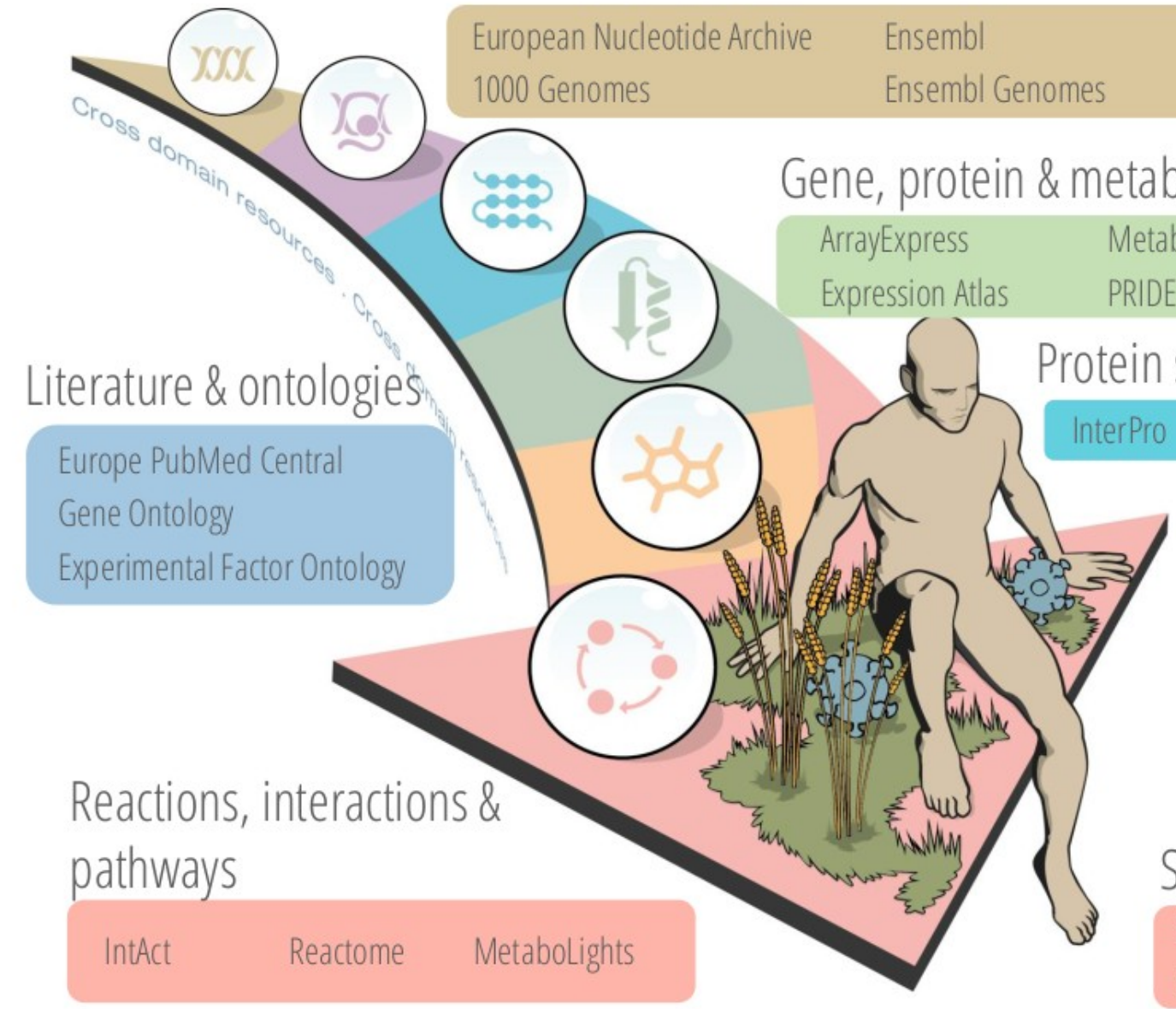
Integration, integration, integration

I wish I could go to one place only and get as much information in an easy fashion

Yes, one one-stop shop with comprehensive data that I can trust and rank, with intuitive visualization

That’d be fab! It’d be much quicker to carry out my experiments in the lab identifying and prioritizing new targets

Public databases for drug discovery



European Nucleotide Archive
1000 Genomes
Ensembl
Ensembl Genomes
European Genome-phenome Archive
Metagenomics portal

Gene, protein & metabolite expression

ArrayExpress
Expression Atlas
Metabolights
PRIDE

Literature & ontologies

Europe PubMed Central
Gene Ontology
Experimental Factor Ontology

Protein sequences, families & motifs

InterPro
Pfam
UniProt

Molecular structure

Protein Data Bank in Europe
Electron Microscopy Data Bank

Chemical biology

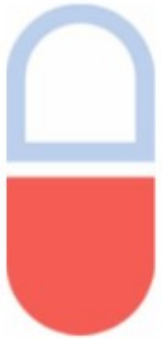
ChEMBL
ChEBI

Reactions, interactions & pathways

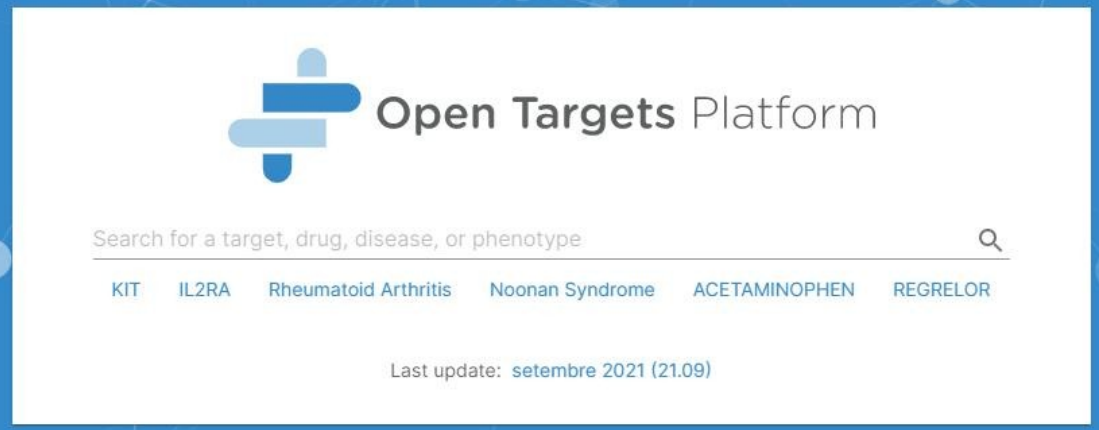
IntAct
Reactome
MetaboLights

Systems

BioModels
BioSamples
Enzyme Portal



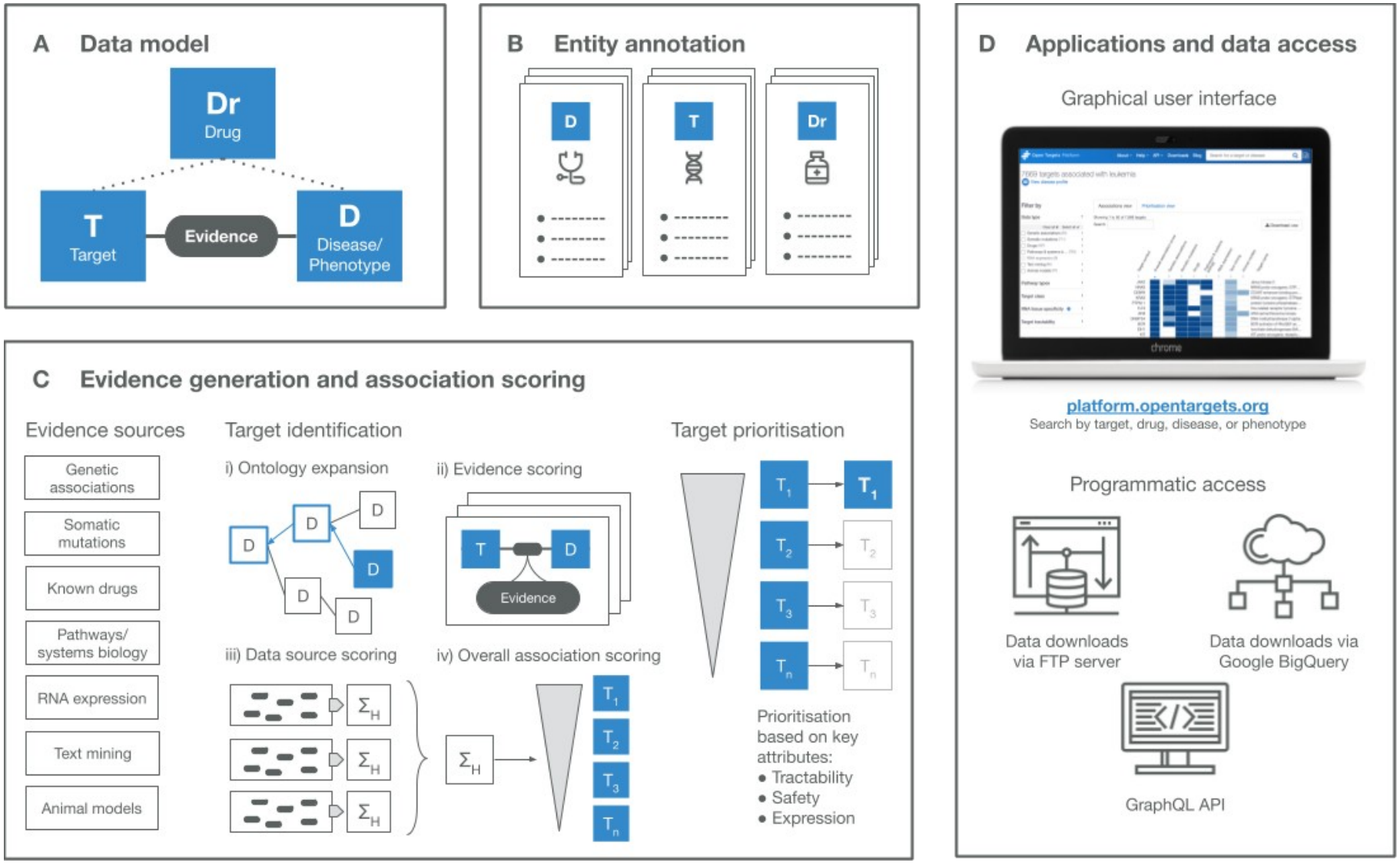
Open Targets



Open Targets is an innovative, large-scale, multi-year, public-private partnership that uses human genetics and genomics data for systematic drug target identification and prioritization.

