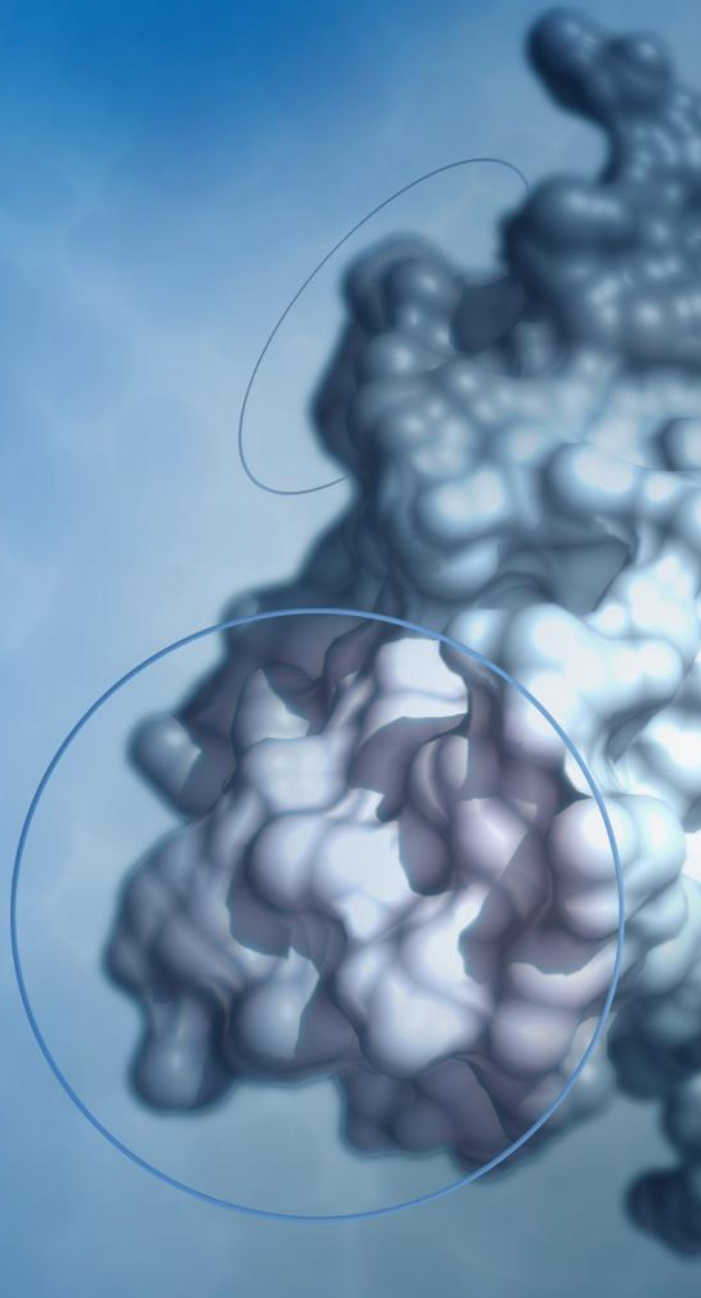
Open Targets Platform

Data integration case study

Part of “Summer School of Bioinformatics”
26th-30th June 2017



Denise Carvalho-Silva

Scientific Outreach Officer
Core Bioinformatics and Computational Pipelines
Open Targets, EMBL-EBI
Wellcome Genome Campus

Open Targets

Objectives

The **Open Targets Platform**: integrated portal for drug identification

The **Open Targets Consortium**

How to **get in touch** with us

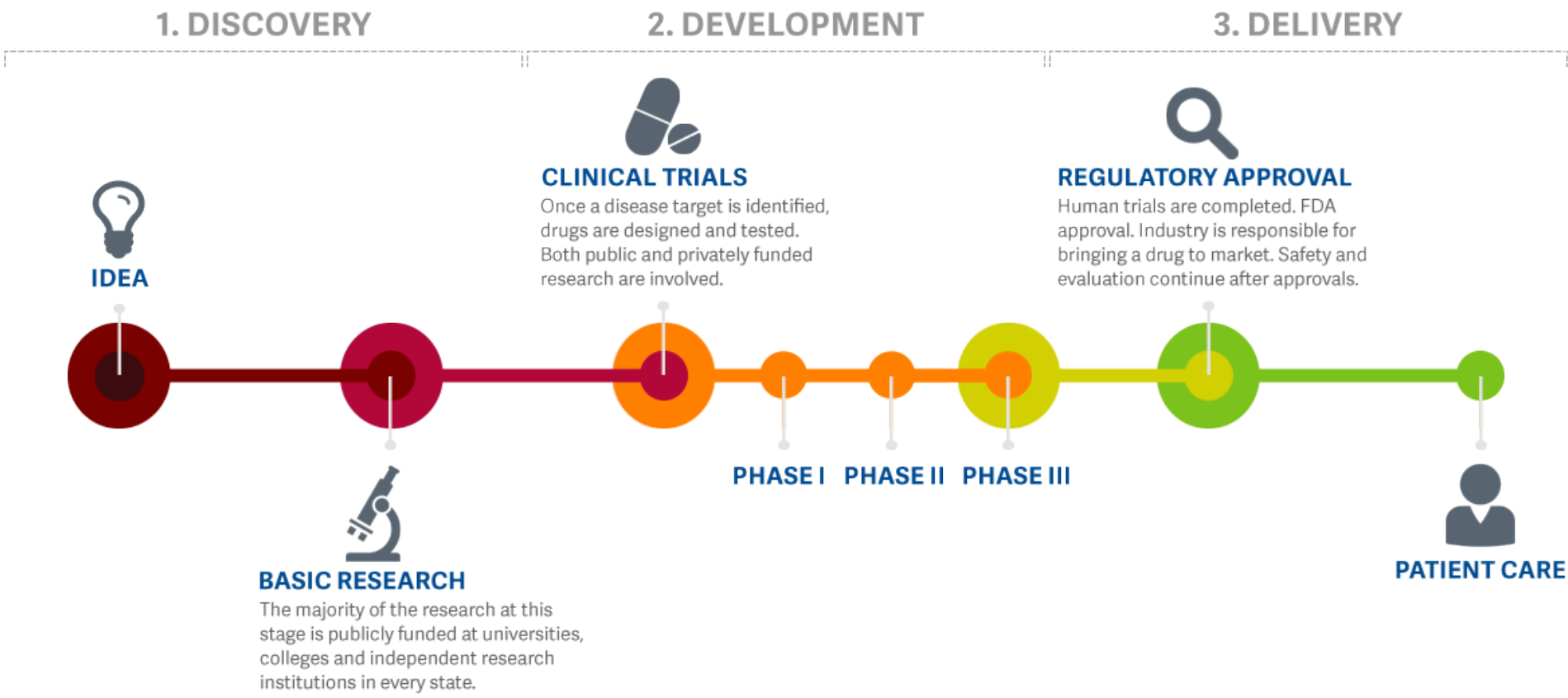
Open Targets

Outline

- Disease and Drug Discovery: where to start
- Open Targets: Platform and consortium
- Wrap up

