Open PHACTS
Open Pharmacological Space

The Open PHArmacological Concepts Triple Store: Solutions and the Foundation

Egon Willighagen
Dept of Bioinformatics – BiGCaT, Maastricht University
@egonwillighagen, #oteu14

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The Innovative Medicines Initiative

- EC funded public-private partnership for pharmaceutical research
- Focus on key problem
  - Efficacy, Safety, Education & Training, **Knowledge Management**

The Open PHACTS Project

- Create a *semantic integration hub ("Open Pharmacological Space")…*
- Delivering services to support

- Work split into clusters:
  - Technical Build (*focus here)*
  - Scientific Drive
  - Community & Sustainability

The Project

DOI: 10.1016/j.drudis.2012.05.016

Project Partners

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Who is involved?

31 partners

Associate Partners

Open PHACTS
Open Pharmacological Space

orphanet

IDEA consult

eagle genomics

Sage BIONETWORKS

Global Health Equity Foundation
research · advocacy · capacity building

VIVO connect share discover

mobileflow

Concept Web Alliance

Nūmedicus

MGH 1811

codeN

ACD/Labs

Genetta SOFT

thehyve

CERTARA
Implementing Translational Science

THE NATIONAL CENTER FOR BIOMEDICAL ONTOLOGY

INDIANA UNIVERSITY

IRB BARCELONA
INSTITUTE FOR RESEARCH IN BIOMEDICINE

ih Ian Harrow Consulting

AUREUS SCIENCES

GVK BIO
Accelerating Research

Sequenomics

accelrys

Erasmus MC

Parc Científic de Barcelona
B·KC

IUPHAR DATABASE
International Union of Basic and Clinical Pharmacology

THOMSON REUTERS

Research Questions

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Number	sum	Nr of 1	Question
15	**12**	**9**	**All oxido,reductase inhibitors active <100nM in both human and mouse**
18	14	8	Given compound X, what is its predicted secondary pharmacology? What are the on and off,target safety concerns for a compound? What is the evidence and how reliable is that evidence (journal impact factor, KOL) for findings associated with a compound?
24	13	8	Given a target find me all actives against that target. Find/predict polypharmacology of actives. Determine ADMET profile of actives.
32	13	8	For a given interaction profile, give me compounds similar to it.
37	13	8	The current Factor Xa lead series is characterised by substructure X. Retrieve all bioactivity data in serine protease assays for molecules that contain substructure X.
38	13	8	Retrieve all experimental and clinical data for a given list of compounds defined by their chemical structure (with options to match stereochemistry or not).
41	13	8	A project is considering Protein Kinase C Alpha (PRKCA) as a target. What are all the compounds known to modulate the target directly? What are the compounds that may modulate the target directly? i.e. return all cmpds active in assays where the resolution is at least at the level of the target family (i.e. PKC) both from structured assay databases and the literature.
44	13	8	Give me all active compounds on a given target with the relevant assay data
46	13	8	Give me the compound(s) which hit most specifically the multiple targets in a given pathway (disease)
59	14	8	Identify all known protein-protein interaction inhibitors

DOI: 10.1016/j.drudis.2013.05.008

What do we need?

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"What is the selectivity profile of known p38 inhibitors?"

"Let me compare MW, logP and PSA for known oxidoreductase inhibitors"

"Find me compounds that inhibit targets in NFkB pathway assayed in only functional assays with a potency <1 µM"