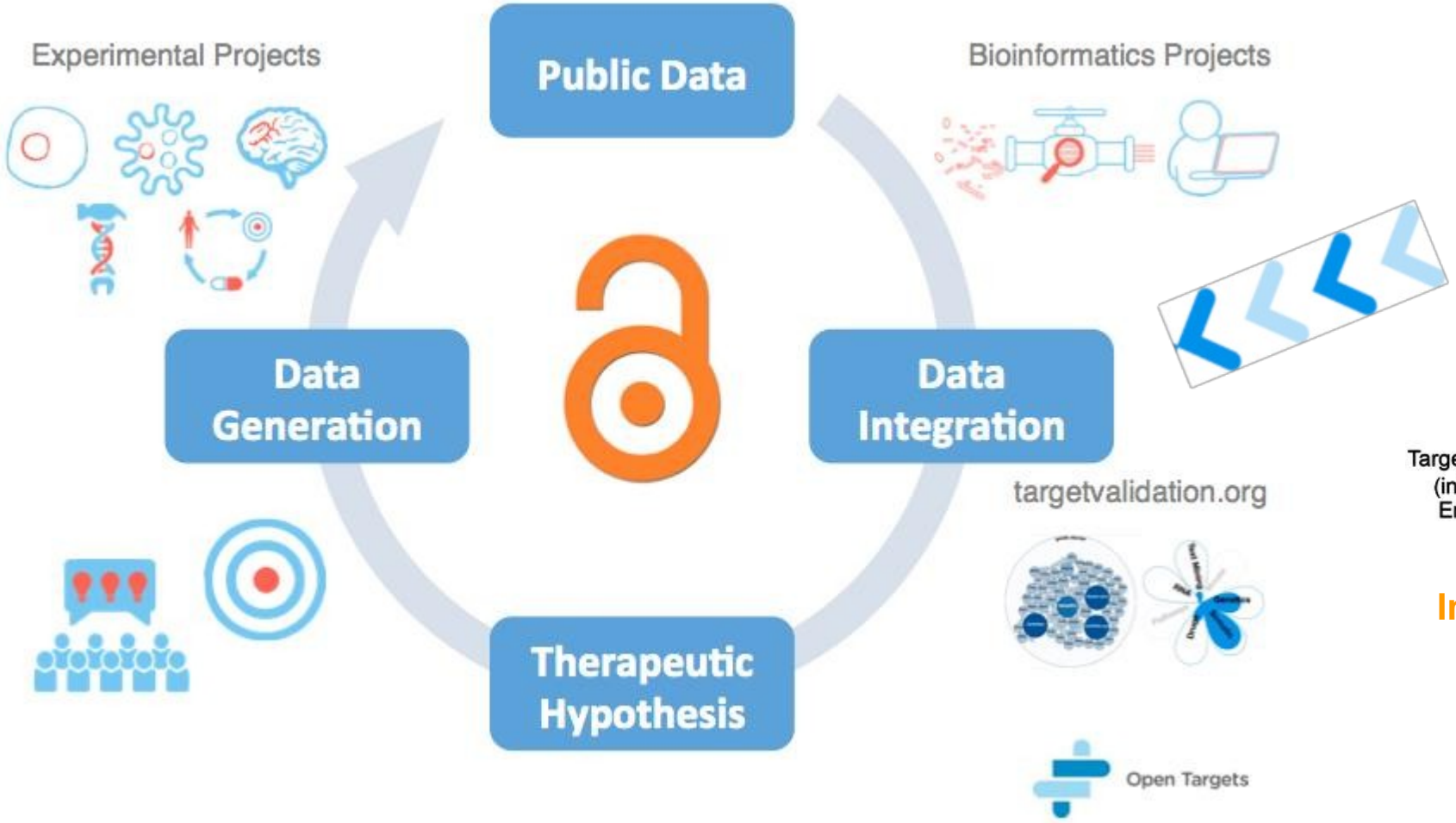
https://platform.opentargets.org/

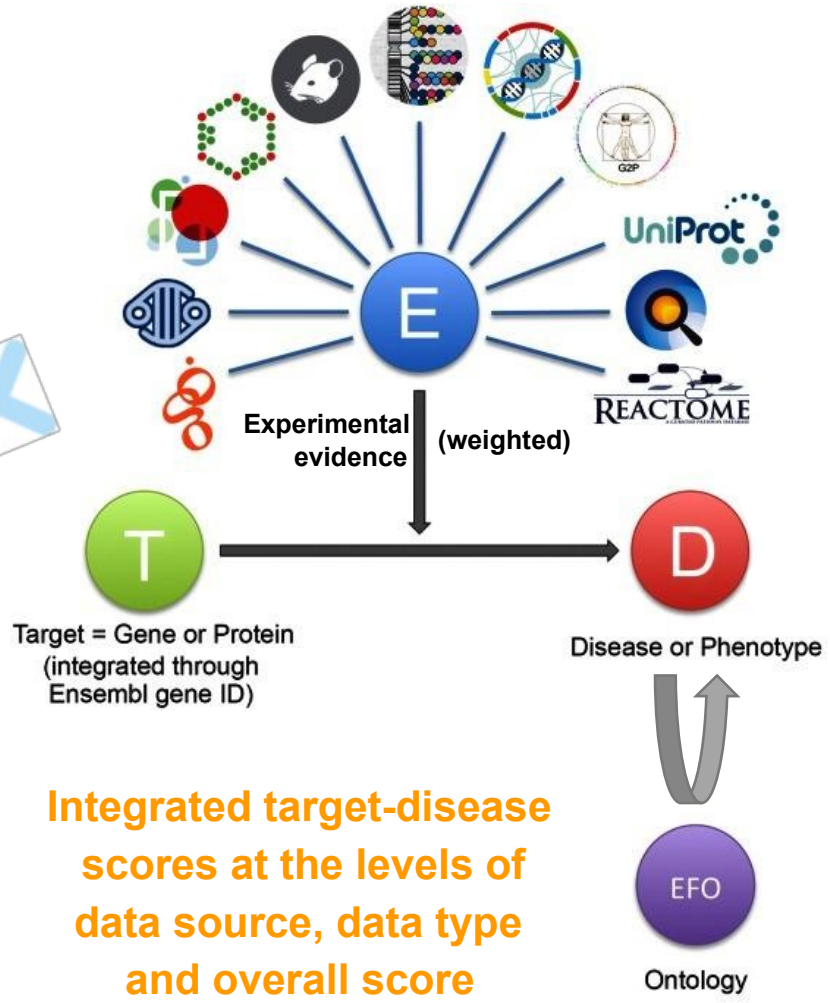
Open Targets



https://platform-docs.opentargets.org/getting-started

Open Targets





Integrated target-disease scores at the levels of data source, data type and overall score

Open Targets: sources of data

PhenoDigm: association of mouse models with disease
http://www.sanger.ac.uk/science/tools/phenodigm

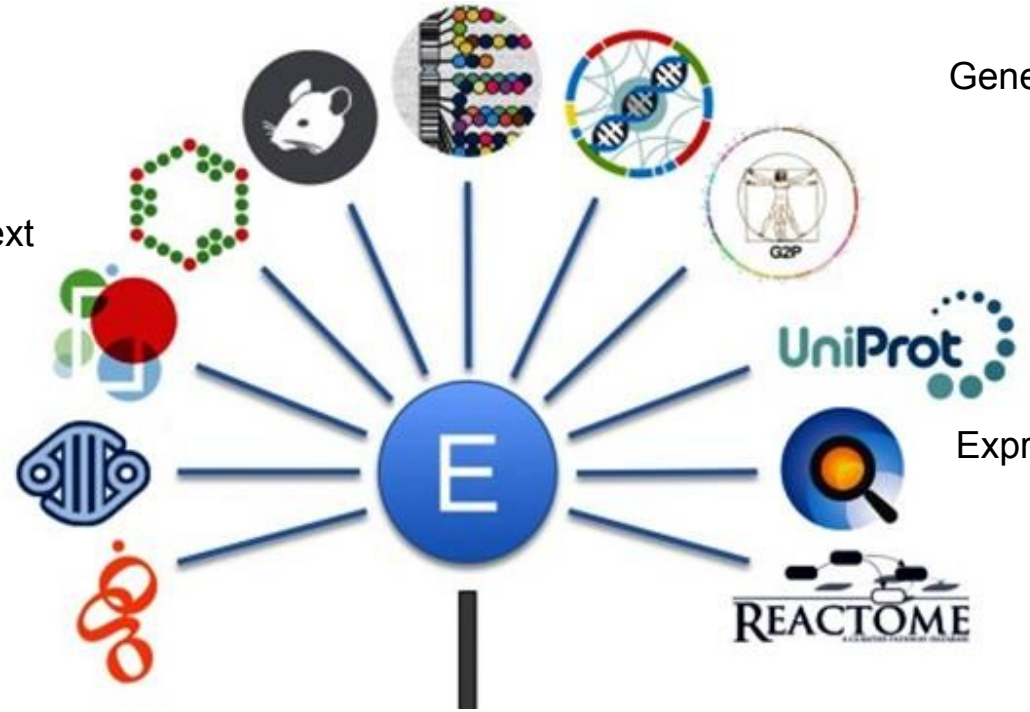
ChEMBL: known drugs linked to a disease and a known target
https://www.ebi.ac.uk/chembl