Open Targets

Drug discovery path: timeline

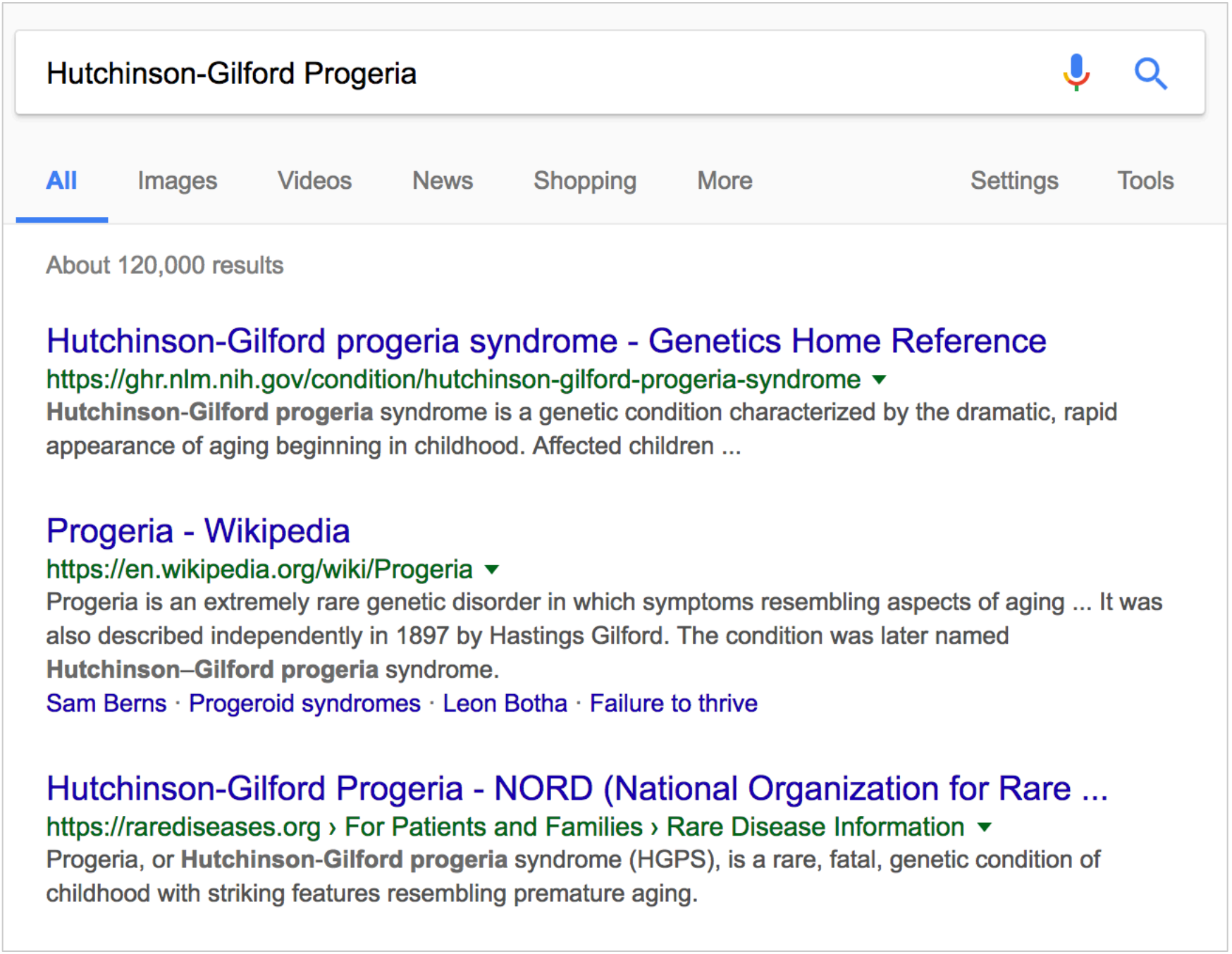


Where to start?

We are looking for better understanding of Hutchinson – Gilford progeria syndrome.

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

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


Hutchinson-Gilford Progeria
All
Images
Videos
News
Shopping
More
Settings
Tools
About 120,000 results
Hutchinson-Gilford progeria syndrome - Genetics Home Reference
https://ghr.nlm.nih.gov/condition/hutchinson-gilford-progeria-syndrome
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
Progeria is an extremely rare genetic disorder in which symptoms resembling aspects of aging ... It was also described independently in 1897 by Hastings Gilford. The condition was later named Hutchinson–Gilford progeria syndrome.
Sam Berns · Progeroid syndromes · Leon Botha · Failure to thrive
Hutchinson-Gilford Progeria - NORD (National Organization for Rare ...
https://rarediseases.org › For Patients and Families › Rare Disease Information
Progeria, or Hutchinson-Gilford progeria syndrome (HGPS), is a rare, fatal, genetic condition of childhood with striking features resembling premature aging.

PubMed | Hutchinson-Gilford Progeria | Search

Create RSS | Create alert | Advanced | Help

Format: Summary | **Sort by**: Most Recent | **Send to** | **Filters:** Manage Filters

Search Tip

Sort by **Best Match** to display results from highest to lowest relevance to your search terms.