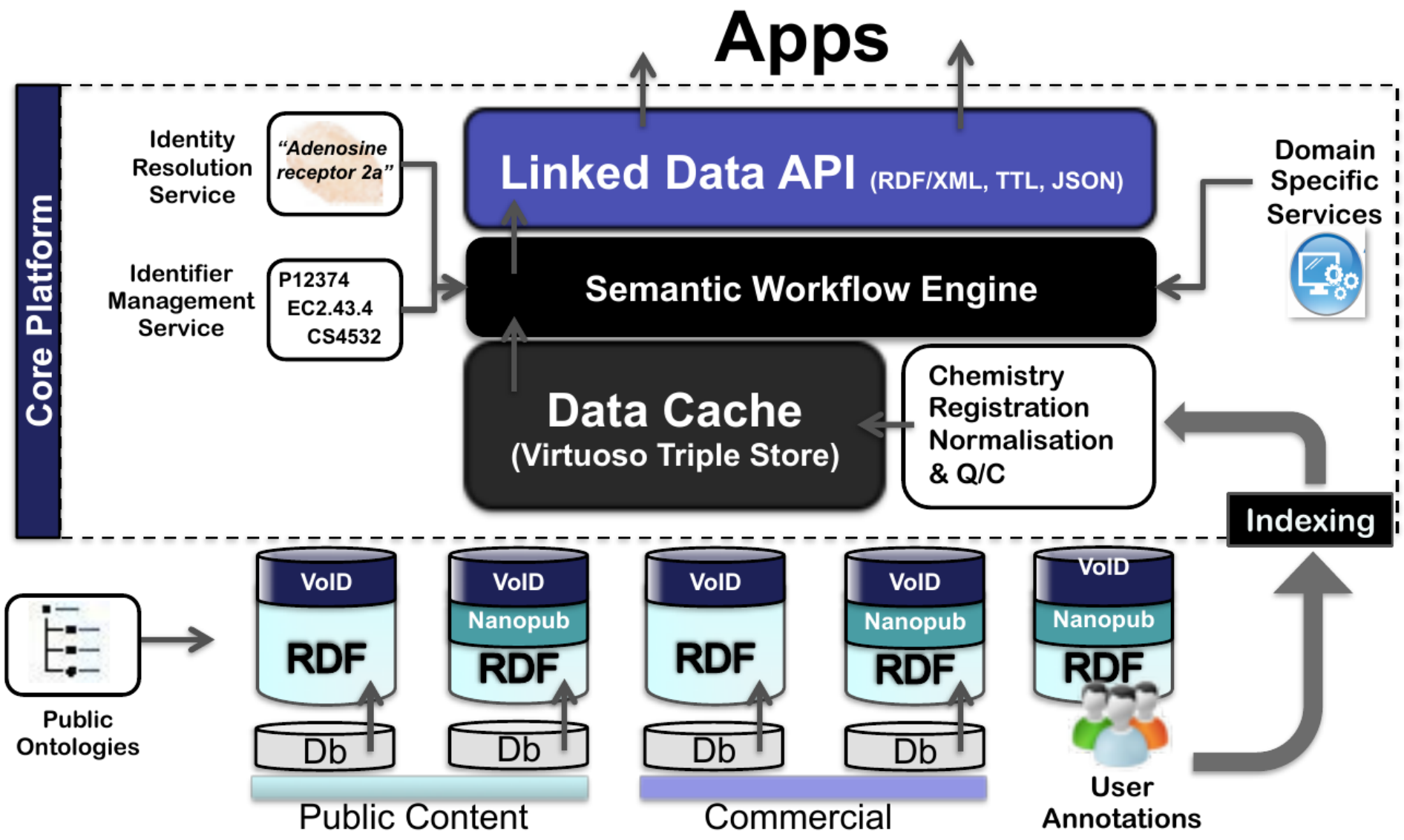
ChEMBL | DrugBank | Gene Ontology | Wikipathways | GeneGo

