



Open PHACTS

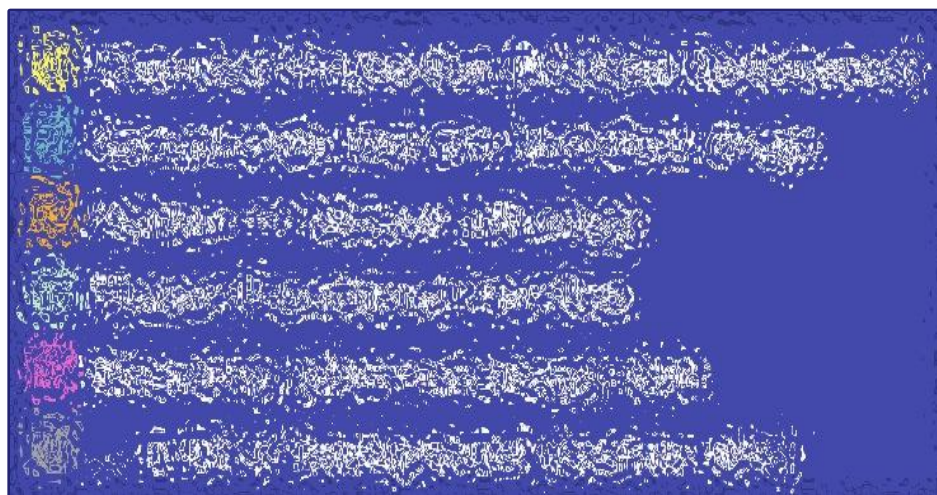
Practical Semantics For Drug Discovery

Lee Harland (CTO)

Bio-IT World 2014



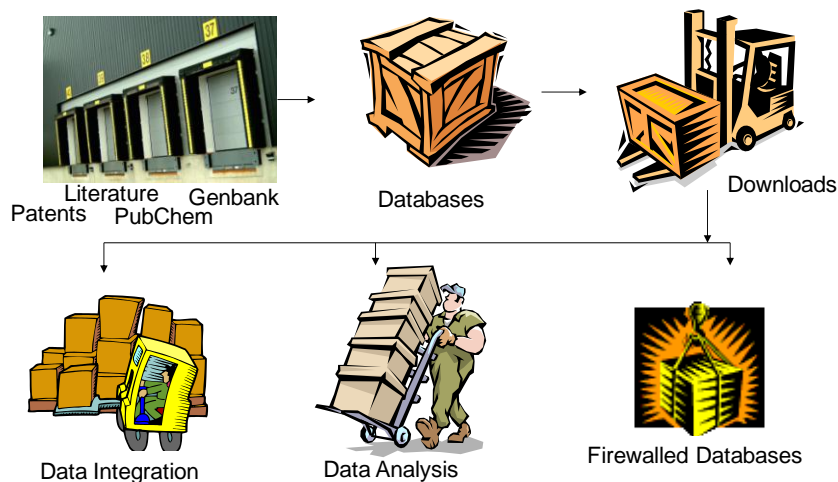
“Let me compare **MW**, **logP**
and **PSA** for **launched**
inhibitors of **human &**
mouse oxidoreductases”





Pre-competitive Informatics:

Pharma are all accessing, processing, storing & re-processing external research data



**X Repeat @
each company**



**A single, shared
solution.**

**Funded under IMI
March 2011-14**

Lowering industry firewalls: pre-competitive informatics in drug discovery
Nature Reviews Drug Discovery (2009) 8, 701-708 doi:10.1038/nrd2944




Open PHACTS Mission:
Integrate Multiple Research
Biomedical Data Resources
Into A Single **Open & Free**
Access Point




The Open PHACTS Discovery Platform

- **Cloud-Based “Production” Level System. Secure & Private**
- **Guided By Business Questions**
- **Uses Semantic Web Technology But provides a simple REST-ful API for the everyone else**





Drug Discovery Today
Volume 18, Issues 17–18, September 2013, Pages 843–852




Review


Scientific competency questions as the basis for semantically enriched open pharmacological space development

Kamal Azzaoui¹, Edgar Jacoby¹⁴, Stefan Senger², Emiliano Cuadrado Rodríguez³, Mabel Loza³, Barbara Zdrazil⁴, Marta Pinto⁴, Antony J. Williams⁵, Victor de la Torre⁶, Jordi Mestres⁷, Manuel Pastor⁷, Olivier Taboureau⁸, Matthias Rarey⁹, Christine Chichester¹⁰, Steve Pettifer¹¹, Niklas Blomberg^{12, a}, Lee Harland¹³, Bryn Williams-Jones¹³, Gerhard F. Ecker⁴.  