Try it Now

Search results

Items: 1 to 20 of 580

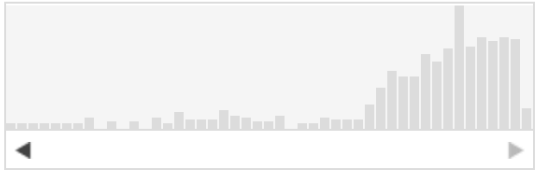
<< First | < Prev | Page 1 of 29 | Next > | Last >>

1. Nuclear lamins and progerin are dispensable for antioxidant Nrf2 response to arsenic and cadmium.
   Hashimoto K, Majumdar R, Tsuji Y.
   Cell Signal. 2017 Feb 14;33:69-78. doi: 10.1016/j.cellsig.2017.02.012. [Epub ahead of print]
   PMID: 28229933
   Similar articles

2. Biomechanical Strain Exacerbates Inflammation on a **Progeria**-on-a-Chip Model.
   Ribas J, Zhang YS, Pitrez PR, Leijten J, Miscuglio M, Rouwkema J, Dokmeci MR, Nissan X, Ferreira L, Khademhosseini A.
   Small. 2017 Feb 17. doi: 10.1002/smll.201603737. [Epub ahead of print]
   PMID: 28211642
   Similar articles

3. Metformin Alleviates Aging Cellular Phenotypes in **Hutchinson-Gilford Progeria** Syndrome Dermal Fibroblasts.

Results by year



Download CSV

Related searches

hutchinson-gilford progeria syndrome review

lamin a truncation in **hutchinson-gilford progeria**

hutchinson-gilford progeria syndrome treatment

PMC Images search for *Hutchinson-Gilford Progeria*

EMBL-EBI | Services | Research | Training | About us | EMBL-EBI Hinxton

EBI Search

Hutchinson–Gilford progeria

Examples: VAV_HUMAN , tpi1 , Sulston ...

Build Query

Help & Documentation | About EBI Search | Feedback

Search results for ***Hutchinson–Gilford progeria***

Showing **23** results out of **880** in All results

Filter your results

Source

All results (880)

- Genomes & metagenomes (1)
- Nucleotide sequences (97)
- Protein sequences (3)
- Gene expression (41)
- Reactions, pathways & diseases (14)
- Protein families (1)
- Literature (604)
- Samples & ontologies (111)
- EBI web (8)

Literature (604 results)

Hutchinson-Gilford progeria syndrome with G608G LMNA mutation.

Kim HK, Lee JY, Bae EJ, Oh PS, Park WI, Lee DS, Kim JI, Lee HJ

(2011 Dec), Journal of Korean medical science 26 (12) 1642-5

Related data | Views

Source: MEDLINE
ID: 22148005

[**Progeria** infantum (**Hutchinson**--**Gilford**)].

CHYLEWSKI W

(1962 Sep-Oct) Przeglad dermatologiczny 49 413-8

Related data | Views

Source: MEDLINE
ID: 14021286

Hutchinson-

Ullrich NJ, Gorc

(2015), Handbo

ChEMBL

REACTOME
A CURATED PATHWAY DATABASE

IntAct

PDBe

Integration, Integration, Integration

- One-stop shop
- Comprehensive data
- Easy-to-use and intuitive visualisation

Open Targets

Open Targets Platform*

- Developed by the Open Targets team at EMBL-EBI
  - Identification of target – disease associations
  - Access to comprehensive information on targets
  - Better understanding of disease biology

https://www.targetvalidation.org/

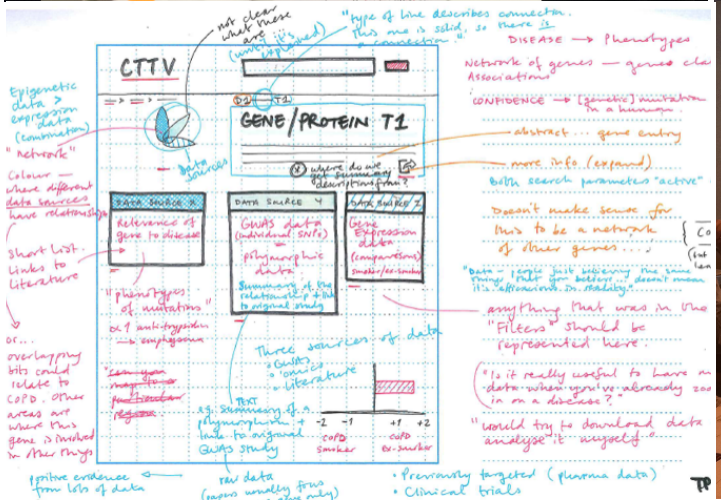
* First release: December 2015

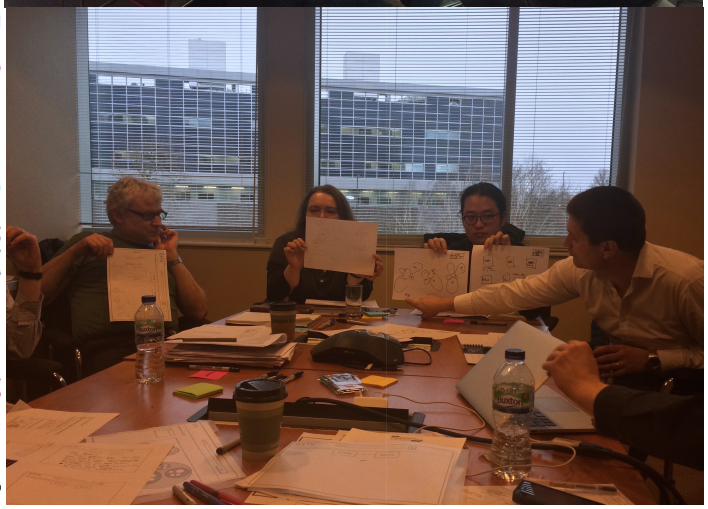
Open Targets

Developing the Open Targets Platform

Step 1

Interviewed ~100 people working with target identification at GSK





Developing the Open Targets Platform

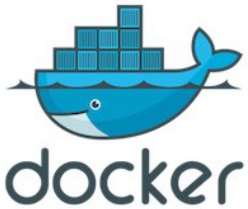
Step 2

Made the selection of data providers

Data sources	Data types
GWAS catalog, UniProt, EVA, G2P	Genetic associations
Cancer Gene Census, EVA, IntOgen	Somatic mutations
Expression Atlas	RNA expression
ChEMBL	Drugs
Reactome	Affected pathways
Europe PMC	Text mining
PhenoDigm	Animal models
Your favourite data?	**Let us know!**