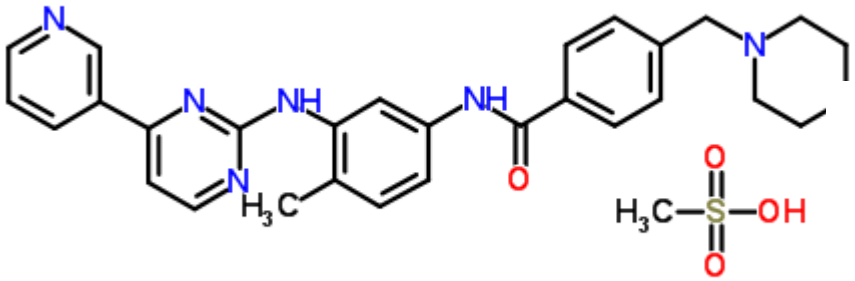
ChEBI | Uniprot | UMLS | GVKBio

ConceptWiki | ChemSpider | TrialTrove | TR Integrity

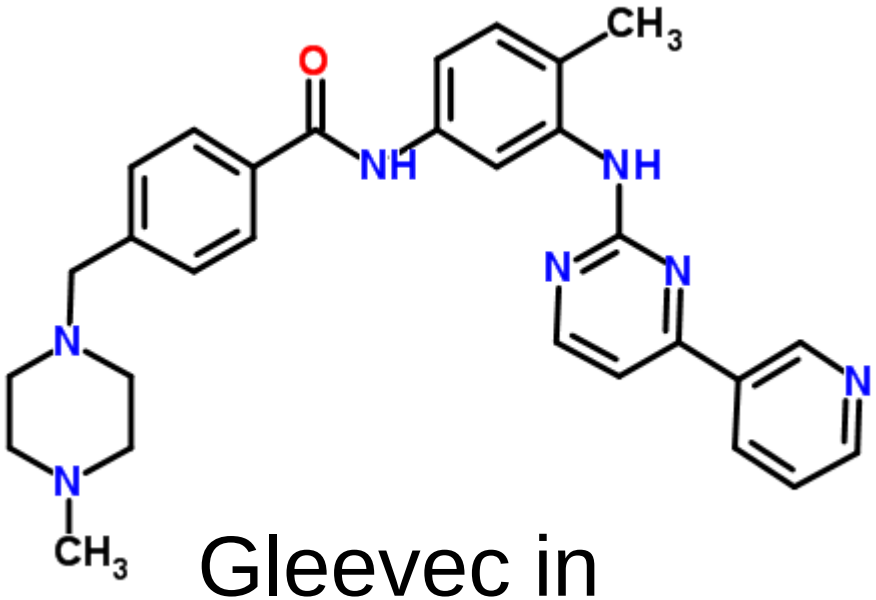
The Open PHACTS infrastructure can support many different domains & questions

Solutions


Apps
Core Platform
Identity Resolution Service
"Adenosine receptor 2a"
Identifier Management Service
P12374
EC2.43.4
CS4532
Linked Data API (RDF/XML, TTL, JSON)
Semantic Workflow Engine
Data Cache
(Virtuoso Triple Store)
Domain Specific Services
Chemistry Registration Normalisation & Q/C
Indexing
Public Ontologies
VoID
RDF
Db
Nanopub
Public Content
Commercial
User Annotations

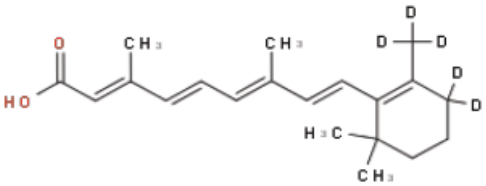


Gleevec in ChemSpider and ChEMBL (imatinib mesylate)



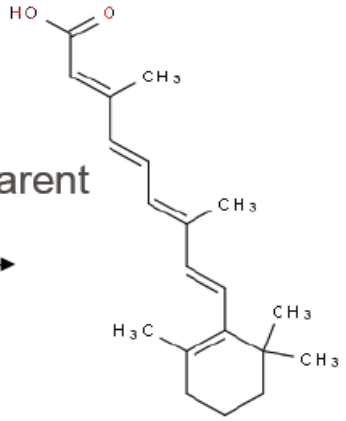
Gleevec in DrugBank (actually imatinib)


ilip Chapman-Bell (https://www.flickr.com/photos/oschene/)
Magnifying Lens Price Guide:
2” - $1.99 2.5” - $2.99 3” - $3.99 3.5” - $4.99



http://ops.rsc.org/OPS45975

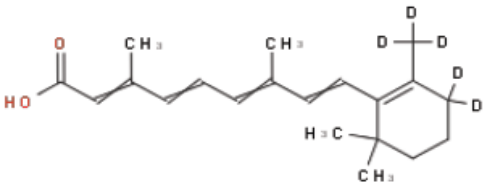
has_isotopically_unspecified_parent
[CHEMINF:000459]



http://ops.rsc.org/OPS45978

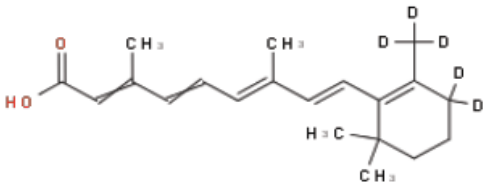
has OPS normalized counterpart
[CHEMINF:000458]

has_stereoundefined_parent
[CHEMINF:000456]



http://ops.rsc.org/OPS45981

is_tautomer_of
[chebi:is_tautomer_of]