<http://dx.doi.org/10.1016/j.drudis.2013.05.008>



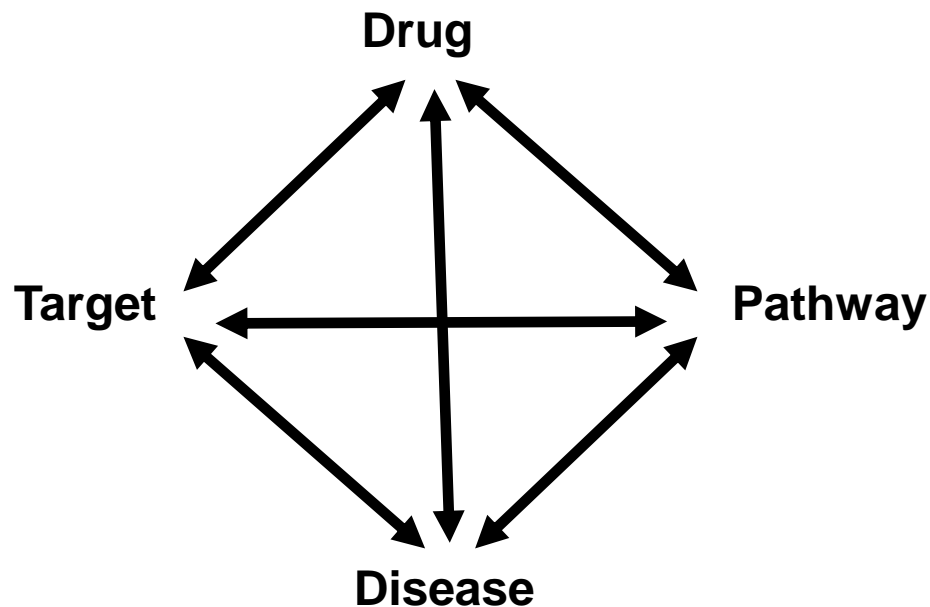
Web Semantics: Science, Services and Agents on the World Wide Web
Available online 8 April 2014
In Press, Accepted Manuscript — Note to users



API-centric Linked data integration: The open PHACTS discovery platform case study

Paul Groth^a.   , Antonis Loizou^a, Alasdair J.G. Gray^d, Carole Goble^b, Lee Harland^c, Steve Pettifer^b

<http://dx.doi.org/10.1016/j.websem.2014.03.003>



<https://dev.openphacts.org/>

OpenPHACTS API

Chemical Structure Exact Search	<code>/structure/exact</code> GET
InchiKey to URL	<code>/structure</code> GET
Inchi to URL	<code>/structure</code> GET
Chemical Structure Similarity Search	<code>/structure/similarity</code> GET
SMILES to URL	<code>/structure</code> GET
Chemical Structure Substructure Search	<code>/structure/substructure</code> GET
Get concept description	<code>/getConceptDescription</code> GET
Map free text to a concept URL based on semantic tag	<code>/search/byTag</code> GET
Map URL	<code>/mapURL</code> GET
Map free text to a concept URL	<code>/search/freetext</code> GET
Get ChEBI Ontology Class Members	<code>/compound/chebi/members</code> GET
Get ChEBI Ontology Root Classes	<code>/compound/chebi/root</code> GET
Get ChEBI Ontology Class	<code>/compound/chebi/node</code> GET
ChEBI Class Pharmacology Count	<code>/compound/chebi/pharmacology/count</code> GET



ChEMBL



GENE ONTOLOGY
Unifying Biology



Compound Information

Compound Classifications

Compound Pharmacology:

Chemical Structure Search: Similarity

Target Class Pharmacology:

Pathway Information: Get Targets

Targets for Disease: List

Tissues for Protein: List

Getting Started Guide:

<http://www.slideshare.net/pgroth/ops-developerwebinarjuly312013>



Adding Further Value



Directly Funding Public Resources





HELLO
my name is

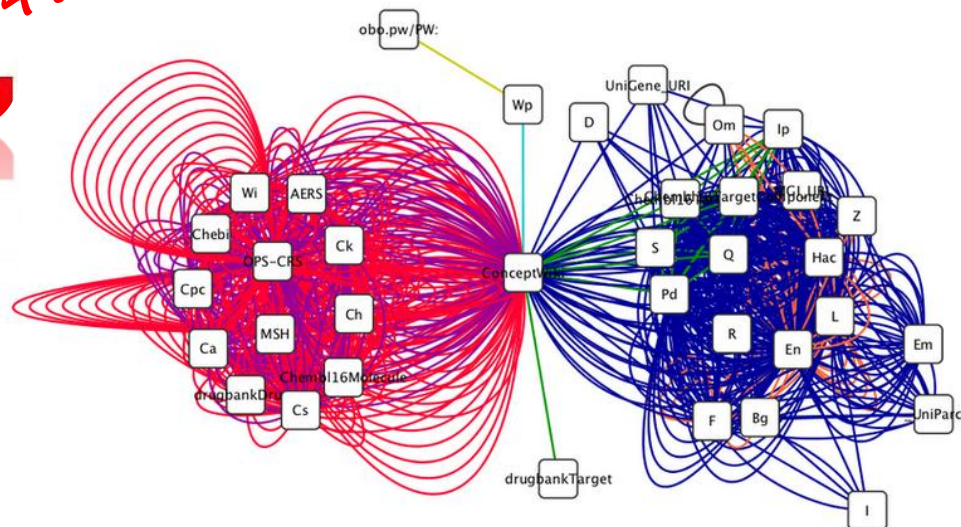
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~~P12047~~