Developing the Open Targets Platform

Step 3 Selected the technology for deployment and storage

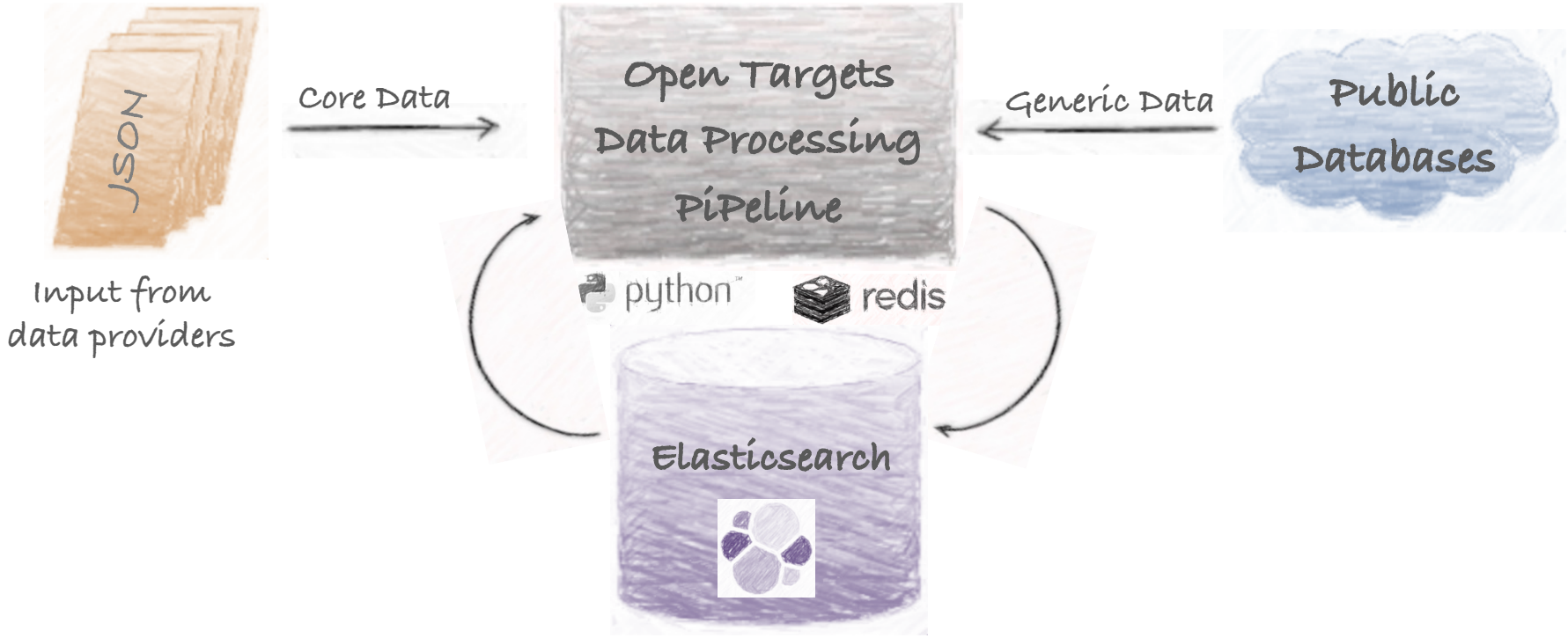


https://blog.opentargets.org/using-containers-with-luigi/

Developing the Open Targets Platform

Step 4

Integration: analysis, ranking, scoring



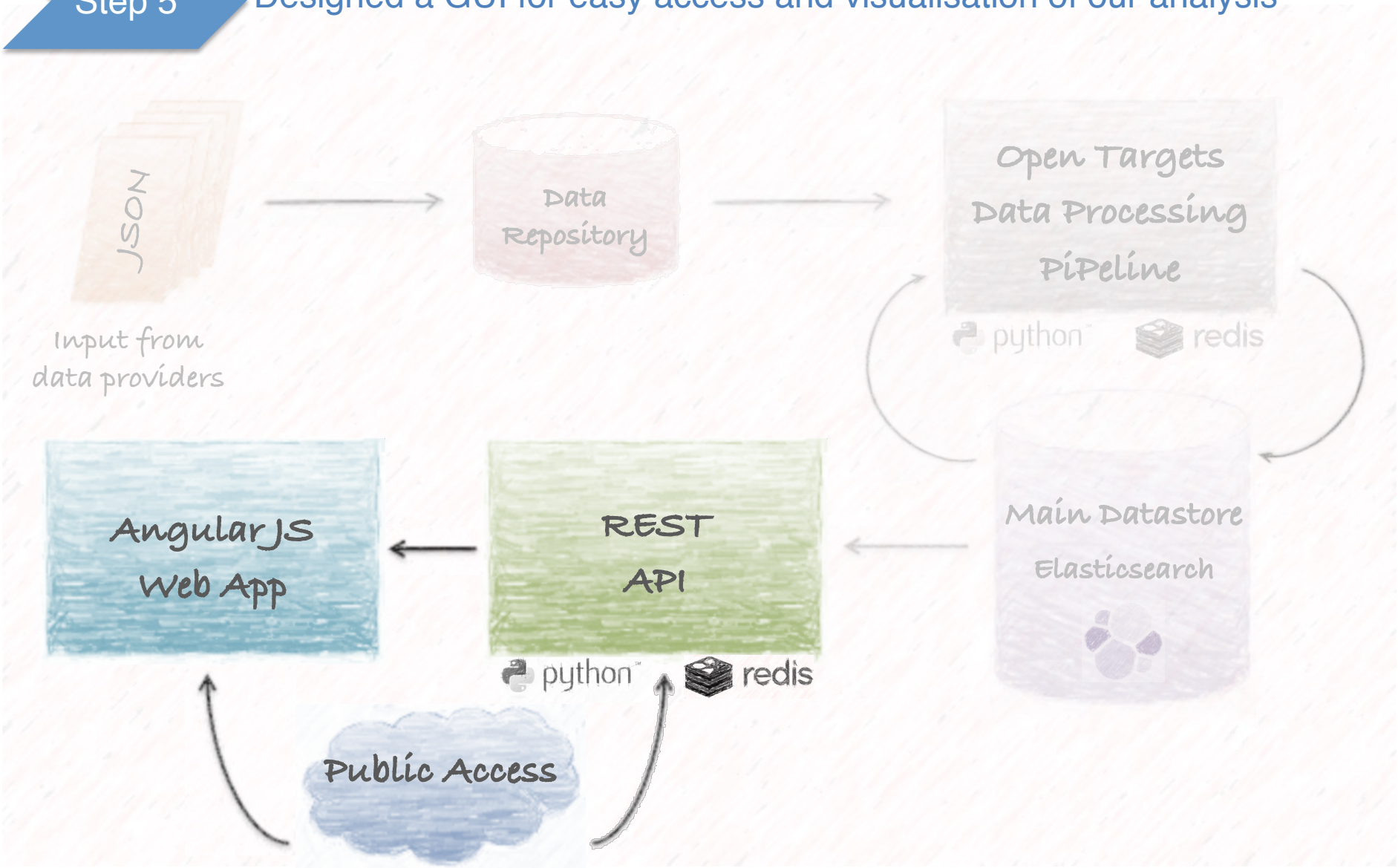
JSON summary document

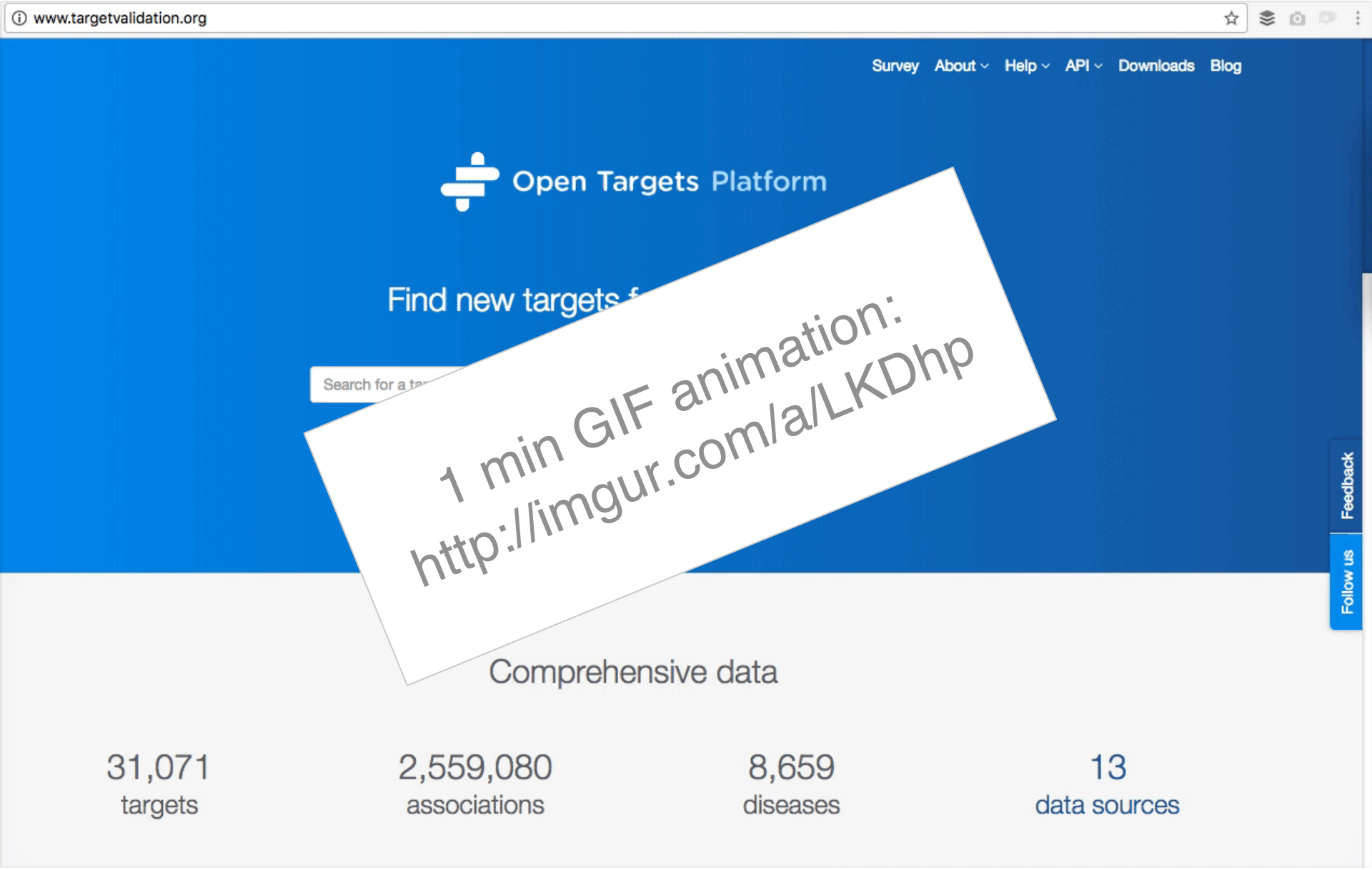

```
hort_name": "Franke A"}, {"last_name": "Alizadeh", "full_name": "Alizadeh Behrooz Z", "short_name": "Alizadeh BZ"}, {"last_r
rkes Miles", "short_name": "Parkes M"}, {"last_name": "B K", "full_name": "B K Thelma", "short_name": "B K T"}, {"last_name"
k J", "short_name": "Daly MJ"}, {"last_name": "Kubo", "full_name": "Kubo Michiaki", "short_name": "Kubo M"}, {"last_name": "
n Carl A", "short_name": "Anderson CA"}, {"last_name": "Weersma", "full_name": "Weersma Rinse K", "short_name": "Weersma RK"
al_data": {"medlineAbbreviation": "Nat. Genet.", "title": "Nature genetics"}}, "target": {"activity": "predicted_damaging",
 "name": "integrin subunit alpha L", "geneid": "ENSG00000005844"}, "id": "ENSG00000005844", "target_type": "gene_evidence"},
ceID": "gwas_catalog", "variant": {"type": "snp single", "id": "http://identifiers.org/dbsnp/rs11150589"}, "disease": {"efo_
bels": ["immune system disease", "digestive system disease"], "codes": ["EFO_0000405", "EFO_0000540"]}, "path": [["EFO_00004
40", "EFO_0005140", "EFO_0003767"]], "efo_id": "http://www.ebi.ac.uk/efo/EFO_0003767", "label": "inflammatory bowel disease"
_association_fields": {"pubmed_refs": "http://europepmc.org/abstract/MED/26192919", "object": "http://www.ebi.ac.uk/efo/EFO_
ntifiers.org/dbsnp/rs11150589", "study_name": "cttv009_gwas_catalog", "sample_size": "96486", "gwas_panel_resolution": "9000