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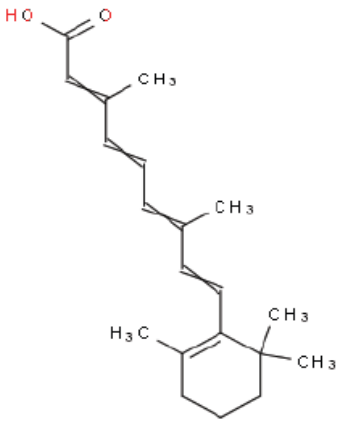


http://ops.rsc.org/OPS45991

Equivalence rules

The BridgeDb vocabulary adds metadata that provides a justification for treating two URIs alike, thus allowing the researcher to determine whether their circumstances fit.

owl:sameAs ≤ skos:exactMatch ≤ skos:closeMatch ≤ rdfs:seeAlso

The ChEBI and CHEMINF ontologies provide a rich set of relations (many of which developed for this project) to relate one molecule to another.

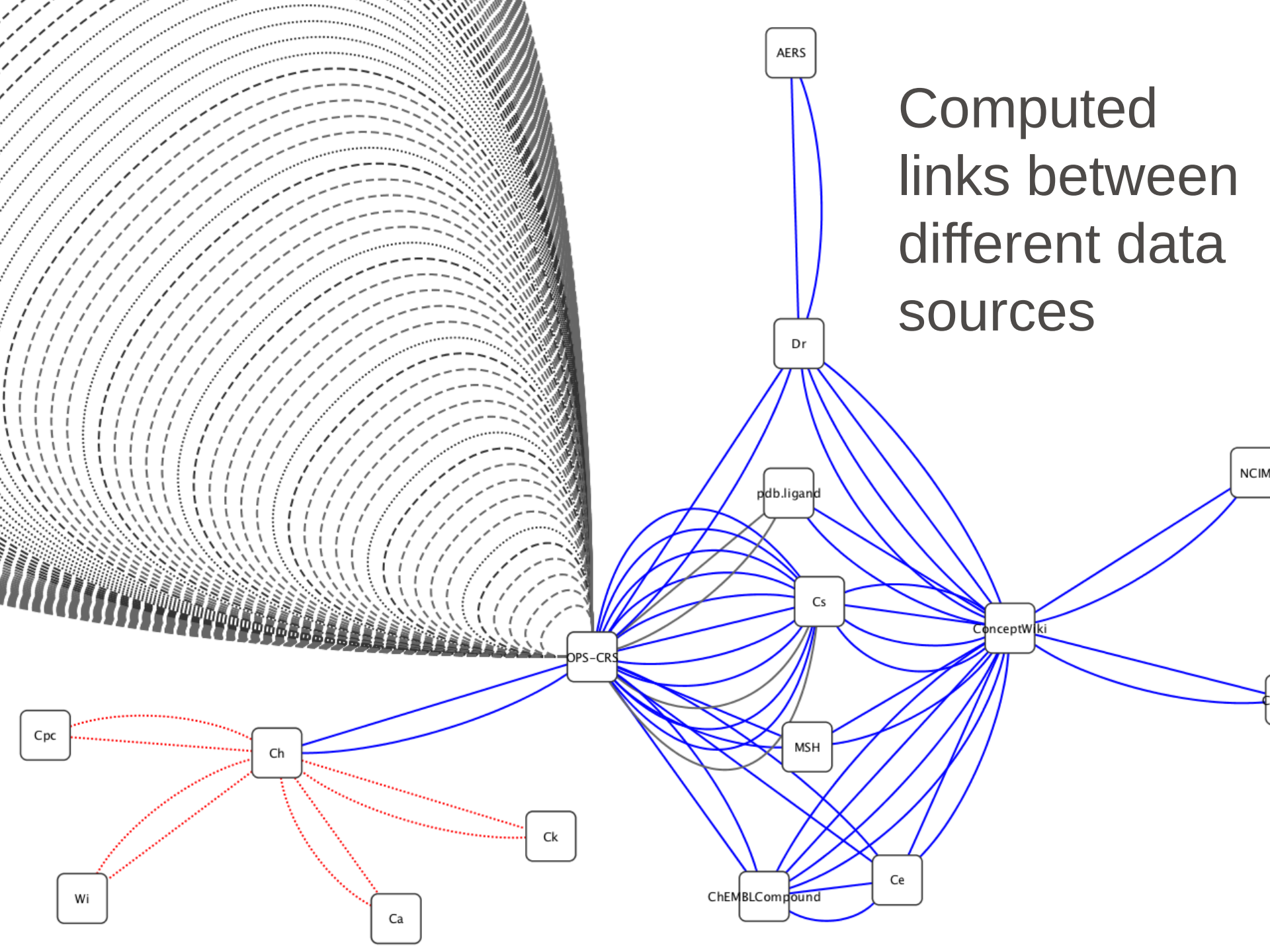
Where do mappings come from?