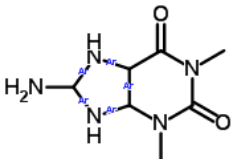
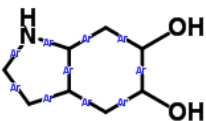
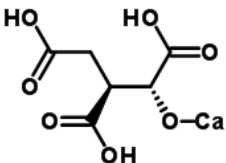
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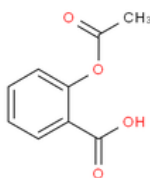




Quality Assurance

1556		Error an atom has the wrong valence
1586		Error an atom has the wrong valence
1623		Error an atom has the wrong valence

ChemSpider Validation & Standardization Platform
<http://bit.ly/NZF5VB>



Aspirin

[Structure](#)

[Draw Molecule](#)



AlogP

1.19

H-Bond Acceptors

4

H-Bond Donors

1

Mol Weight

180.157

The prototypical analgesic used in the treatment of mild to moderate pain. It has anti-inflammatory and antipyretic properties and acts as an inhibitor of cyclooxygenase which results in the inhibition of the biosynthesis of prostaglandins. Aspirin also inhibits platelet aggregation and is used in the prevention of arterial and venous thrombosis. (From Martindale, The Extra Pharmacopoeia, 30th ed, p5)

ChemSpider ID [OPS403534](#)

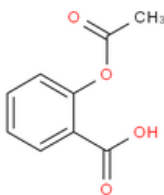
SMILES [CC\(=O\)OC1=CC=CC=C1C\(=O\)O](#)

Standard InChI [InChI=1S/C9H8O4/c1-6\(10\)13-8-5-3-2-4-7\(8\)9\(11\)12/h2-5H,1H3,\(H,11,12\)](#)

Standard InChIKey [BSYNRYMUTXBXSQ-UHFFFAOYSA-N](#)

Protein Binding High (99.5%) to albumin. Decreases as plasma salicylate concentration increases, with reduced plasma albumin concentration or renal dysfunction, and during pregnancy.

Toxicity Oral, mouse: LD₅₀ = 250 mg/kg; Oral, rabbit: LD₅₀ = 1010 mg/kg; Oral, rat: LD₅₀ = 200 mg/kg. Effects of overdose include: tinnitus, abdominal pain, hypokalemia, hypoglycemia, pyrexia, hyperventilation, dysrhythmia, hypotension, hallucination, renal failure, confusion, seizure, coma, and death.



Aspirin

Pharmacology (2677)

Structure

[Draw Molecule](#)

The prototypical analgesic with antipyretic properties and active in the biosynthesis of prostaglandins, leading to arterial and venous thrombosis.

AlogP

1.19 

H-Bond Acceptors

5 

H-Bond Donors


2 


Mol Weight


180.157

ChemSpider ID [OPS403534](#)

SMILES [CC\(=O\)OC1=CC=CC=C1C\(=O\)O](#) 

Standard InChI [InChI=1S/C9H8O4/c1-6\(10\)13-8-5-3-2-4-7\(8\)9\(11\)12/h2-5H,1H3,\(H,11\)12](#) 

Standard InChIKey [BSYNRYMUTXBXSQ-UHFFFAOYSA-N](#) 

Protein Binding High (99.5%) to albumin. Decreases as plasma salicylate concentration increases, with reduced plasma albumin concentration or renal dysfunction, and during pregnancy. 

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This XML file does not appear to have any style information associated with it. The document tree is shown below.