Europe PMC: mining titles, abstracts, full text
https://europepmc.org

COSMIC: Catalog Of Somatic Mutations In Cancer
http://cancer.sanger.ac.uk/cosmic/census

IntOGen: Integrative Onco Genomics
http://www.intogen.org

Genome Wide Association Studies
https://www.ebi.ac.uk/gwas



European Variation Archive: germline and somatic variants
https://www.ebi.ac.uk/eva

Gene2Phenotype: variants, genes, phenotypes in developmental disorders
https://www.ebi.ac.uk/gene2phenotype

Protein: sequence, annotation, function
https://www.ebi.ac.uk/uniprot

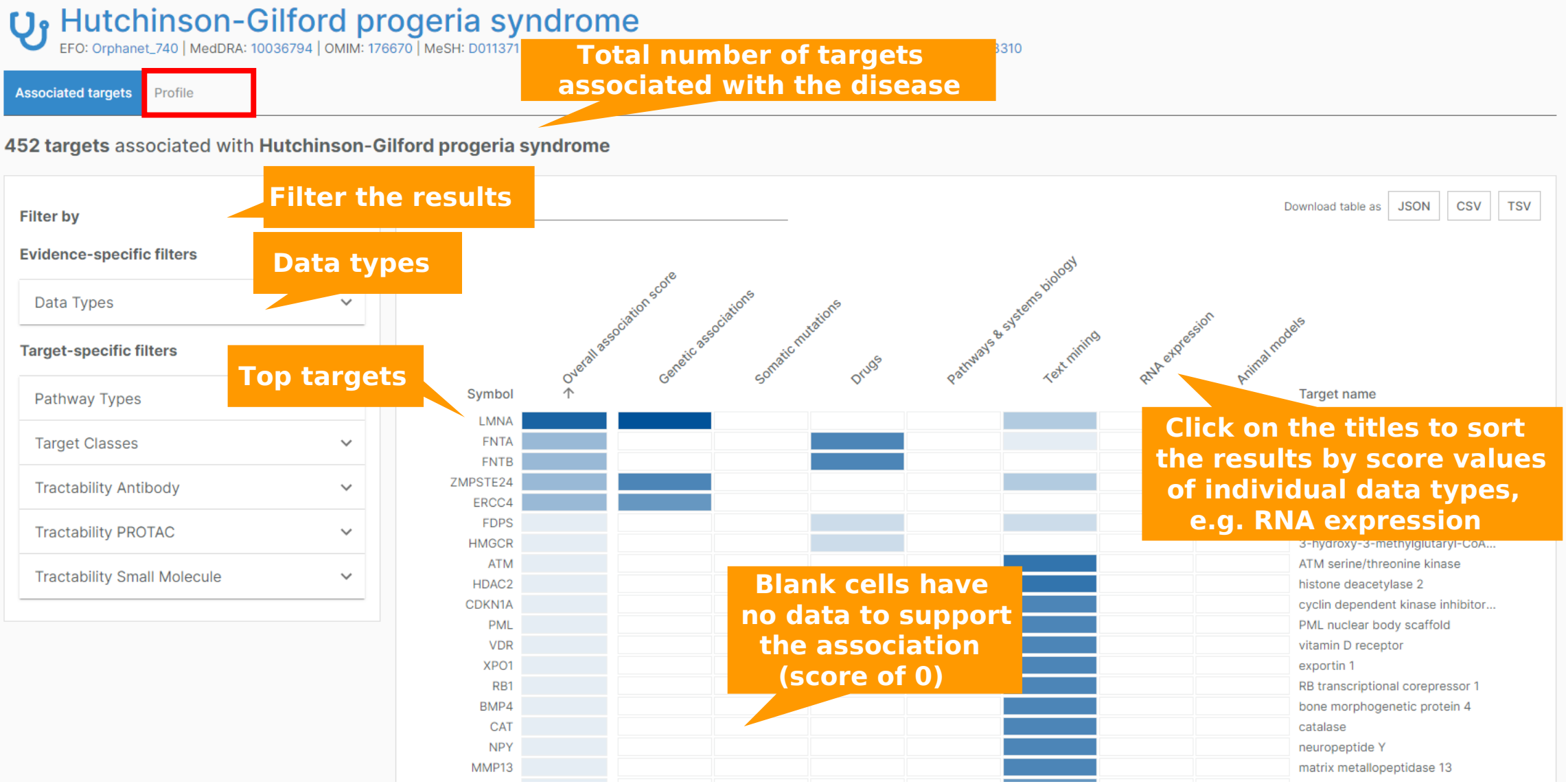
Expression Atlas: baseline/differential expression
https://www.ebi.ac.uk/gxa

Biochemical reactions and pathways
https://reactome.org

Open Targets: examples of questions

- Which targets are associated with a disease?
- What evidence supports this target-disease association?
- Are there FDA-approved drugs for this association?
- For a target, are there other diseases associated with it?
- If so, can I get associations for diseases from different therapeutic areas?
- What else can I find out about my drug target?
- Can I find out about the mechanisms of the disease?

Open Targets Use Case: Hutchinson-Gilford progeria syndrome



Open Targets Use Case: Hutchinson-Gilford progeria syndrome

O KD CS B

Hutchins

Information about the disease

EFO: Orphanet_740 | … 3300 | NCIt: C34951 | ICD10: E34.8 | MONDO: 0008310

Associated targets | **Profile**

Description

Hutchinson-Gilford progeria syndrome is a rare, fatal, autosomal dominant and premature aging disease, beginning in childhood and characterized by growth reduction, failure to thrive, a typical facial appearance (prominent forehead, protuberant eyes, thin nose with a beaked tip, thin lips, micrognathia and protruding ears) and distinct dermatologic features ... [show more]

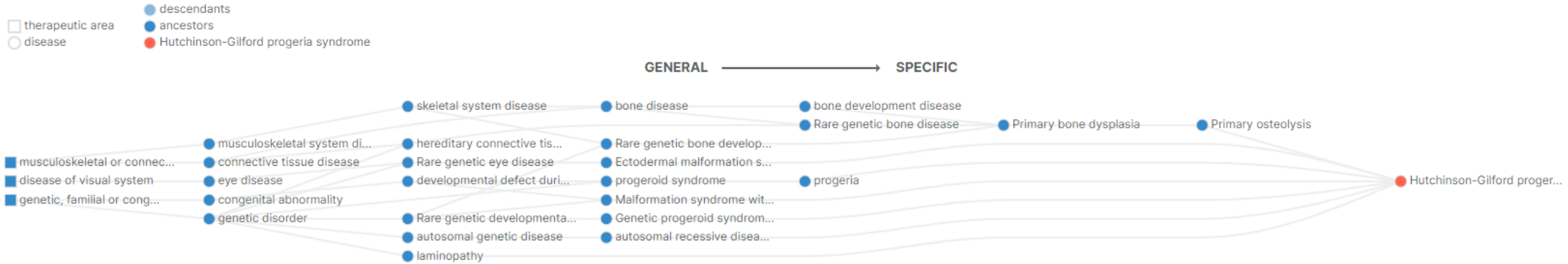
Synonyms

progeria | Progeria | HGPS | premature senility syndrome | Hutchinson-Gilford disease | Hutchinson-Gilford progeria syndrome | Hutchinson Gilford syndrome | Hutchinson Gilford progeria syndrome | progeria syndrome, childhood-onset

O Ontology	KD Known Drugs	CS Clinical signs and symptoms	B Bibliography
Belongs to 3 therapeutic areas	*3 drugs with 4 targets*	*104 phenotypes*	*1.692 publications*

Ontology

*Ontology subgraph including children, ancestors and therapeutic areas of **Hutchinson-Gilford progeria syndrome**. Source: EFO.*



Known Drugs

Open Targets Use Case: Hutchinson-Gilford progeria syndrome

Known Drugs

*Clinical precedence for investigational or approved drugs indicated for **Hutchinson-Gilford progeria syndrome** and curated mechanism of action. Source: ChEMBL.*