: "http://identifiers.org/ensembl/ENSG00000005844"}, "evidence": {"variant2disease": {"gwas_sample_size": 96486, "unique_exp
pepmc.org/abstract/MED/26192919", "gwas_panel_resolution": 9000000, "provenance_type": {"literature": {"references": [{"lit_
act/MED/26192919"}]}, "expert": {"status": true, "statement": "Primary submitter of data"}, "database": {"dbxref": {"version
"id": "http://identifiers.org/gwascatalog"}, "id": "GWAS Catalog", "version": "2017-03-23T03:44:36+00:00"}}, "is_associated"
": "pvalue", "method": {"description": "pvalue for the snp to disease association."}, "value": 9e-07}, "evidence_codes": ["h
 "http://purl.obolibrary.org/obo/ECO_0000205", "http://purl.obolibrary.org/obo/ECO_0000205", "http://identifiers.org/eco/ctt
rted": "2017-03-23T03:44:36+00:00"}, "evidence_codes_info": [[{"eco_id": "GWAS", "label": "Genome-wide association study evi
ing_pipeline", "label": "CTTV-custom annotation pipeline"}], [{"eco_id": "ECO_0000205", "label": "curator inference"}], [{"e
upstream_gene_variant"}]], "gene2variant": {"functional_consequence": "http://purl.obolibrary.org/obo/SO_0001631", "provenan
true, "statement": "Primary submitter of data"}, "database": {"dbxref": {"version": "2017-03-23T03:44:36+00:00", "id": "http
, "id": "GWAS Catalog", "version": "2017-03-23T03:44:36+00:00"}}, "is_associated": true, "resource_score": {"type": "probabi
codes": ["http://purl.obolibrary.org/obo/ECO_0000205", "http://identifiers.org/eco/cttv_mapping_pipeline"], "date_asserted":
evidence_codes": ["GWAS", "cttv_mapping_pipeline", "ECO_0000205", "SO_0001631"]}, "validated_against_schema_version": "1.2.5
res": {"association_score": 0.24183029962242697}, "type": "genetic_association", "id": "f8aa5612c7f01940f3958914fc6074ba"}
loads denise$
```