1. Chemical Registration Service
2. BridgeDb
    1. Metabolites: HMDB, ChEBI
    2. Genes / Proteins: Ensembl (*)

ChemSpider
Search and share chemistry

BridgeDb

*) Andra Waagmeester and Alex Pico (WikiPathways).



Computed links between different data sources

Other Data Challenges

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STANDARD_TYPE	UNIT_COUNT
AC50	7
Activity	421
EC50	39
IC50	46
ID50	42
Ki	23
Log IC50	4
Log Ki	7
Potency	11
log IC50	0

>5000 types

STANDARD_TYPE	STANDARD_UNITS	COUNT(*)
IC50	nM	829448
IC50	ug.mL-1	41000
IC50		38521
IC50	ug/ml	2038
IC50	ug ml-1	509
IC50	mg kg-1	295
IC50	molar ratio	178
IC50	ug	117
IC50	%	113
IC50	uM well-1	52
IC50	p.p.m.	51
IC50	ppm	36
IC50	uM-1	25
IC50	nM kg-1	25
IC50	milliequivalent	22
IC50	kJ m-2	20

Implemented using the Quantities, Dimension, Units, Types Ontology (http://www.qudt.org/)

~ 100 units

Application Programming Interface

What can be explored?

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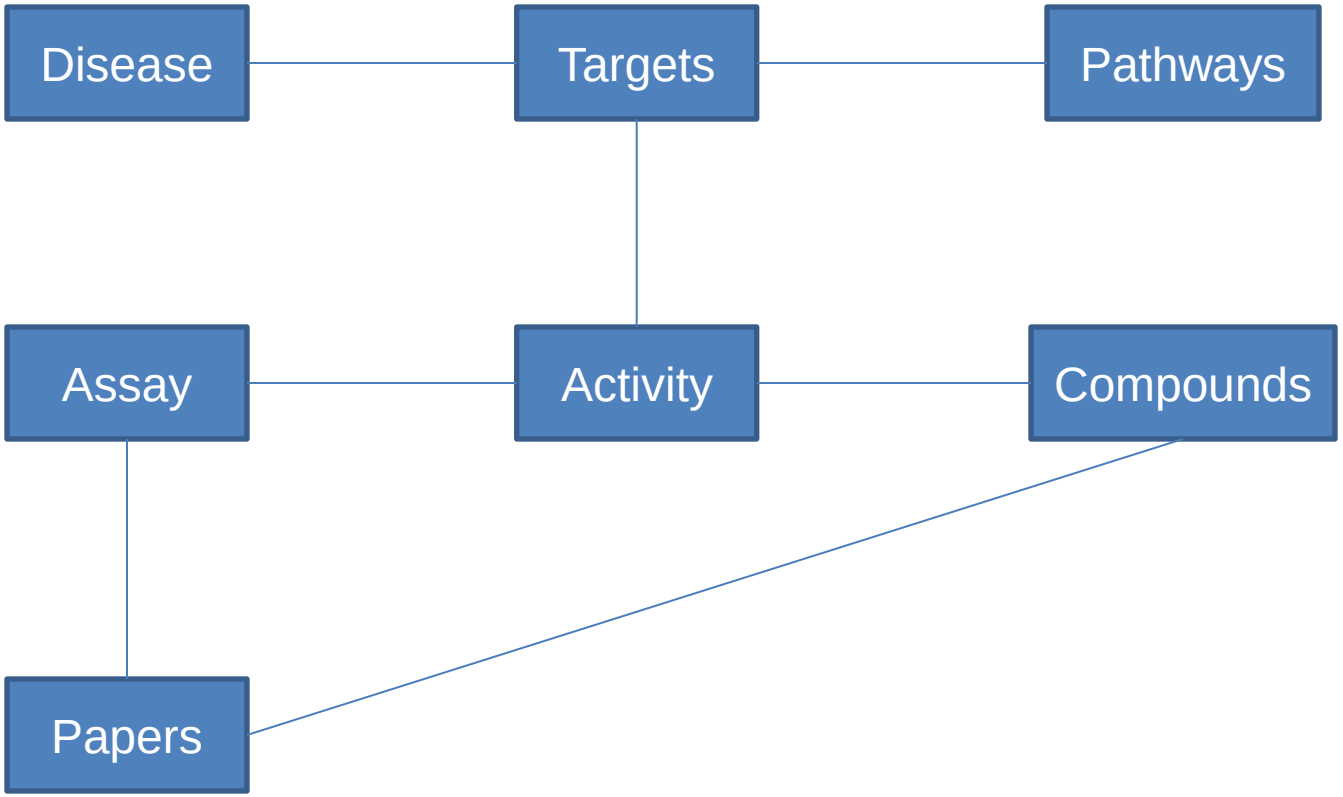

Access via REST-like API

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The API

dev.openphacts.org/docs/1.4

Chemical Structure Exact Search	/structure/exact	GET
InchiKey to URL	/structure	GET
Inchi to URL	/structure	GET
Chemical Structure Similarity Search	/structure/similarity	GET
SMILES to URL	/structure	GET
Chemical Structure Substructure Search	/structure/substructure	GET
Get concept description	/getConceptDescription	GET

Hiding a SPARQL end point

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dev.openphacts.org/docs/1.4