Known drugs

Search

Download table as JSON CSV TSV

Disease information		Drug information				Target information		Clinical trials information		
Disease	Drug	Type	Mechanism Of Action	Action Type	Symbol	Name	Phase	Status	Source
Hutchinson-Gilford progeria syndrome	LONAFARNIB	Small molecule	Protein farnesyltransferase inhibitor	Inhibitor	FNTB	farnesyltransferase, CAAX box, beta	Phase IV	N/A	FDA
Hutchinson-Gilford progeria syndrome	LONAFARNIB	Small molecule	Protein farnesyltransferase inhibitor	Inhibitor	FNTA	farnesyltransferase, CAAX box, alpha	Phase IV	N/A	FDA
Hutchinson-Gilford progeria syndrome	PRAVASTATIN	Small molecule	HMG-CoA reductase inhibitor	Inhibitor	HMGCR	3-hydroxy-3-methylglutaryl-CoA reductase	Phase II	Completed	2 references
Hutchinson-Gilford progeria syndrome	ZOLEDRONIC ACID	Small molecule	Farnesyl diphosphate synthase inhibitor	Inhibitor	FDPS	farnesyl diphosphate synthase	Phase II	Completed	2 references
Hutchinson-Gilford progeria syndrome	LONAFARNIB	Small molecule	Protein farnesyltransferase inhibitor	Inhibitor	FNTA	farnesyltransferase, CAAX box, alpha	Phase II	Completed	2 references
Hutchinson-Gilford progeria syndrome	LONAFARNIB	Small molecule	Protein farnesyltransferase inhibitor	Inhibitor	FNTB	farnesyltransferase, CAAX box, beta	Phase II	Completed	2 references

Rows per page: 10 1-6 of 6

Clinical signs and symptoms

*Clinical signs and symptoms observed in **Hutchinson-Gilford progeria syndrome**. Source: EFO, MONDO, HPO.*

Search

Download table as JSON CSV TSV

Qualifier	Phenotype	Phenotype ID	Aspect	Frequency	Onset	Modifier	Sex	Evidence	Source	References
	Relative macrocephaly[?]	HP:0004482	P[?]	Frequent	N/A	N/A	N/A	TAS[?]	HPO	ORPHA:740
	Hip pain[?]	HP:0030838	P[?]	Occasional	N/A	N/A	N/A	TAS[?]	HPO	ORPHA:740
	Short lingual frenulum[?]	HP:0000200	P[?]	Frequent	N/A	N/A	N/A	TAS[?]	HPO	ORPHA:740
	Limitation of movement at ankles[?]	HP:0010505	P[?]	Occasional	N/A	N/A	N/A	TAS[?]	HPO	ORPHA:740
	Stroke[?]	HP:0001297	P[?]	Occasional	N/A	N/A	N/A	TAS[?]	HPO	ORPHA:740
	Ankyloglossia[?]	HP:0010296	P[?]	Frequent	N/A	N/A	N/A	TAS[?]	HPO	ORPHA:740
	Delayed menarche[?]	HP:0012569	P[?]	Frequent	N/A	N/A	N/A	TAS[?]	HPO	ORPHA:740

Open Targets Use Case: Hutchinson-Gilford progeria syndrome

Hutc a syndrome

EFO: Orph 0011371 | UMLS: CN236401, C0033300 | NCIt: C34951 | ICD10: E34.8 | MONDO: 0008310

Back to the targets…

Associated targets | Profile

452 targets associated with **Hutchinson-Gilford progeria syndrome**

Filter by

Evidence-specific filters

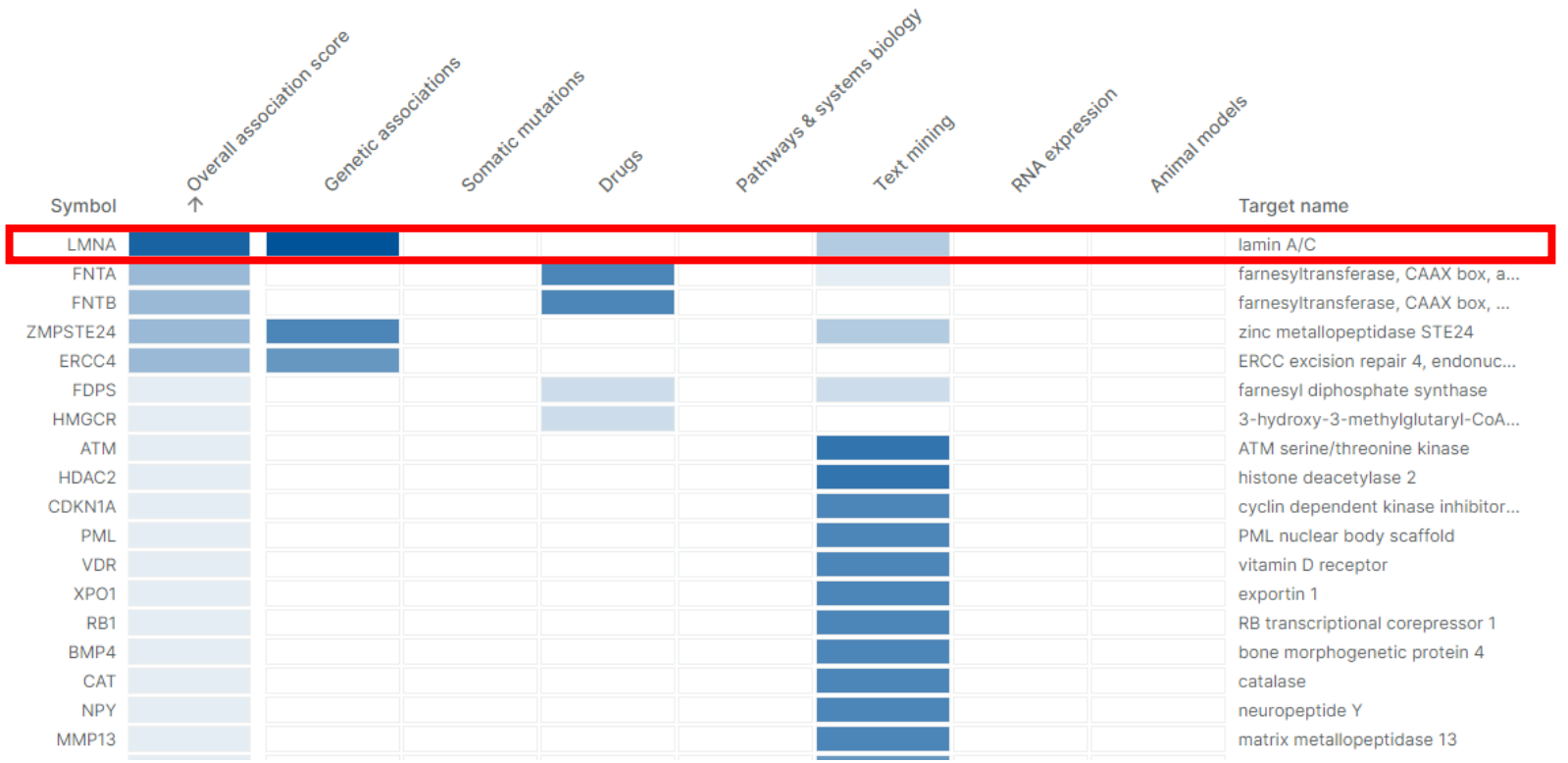
- Data Types

Target-specific filters

- Pathway Types
- Target Classes
- Tractability Antibody
- Tractability PROTAC
- Tractability Small Molecule

Search

Download table as JSON CSV TSV



Symbol	Target name
LMNA	lamin A/C
FNTA	farnesyltransferase, CAAX box, a...
FNTB	farnesyltransferase, CAAX box, ...
ZMPSTE24	zinc metallopeptidase STE24
ERCC4	ERCC excision repair 4, endonuc...
FDPS	farnesyl diphosphate synthase
HMGCR	3-hydroxy-3-methylglutaryl-CoA...
ATM	ATM serine/threonine kinase
HDAC2	histone deacetylase 2
CDKN1A	cyclin dependent kinase inhibitor...
PML	PML nuclear body scaffold
VDR	vitamin D receptor
XPO1	exportin 1
RB1	RB transcriptional corepressor 1
BMP4	bone morphogenetic protein 4
CAT	catalase
NPY	neuropeptide Y
MMP13	matrix metallopeptidase 13

Open Targets Use Case: Hutchinson-Gilford progeria syndrome

Evidence for LMNA in Hutchinson-Gilford progeria syndrome

LMNA

Description
Lamins are components of the nuclear lamina, a fibrous layer on the nucleoplasmic side of the inner nuclear membrane, which is thought to provide a framework for the nuclear envelope and may also interact with chromatin. Lamin A and C are present in equal amounts in the lamina of mammals. Recruited by DNA repair proteins XRCC4 and IFFO1 to the DNA
... [show more]

Synonyms
Prelamin-A/C | Lamin-A/C | 70 kDa lamin | Renal carcinoma antigen NY-REN-32 | LMNA | LMN1 | HGPS | MADA | mandibuloacral dysplasia type A | CDCD1
... [show more]