* IDs (gene, disease, papers) + curation (e.g. manual) + evidence + source + stats for the score

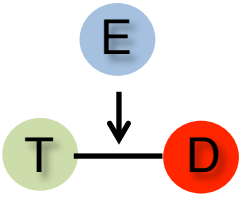
Developing the Open Targets Platform

Step 5 Designed a GUI for easy access and visualisation of our analysis



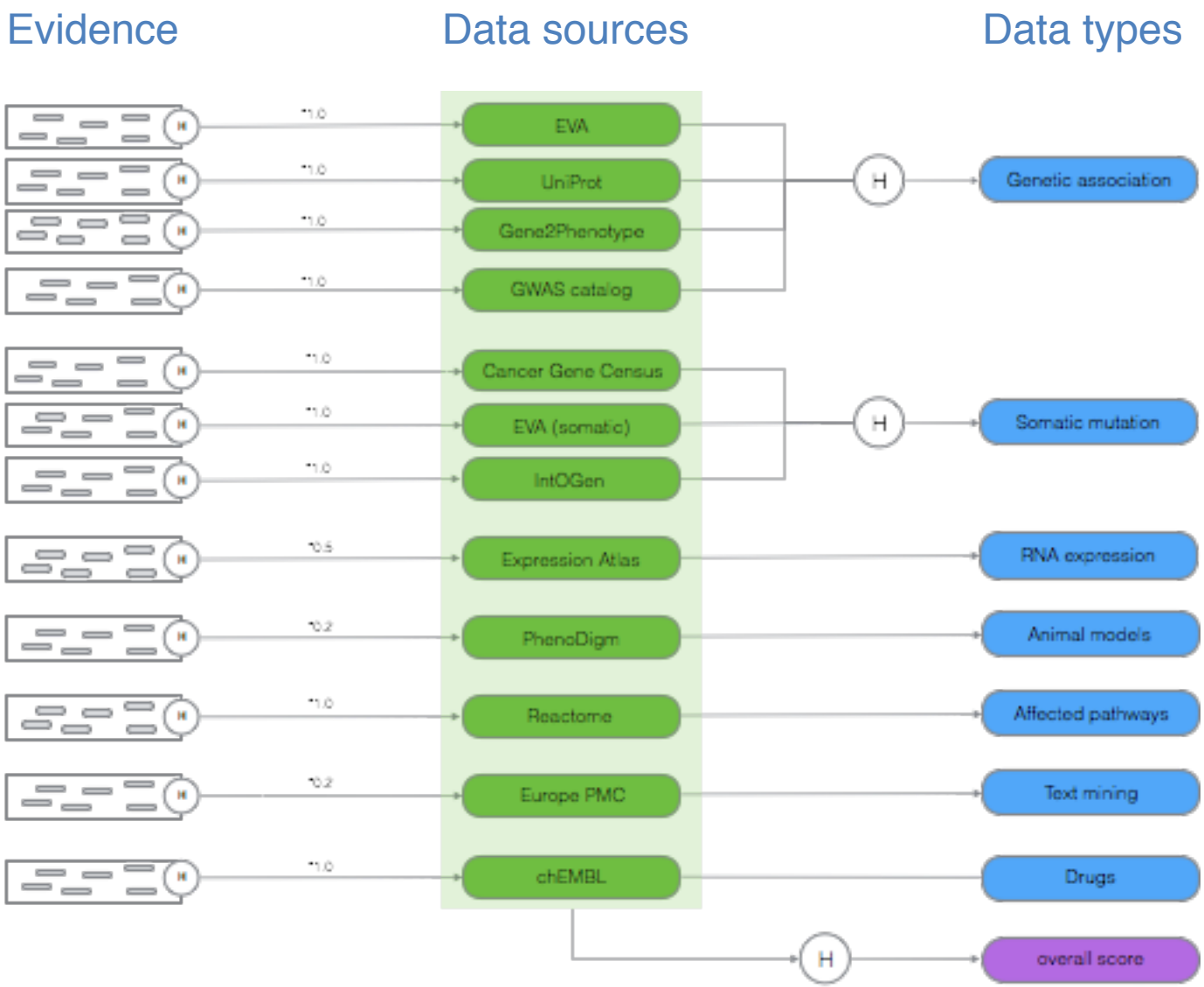

www.targetvalidation.org
Survey
About
Help
API
Downloads
Blog
Open Targets Platform
Find new targets f
Search for a ta
1 min GIF animation:
http://imgur.com/a/LKDhp
Feedback
Follow us
Comprehensive data
31,071
targets
2,559,080
associations
8,659
diseases
13
data sources

How do we associate diseases and phenotypes w/ targets?