Diseases for Target: List

`/disease/byTarget` **GET**

Description

A list of diseases which correspond to {uri}.

Response template:

```
?item foaf:name ?diseaseName ;
    ops:forGene ?dg_gene_uri ;
    void:inDataset ?diseaseDataset .
?dg_gene_uri ops:encodes ?uniprot_target_uri ;
    void:inDataset ?geneDataset .
?uniprot_target_uri skos:exactMatch ?cw_target_uri ;
    void:inDataset <http://purl.uniprot.org> .
?cw_target_uri skos:prefLabel ?cw_prefLabel ;
    void:inDataset <http://www.conceptwiki.org> .
```

The Foundation

The Open PHACTS Foundation - Established May 2013

A not-for-profit, member-owned successor organisation, based in UK:

- Acts a **unique forum** for the scientific community, bringing EFPIA partners together with academia and SMEs.
- Ensures the **sustainability** of the Open PHACTS infrastructure, and provides technical support
- A hub of **relevant scientific research** and development
- Full members **nominate and vote for Directors**, influencing the Foundation's development and strategy

www.openphactsfoundation.org

Timelines

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The Project

- Started in 2011
- Continued in 2014-09
- Until 2016-02

The Foundation

- Started in 2013
- First members in 2014

- GlaxoSmithKline
- Janssen
- Roche

More information:

Project: **www.openphacts.org**
Foundation: **www.openphactsfoundation.org**
Twitter: **@open_phacts**

Access the data:

API: **dev.openphacts.org**
Explorer: **explorer.openphacts.org**

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