Hutchinson-Gilford progeria syndrome

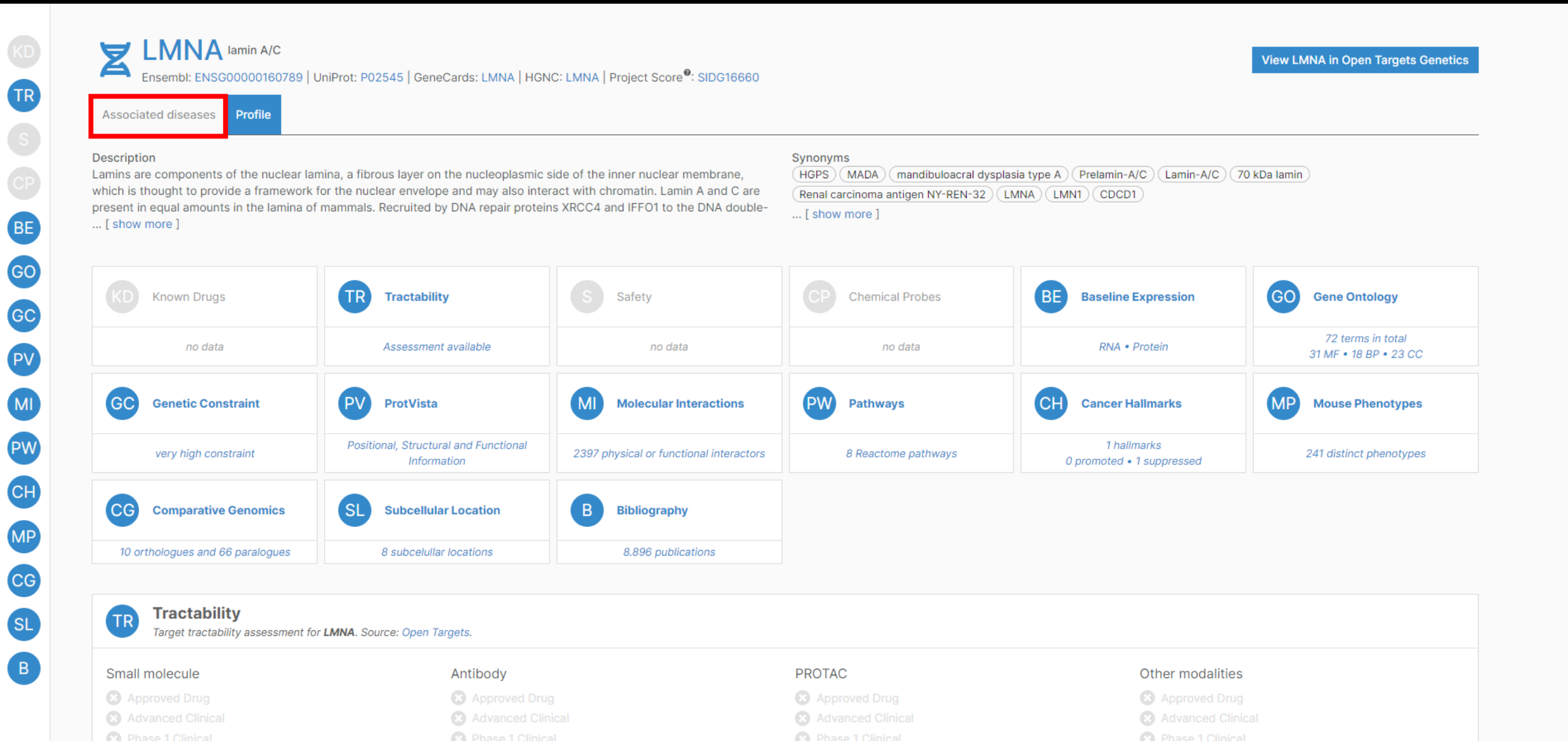
Description
Hutchinson-Gilford progeria syndrome is a rare, fatal, autosomal dominant and premature aging disease, beginning in childhood and characterized by growth reduction, failure to thrive, a typical facial appearance (prominent forehead, protuberant eyes, thin nose with a beaked tip, thin lips, micrognathia and protruding ears) and distinct dermatologic
... [show more]

Synonyms
progeria | Progeria | HGPS | premature senility syndrome | Hutchinson-Gilford disease | Hutchinson-Gilford progeria syndrome | Hutchinson Gilford syndrome | Hutchinson Gilford progeria syndrome | progeria syndrome, childhood-onset

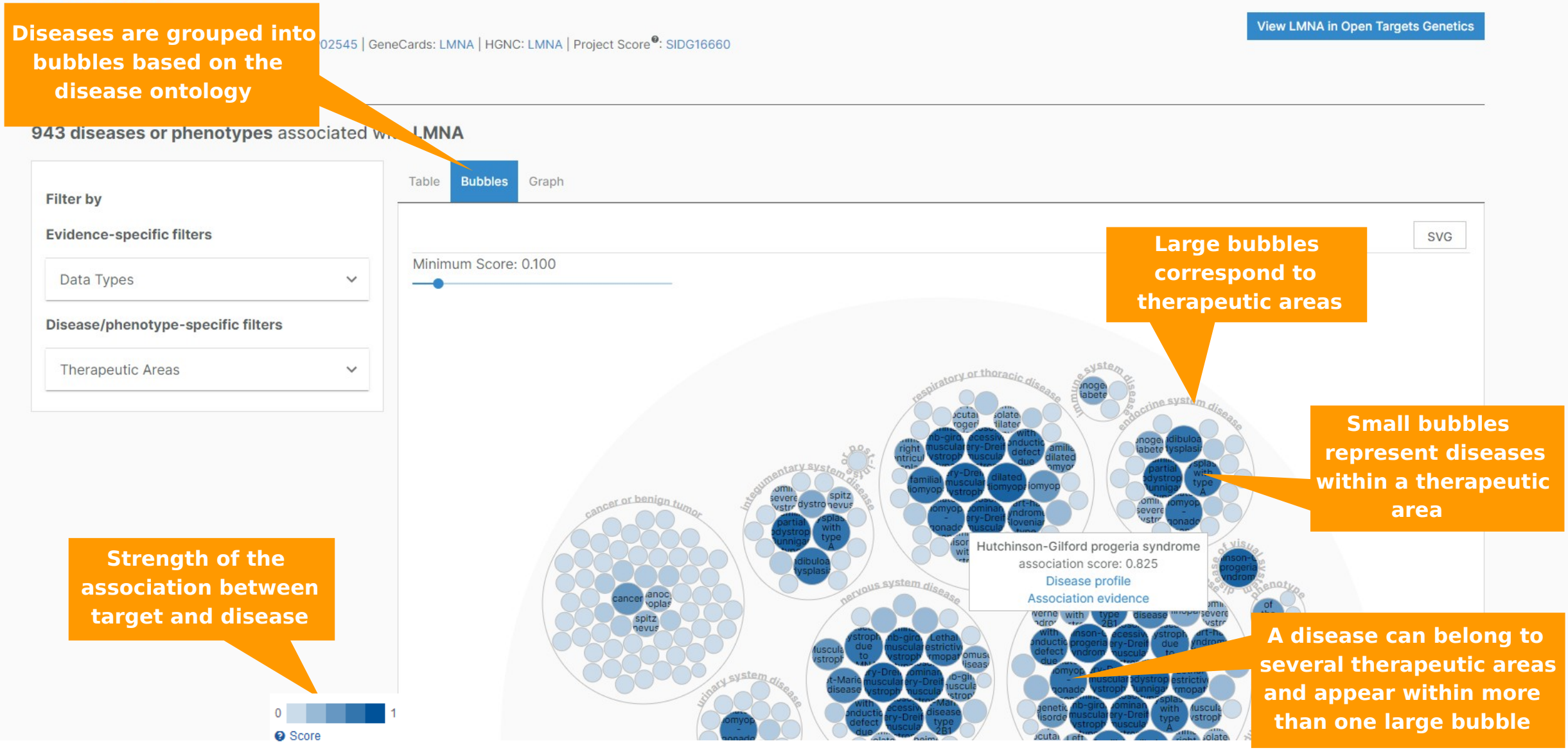
OT Genetics Portal Genetic associations *no data*	PheWAS Catalog Genetic associations *no data*	**ClinVar** Genetic associations *93 entries*	**GEL PanelApp** Genetic associations *6 entries*	**Gene2Phenotype** Genetic associations *2 entries*	**UniProt literature** Genetic associations *1 entry*
UniProt variants Genetic associations *10 entries*	ClinGen Genetic associations *no data*	**Orphanet** Genetic associations *1 entry*	Cancer Gene Census Somatic mutations *no data*	IntOGen Somatic mutations *no data*	ClinVar (somatic) Somatic mutations *no data*
ChEMBL Drugs *no data*	Project Score Pathways & systems biology *no data*	SLAPenrich Pathways & systems biology *no data*	PROGENy Pathways & systems biology *no data*	Reactome Pathways & systems biology *no data*	Gene signatures Pathways & systems biology
Europe PMC Text mining	Expression Atlas RNA expression	PhenoDigm Animal models			

Details of all evidences supporting this association

Open Targets Use Case: Hutchinson-Gilford progeria syndrome



Open Targets Use Case: Hutchinson-Gilford progeria syndrome



InterMine

InterMine | Biologists | Developers | Contact | Resources

http://intermine.org/

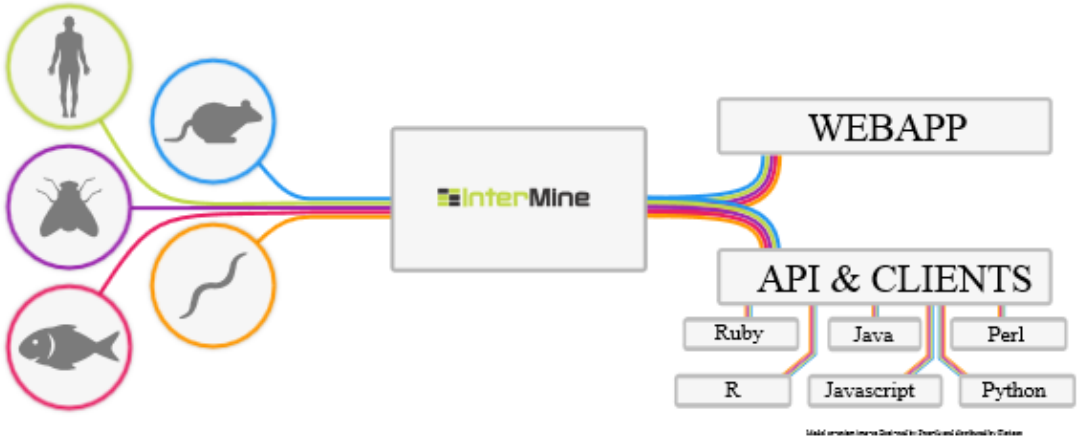
Disparate data in, unified data out

InterMine integrates biological data sources, making it easy to query and analyse data.