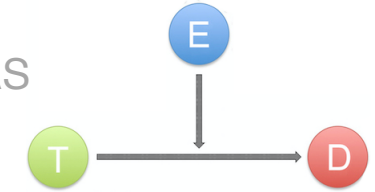
1. Map disease/phenotypes to an ontology using EFO and HPO terms
2. Use genes as proxies for our targets
3. Create target-disease evidence **JSON** documents
4. Calculate for each supporting evidence the likelihood of target T being associated with disease D
5. Compute integrated target-disease scores at the levels of data source, data type and overall score

Score approach and aggregation

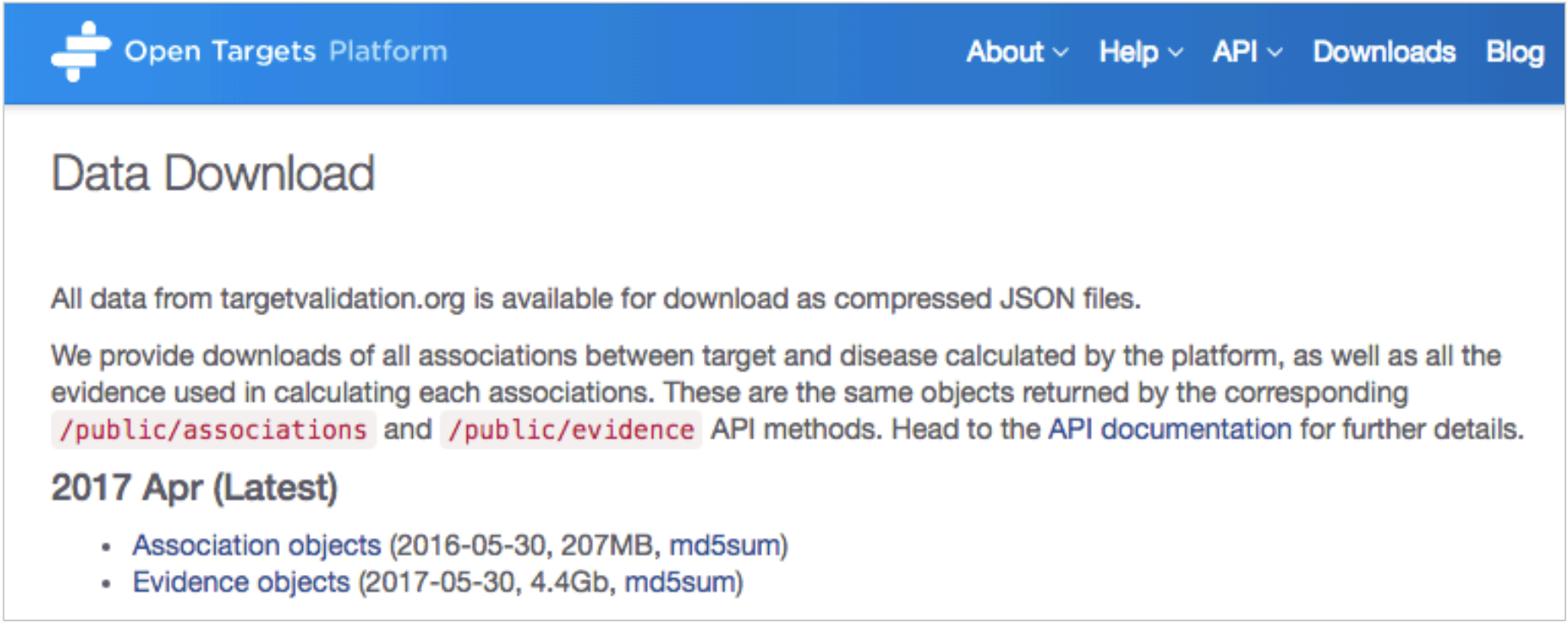


Evidence score e.g. $f * S * C$ (frequency x Severity x Confidence) for GWAS

$H = S_1 + S_2/2^2 + S_3/3^2 + S_4/4^2 + S_i/i^2$



Alternative ways to access the data



http://www.targetvalidation.org/downloads/data

Open Targets REST API

public : Publicly supported stable API.

Open/Hide | List operations | Expand operations

GET	/public/evidence
POST	/public/evidence
GET	/public/evidence/filter
POST	/public/evidence/filter
GET	/public/association
GET	/public/association/filter
POST	/public/association/filter
GET	/public/search
GET	/public/auth/request_token
GET	/public/auth/validate_token
GET	/public/utils/ping
GET	/public/utils/version
GET	/public/utils/stats

https://www.targetvalidation.org/documentation/api

Wrap up

Open Targets Platform:

- Interviewing users from the start
- Keeping up with latest infrastructure
- Improvements driven by users
- Partnerships and collaboration

April 2017 release

Open Targets

Overview Projects People Contact Blog Jobs Platform

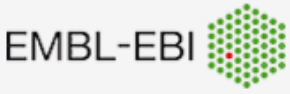
Open Targets is a public-private initiative to transform drug discovery by enabling the systematic identification and prioritisation of targets

Open Targets is working to create an R&D framework that applies to a wide range of human diseases, and is committed to sharing its data openly with the scientific community.

Learn more about us, our projects and get to know our team

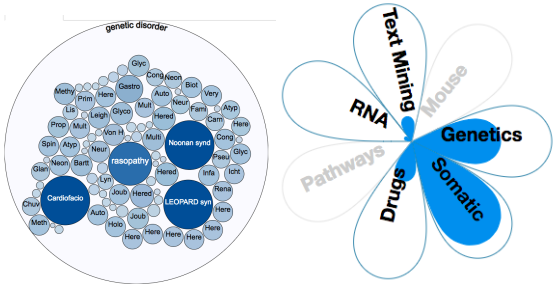
We are committed to openly releasing our data through publications, the internationally recognised databases and the Open Targets Platform. The Open Targets Platform provides an integration of public domain data to enable target identification and prioritisation.

VISIT THE OPEN TARGETS PLATFORM



Two major areas of work in Open Targets

Core bioinformatics pipelines



Integration of available data

Web interface

REST API

Data dumps

Experimental projects

Generate new evidence

CRISPR/Cas9

Organoids and IPS cells

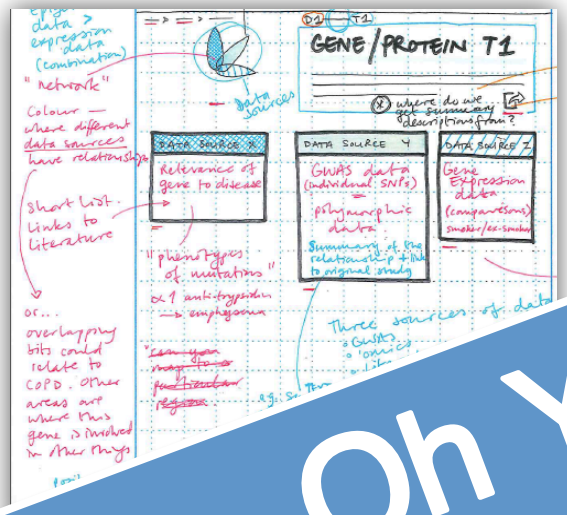
(cellular models for disease)

Concurrent

www.opentargets.org/projects

What makes Open Targets unique?