InterMine is open source (LGPL 2.1) and free to use.

It's a software system that you can install on your own servers to make data available on the web.

There are many different InterMines worldwide, covering a broad range of model organisms and life science research areas.



YeastMine | WormMine | FlyMine | ZebrafishMine | RatMine | MouseMine

PeanutMine | XenMine | LegumeMine | BovineMine | HumanMine | TetraMine

TargetMine | PlanMine | PhytoMine | HymenopteraMine | ChickpeaMine

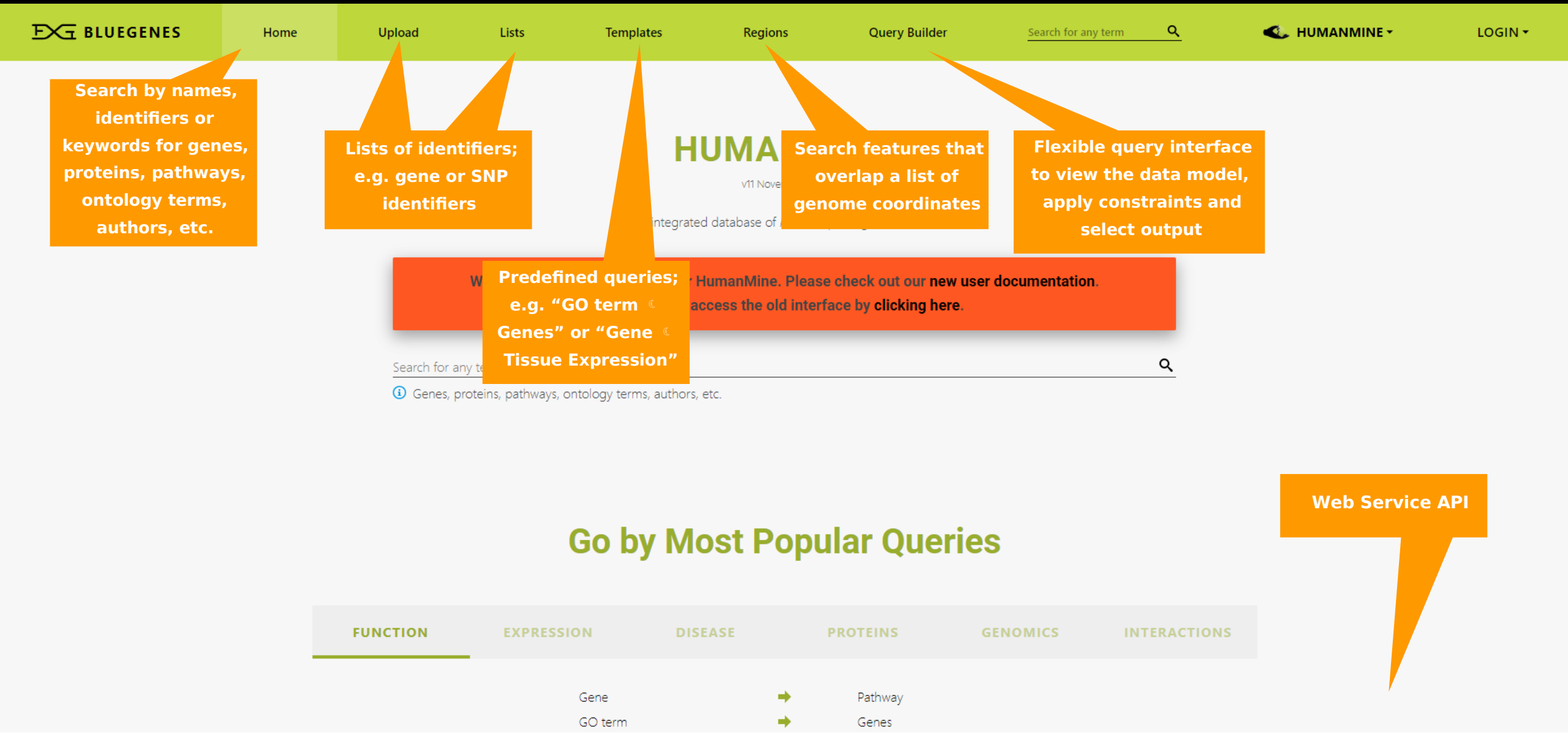
SynBioMine

There's an InterMine for (almost) anyone

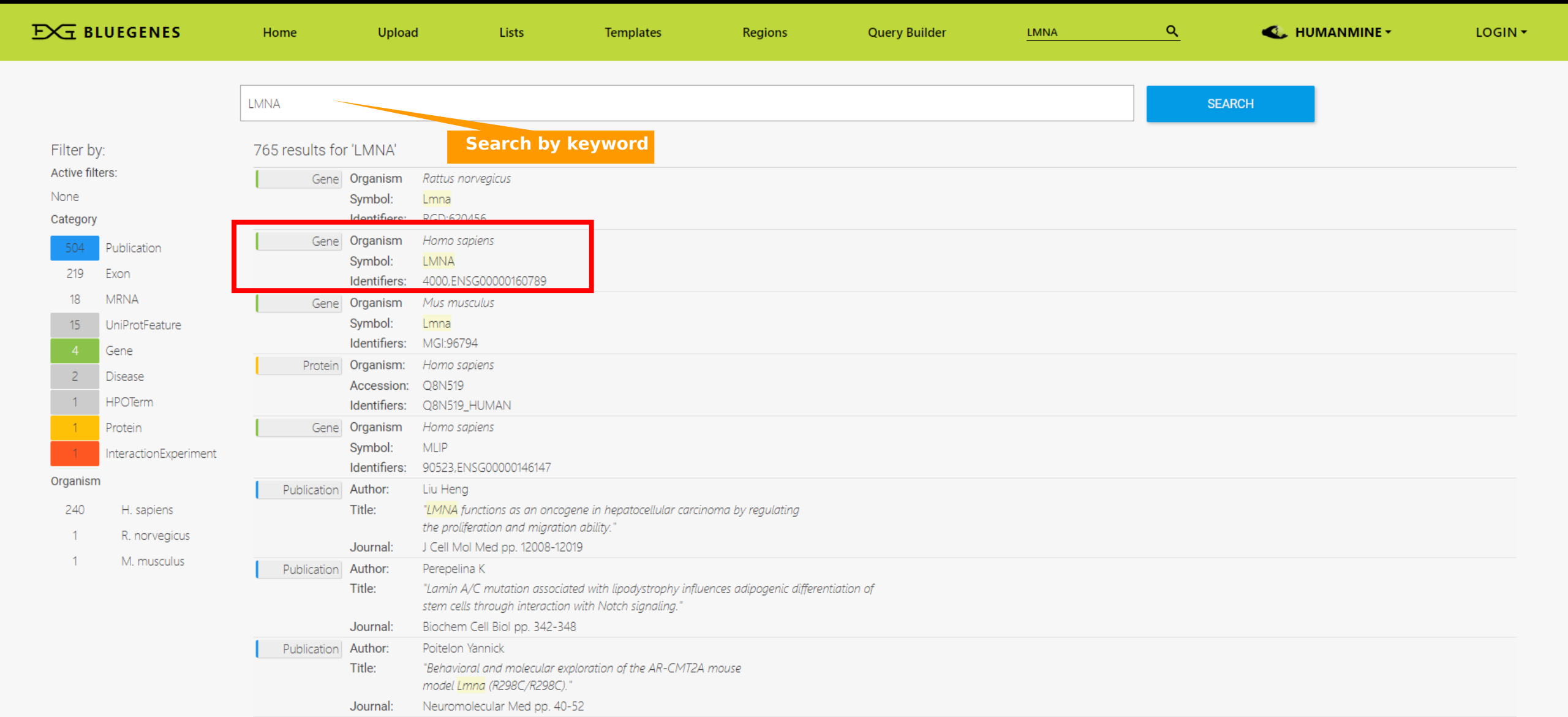
With InterMine you can explore organism and other research data provided by many different organizations, moving between databases using criteria such as homology.

This is a sample of the InterMine installations available - click on one to go straight to that service.