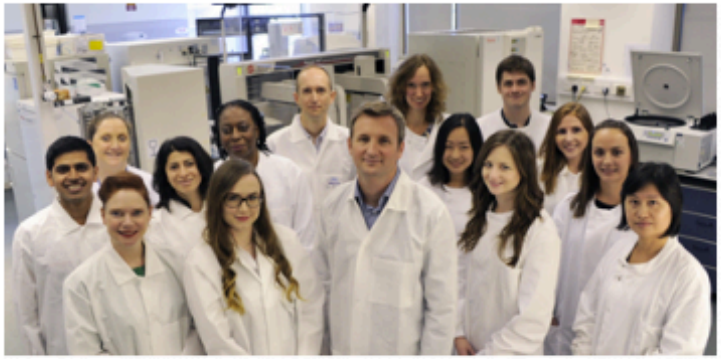
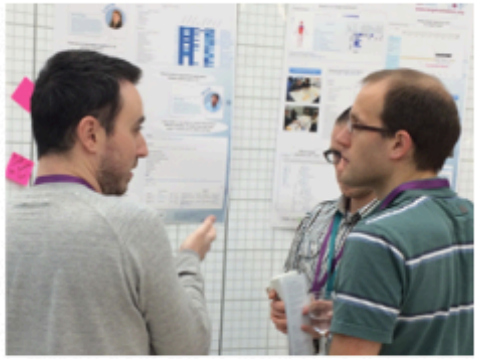
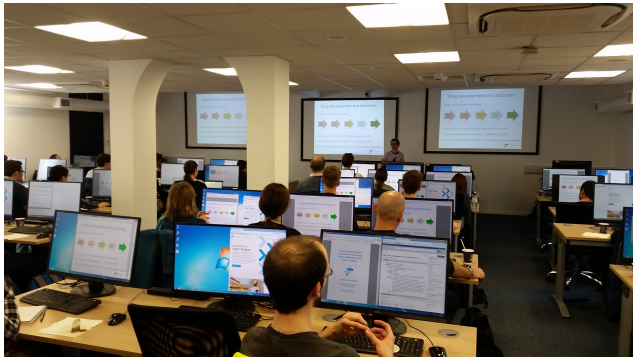
- Addressing many areas of human disease
- Putting our users first
- Working genome wide
- Bringing the partners together



Oh Yes!
And all is 100% free

Acknowledgements



support@targetvalidation.org

Breakthrough Articles from NUCLEIC ACIDS RESEARCH

http://www.narbreakthrough.com/

How to cite us

Published online 8 December 2016

Nucleic Acids Research, 2017, Vol. 45, Database issue ***D985–D994***
doi: 10.1093/nar/gkw1055

Open Targets: a platform for therapeutic target identification and validation

Gautier Koscielny[1,2,*], Peter An[1,3], Denise Carvalho-Silva[1,4], Jennifer A. Cham[1,4], Luca Fumis[1,4], Rippa Gasparyan[1,3], Samiul Hasan[1,2], Nikiforos Karamanis[1,4], Michael Maguire[1,4], Eliseo Papa[1,3], Andrea Pierleoni[1,4], Miguel Pignatelli[1,4], Theo Platt[1,3], Francis Rowland[1,4], Priyanka Wankar[1,3], A. Patrícia Bento[1,4], Tony Burdett[1,4], Antonio Fabregat[1,4], Simon Forbes[1,5], Anna Gaulton[1,4], Cristina Yenyxe Gonzalez[1,4], Henning Hermjakob[1,4,6], Anne Hersey[1,4], Steven Jupe[1,4], Şenay Kafkas[1,4], Maria Keays[1,4], Catherine Leroy[1,4], Francisco-Javier Lopez[1,4], Maria Paula Magarinos[1,4], James Malone[1,4], Johanna McEntyre[1,4], Alfonso Munoz-Pomer Fuentes[1,4], Claire O'Donovan[1,4], Irene Papatheodorou[1,4], Helen Parkinson[1,4], Barbara Palka[1,4], Justin Paschall[1,4], Robert Petryszak[1,4], Naruemon Pratanwanich[1,4], Sirarat Sarntivijal[1,4], Gary Saunders[1,4], Konstantinos Sidiropoulos[1,4], Thomas Smith[1,4], Zbyslaw Sondka[1,5], Oliver Stegle[1,4], Y. Amy Tang[1,4], Edward Turner[1,4], Brendan Vaughan[1,4], Olga Vrousgou[1,4], Xavier Watkins[1,4], Maria-Jesus Martin[1,4], Philippe Sanseau[1,2], Jessica Vamathevan[4], Ewan Birney[1,4], Jeffrey Barrett[1,4,5] and Ian Dunham[1,4,*]

[1]Open Targets, Wellcome Genome Campus, Hinxton, Cambridge, CB10 1SD, UK, [2]GSK, Medicines Research Center, Gunnels Wood Road, Stevenage, SG1 2NY, UK, [3]Biogen, Cambridge, MA 02142, USA, [4]European Bioinformatics Institute (EMBL-EBI), Wellcome Genome Campus, Hinxton, Cambridge, CB10 1SD, UK, [5]Wellcome Trust Sanger Institute, Wellcome Genome Campus, Hinxton, Cambridge, CB10 1SA, UK and [6]National Center for Protein Research, No. 38, Life Science Park Road, Changping District, 102206 Beijing, China

Received August 19, 2016; Revised October 19, 2016; Editorial Decision October 20, 2016; Accepted November 03, 2016

http://nar.oxfordjournals.org/content/45/D1/D985.long

Support, dissemination, GIFs

support@targetvalidation.org

http://tinyurl.com/opentargets-in

@targetvalidate

blog.opentargets.org/

www.facebook.com/OpenTargets/

http://imgur.com/a/JIDCP
http://imgur.com/a/LKDhp