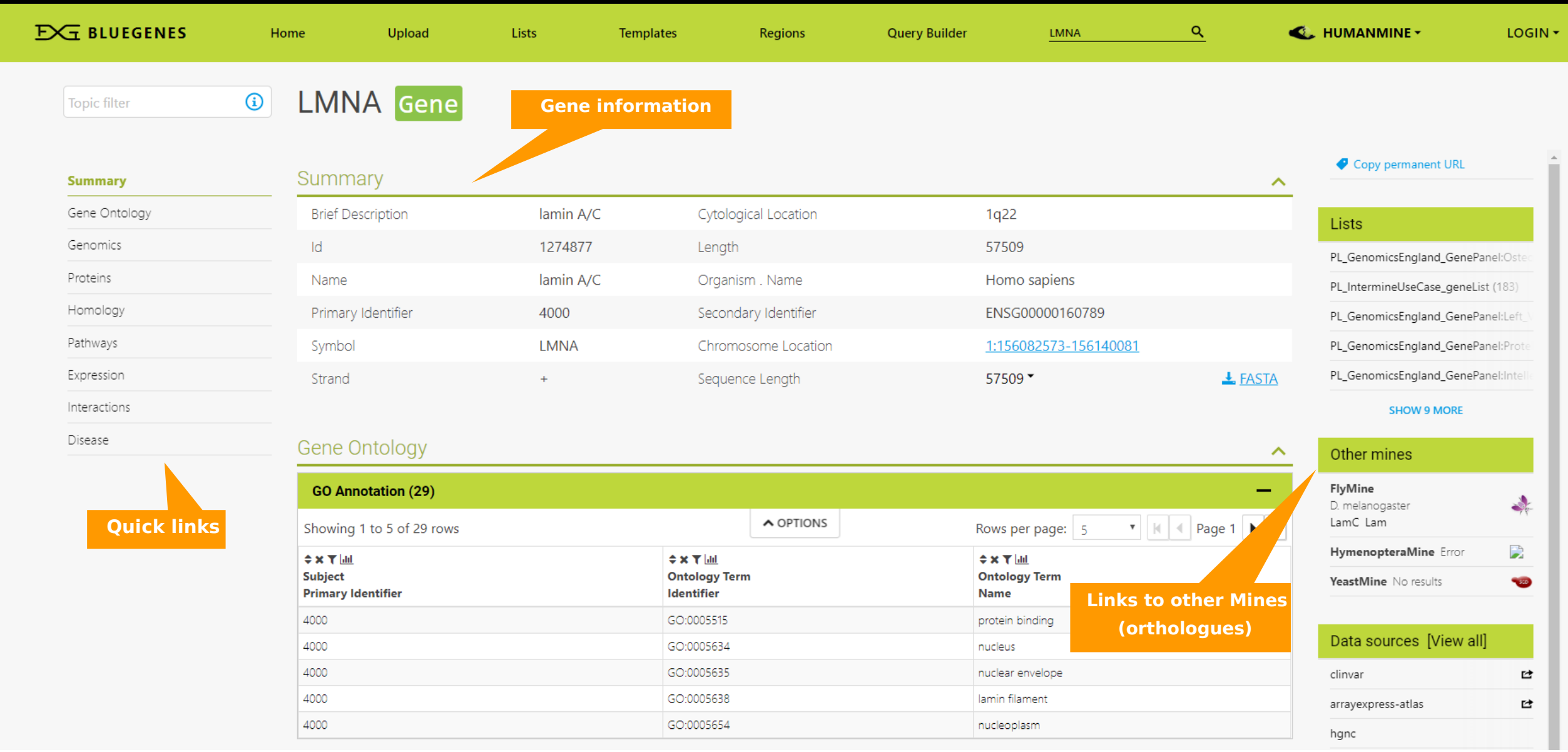
InterMine: Querying the HumanMine



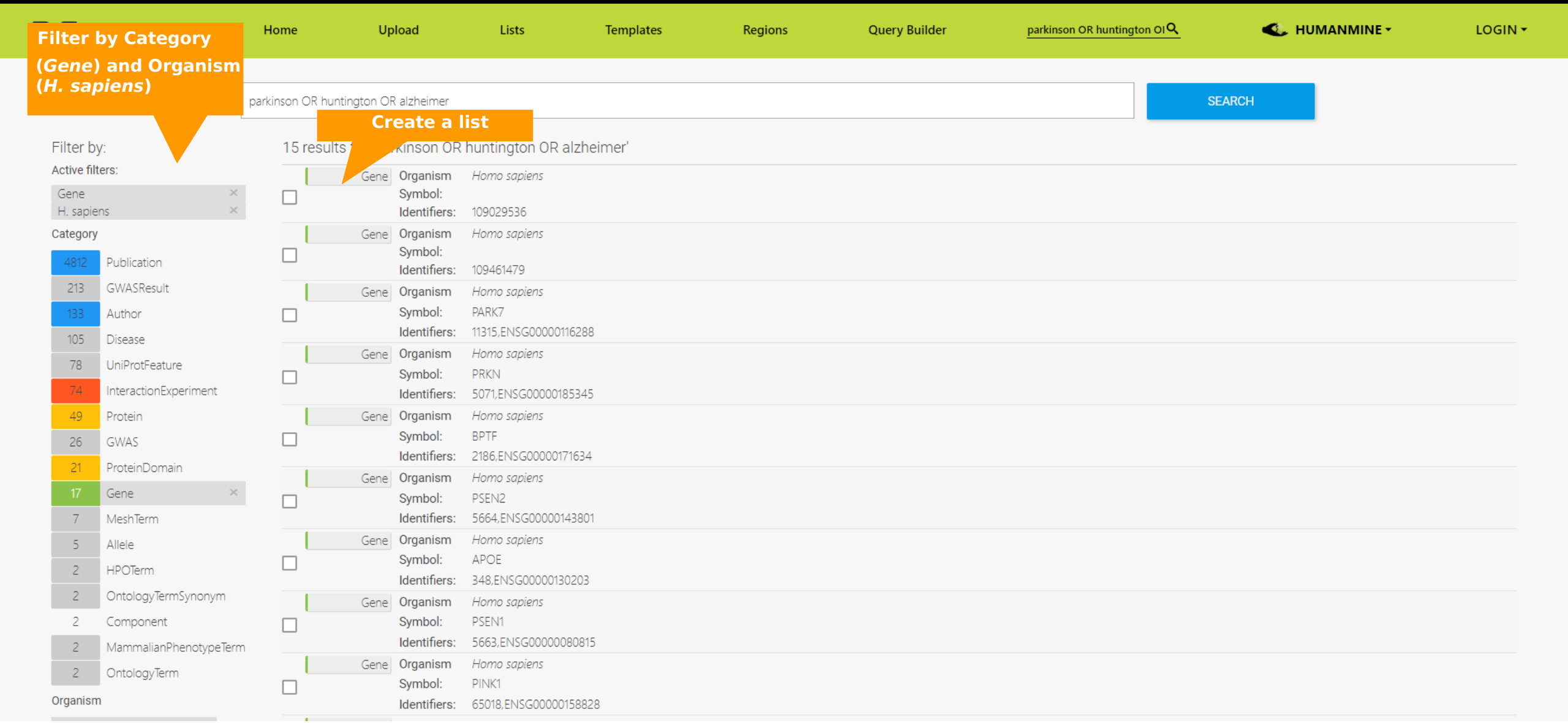
InterMine Use Case: Hutchinson-Gilford progeria (search by keyword)



InterMine Use Case: Hutchinson-Gilford progeria (search by keyword)



InterMine Use Case: neurodegenerative diseases (lists)



InterMine Use Case: neurodegenerative diseases (lists)

BLUEGENES | Home | Upload | Lists | Templates | Regions | Query Builder | Activity | parkinson OR huntington OI | HUMANMINE | LOGIN

Lists

Generate Python, Perl, Java, Ruby, JavaScript, or XML code

Query Results

Back to Search | Recent Queries

ADD COLUMNS | MANAGE FILTERS | MANAGE RELATIONSHIPS | UNDO | SAVE LIST | PYTHON | EXPORT

Showing 1 to 10 of 15 rows — Rows per page: 10 — Page 1

Gene Symbol	Gene Name	Gene Primary Identifier	Gene Secondary Identifier	Gene Length	Organism Name
APOE	apolipoprotein E	348	ENSG00000130203	3598	Homo sapiens
APP	amyloid beta precursor protein	351	ENSG00000142192	290579	Homo sapiens
ATP13A2	ATPase cation transporting 13A2	23400	ENSG00000159363	26015	Homo sapiens
BPTF	bromodomain PHD finger transcription factor	2186	ENSG00000171634	158876	Homo sapiens
GATD1	glutamine amidotransferase class 1 domain containing 1	347862	ENSG00000177225	10407	Homo sapiens
GIGYF2	GRB10 interacting GYF protein 2	26058	ENSG00000204120	163275	Homo sapiens
LRRK2	leucine rich repeat kinase 2	120892	ENSG00000188906	144396	Homo sapiens
PARK7	Parkinsonism associated deglycase	11315	ENSG00000116288	23795	Homo sapiens
PINK1	PTEN induced kinase 1	65018	ENSG00000158828	18054	Homo sapiens
PRKN	parkin RBR E3 ubiquitin protein ligase	5071	ENSG00000185345	1380386	Homo sapiens

Max p-value: 0.05 — Test Correction: Holm-Bonferroni

Background population: Choose a list

Filter enrichment results: Text to filter items

Gene Ontology Enrichment (0)

Ontology: biological_process

Publication Enrichment

Pathway Enrichment (3) VIEW

DataSet: All

Item (matches)	p-value
Amyloid fiber formation (4)	6.163200e-3
Nuclear signaling by ERBB4 (3)	7.305433e-3
Signaling by ERBB4 (3)	4.210130e-2

Protein Domain Enrichment (2) VIEW

Item (matches)	p-value
Peptidase A22A, presenilin (2)	7.659308e-3
Presenilin, C-terminal (2)	7.659308e-3

Much more information below the table!!!

Widgets

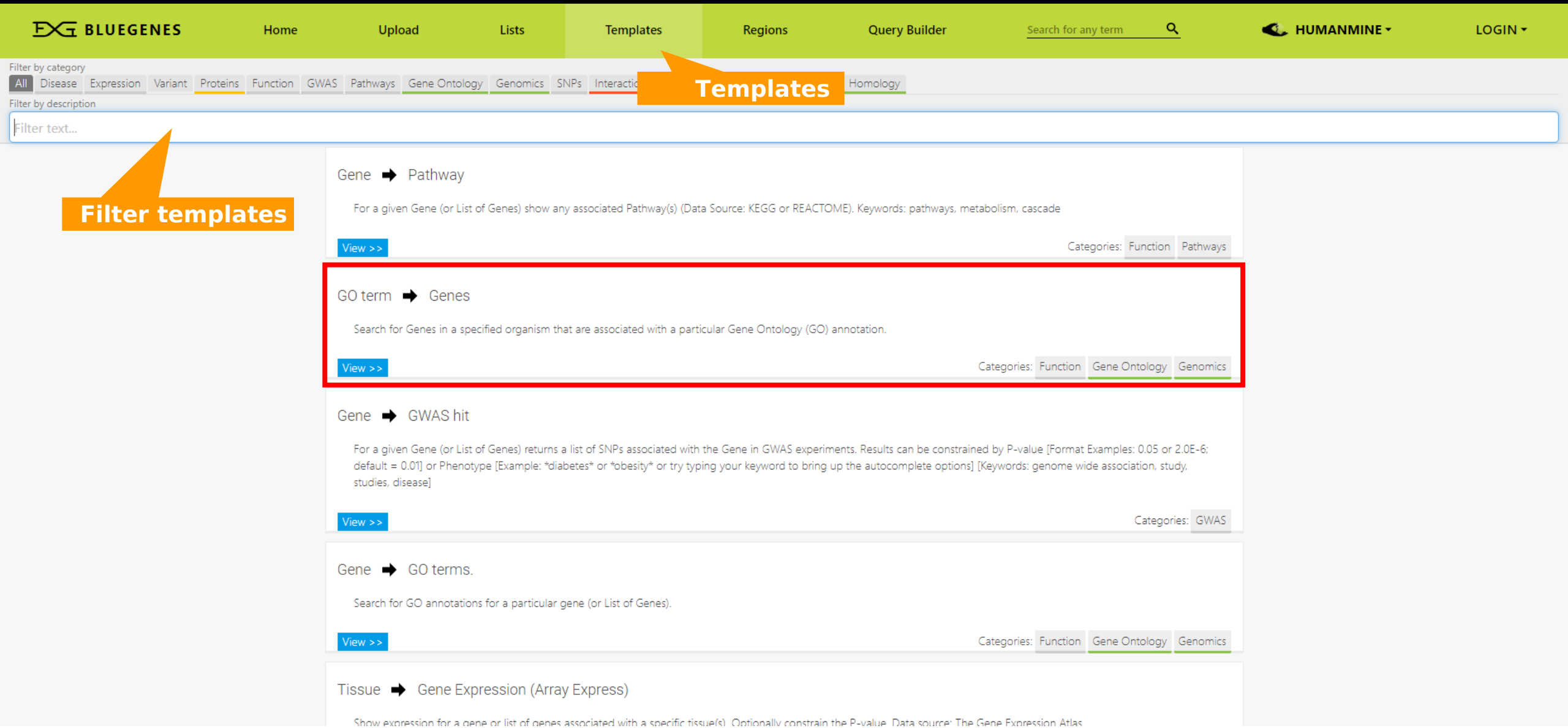
Chromosome Distribution

Actual: number of items in this list found on each chromosome. Expected: given the total number of items on the chromosome and the number of items in this list, the number of items expected to be found on each chromosome.

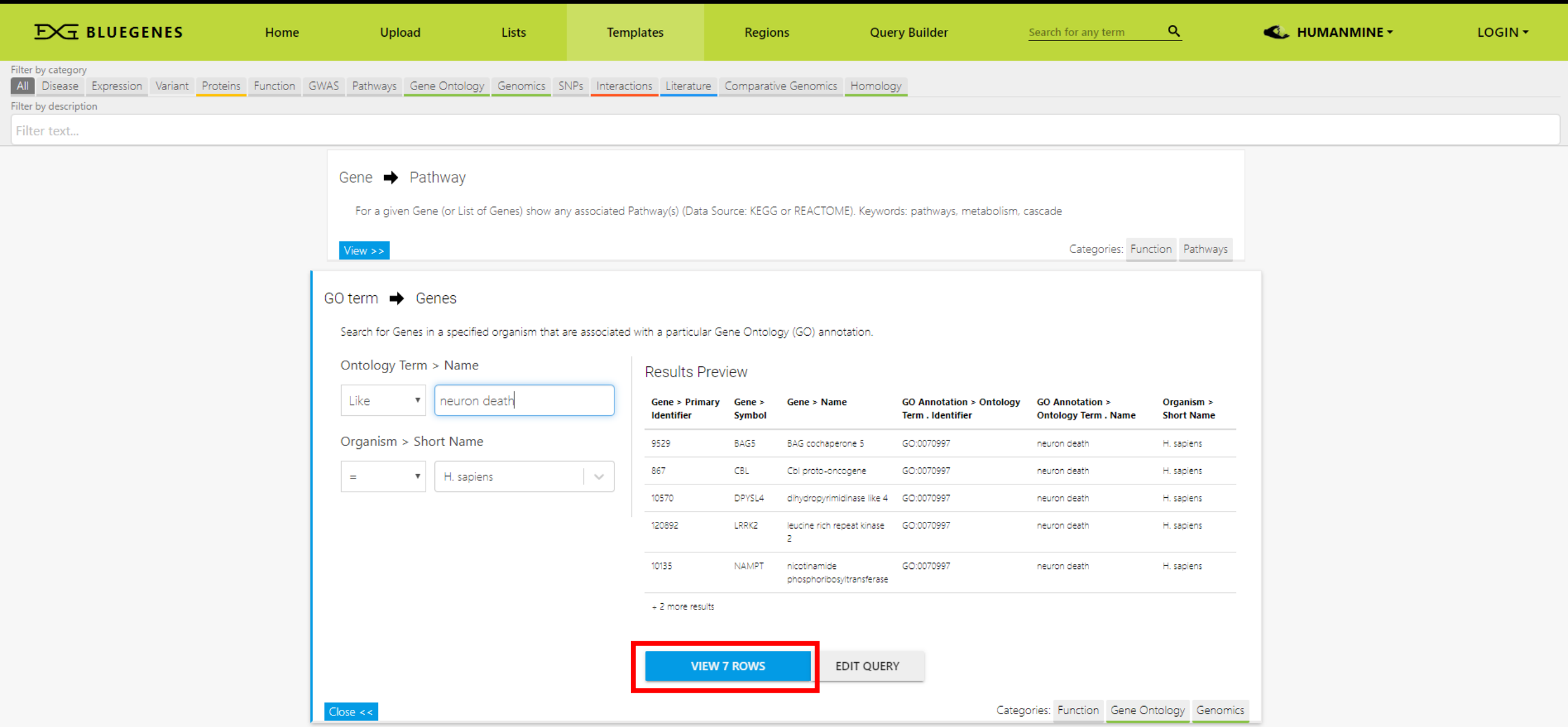
Interactions

Genes (from the list or not) that interact with genes in this list. Counts may include the same interaction more than once if observed in multiple experiments.

InterMine Use Case: genes involved in neuron death (templates)



InterMine Use Case: genes involved in neuron death (templates)



InterMine Use Case: genes involved in neuron death (templates)

BLUEGENES | Home | Upload | Lists | Templates | Regions | Query Builder | Activity | Search for any term | HUMANMINE | LOGIN

Query Results

Back to Templates | Recent Queries

ADD COLUMNS | MANAGE FILTERS | MANAGE RELATIONSHIPS | UNDO | SAVE LIST | PYTHON | EXPORT

Showing 1 to 7 of 7 rows

Rows per page: All (7) | Page 1

Gene Primary Identifier	Gene Symbol	Gene Name	Ontology Term Identifier	Ontology Term Name	Organism Short Name
9529	BAG5	BAG cochaperone 5	GO:0070997	neuron death	H. sapiens
867	CBL	Cbl proto-oncogene	GO:0070997	neuron death	H. sapiens
10570	DPYSL4	dihydropyrimidinase like 4	GO:0070997	neuron death	H. sapiens
120892	LRRK2	leucine rich repeat kinase 2	GO:0070997	neuron death	H. sapiens
10135	NAMPT	nicotinamide phosphoribosyltransferase	GO:0070997	neuron death	H. sapiens
9481	SLC25A27	solute carrier family 25 member 27	GO:0070997	neuron death	H. sapiens
6548	SLC9A1	solute carrier family 9 member A1	GO:0070997	neuron death	H. sapiens

Enrichment

Enrichment column: Gene

Max p-value: 0.05

Test Correction: Holm-Bonferroni

Background population: Choose a list

Filter enrichment results: Text to filter items

Gene Ontology Enrichment (0)

Ontology: biological_process

Publication Enrichment

Pathway Enrichment (0)

DataSet: All

Protein Domain Enrichment (0)

Widgets

Chromosome Distribution

Actual: number of items in this list found on each chromosome. Expected: given the total number of items on the chromosome and the number of items in this list, the number of items expected to be found on each chromosome.

All Genes in the table have been analysed in this widget.

Organism: Homo sapiens

Actual | Expected

Interactions

Genes (from the list or not) that interact with genes in this list. Counts may include the same interaction more than once if observed in multiple experiments.

All Genes in the table have been analysed in this widget.

VIEW ALL

BioEntity.primaryIdentifier	BioEntity.name
3308	heat shock protein family A