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Open PHACTS Working Draft

Dataset Descriptions for the Open Pharmacological Space

Open PHACTS Working Draft 12 September 2013

This version:
<http://www.openphacts.org/specs/2013/WD-datadesc-20130912/>

Latest published version:
<http://www.openphacts.org/specs/datadesc/>

Previous version:
<http://www.openphacts.org/specs/2012/WD-datadesc-20121019/>

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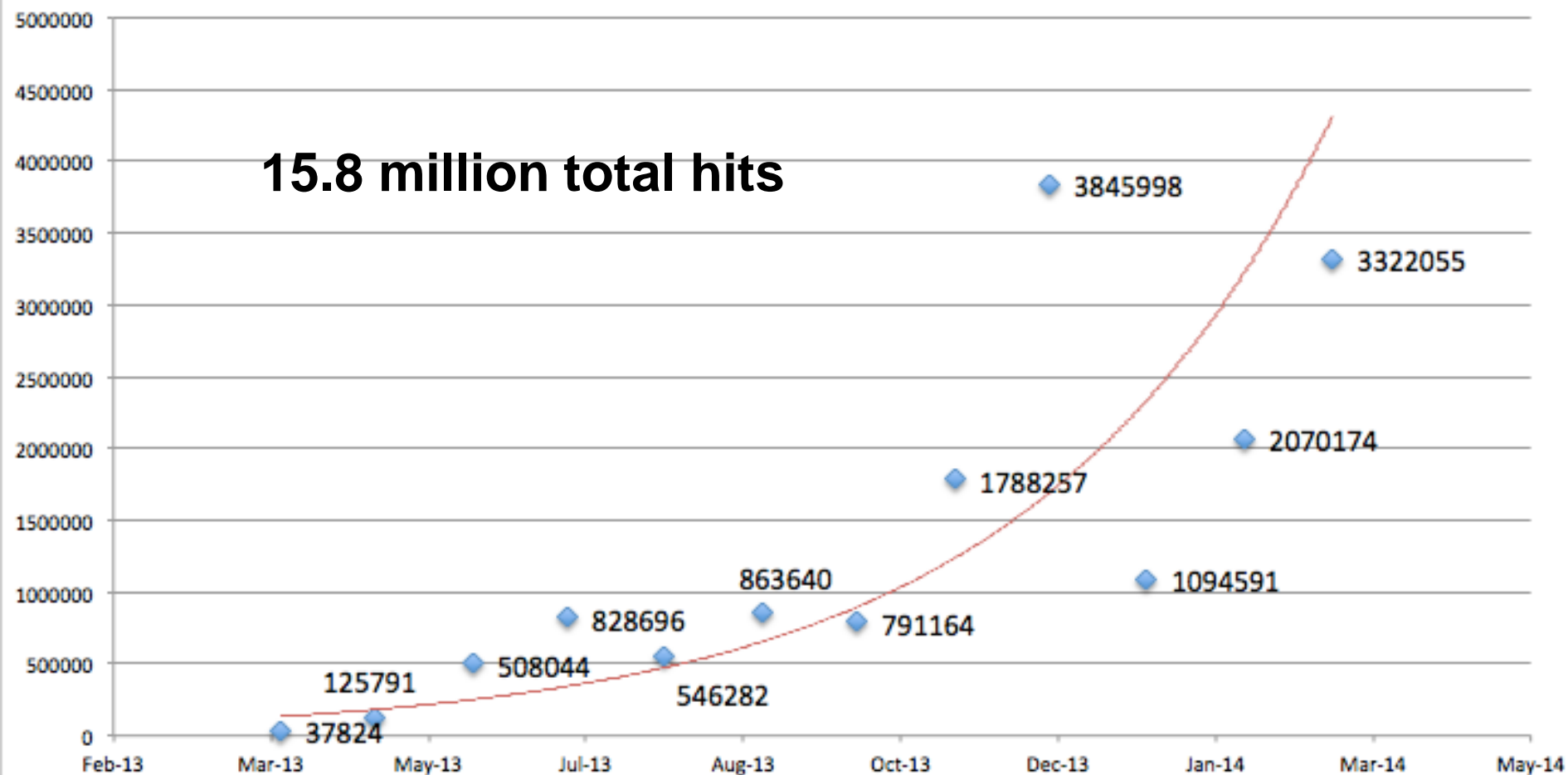
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Is Anybody Using It?



API Hits (April 2013 – March 2014)





Open PHACTS
Open Pharmacological Space

An “App Store”?



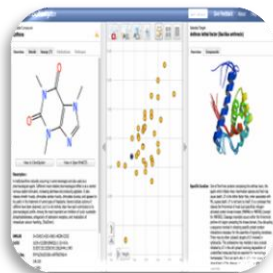
Explorer



Explorer2



ChemBioNavigator



Target Dossier



Pharmatrek



Helium



MOE



Collector



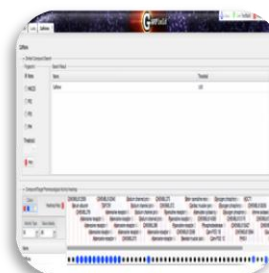
Cytophacts



Utopia



Garfield



SciBite



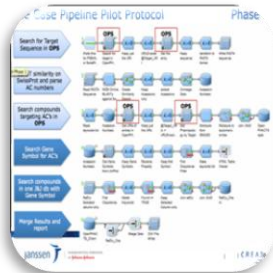
KNIME



Mol. Data Sheets



PipelinePilot



scinav.it



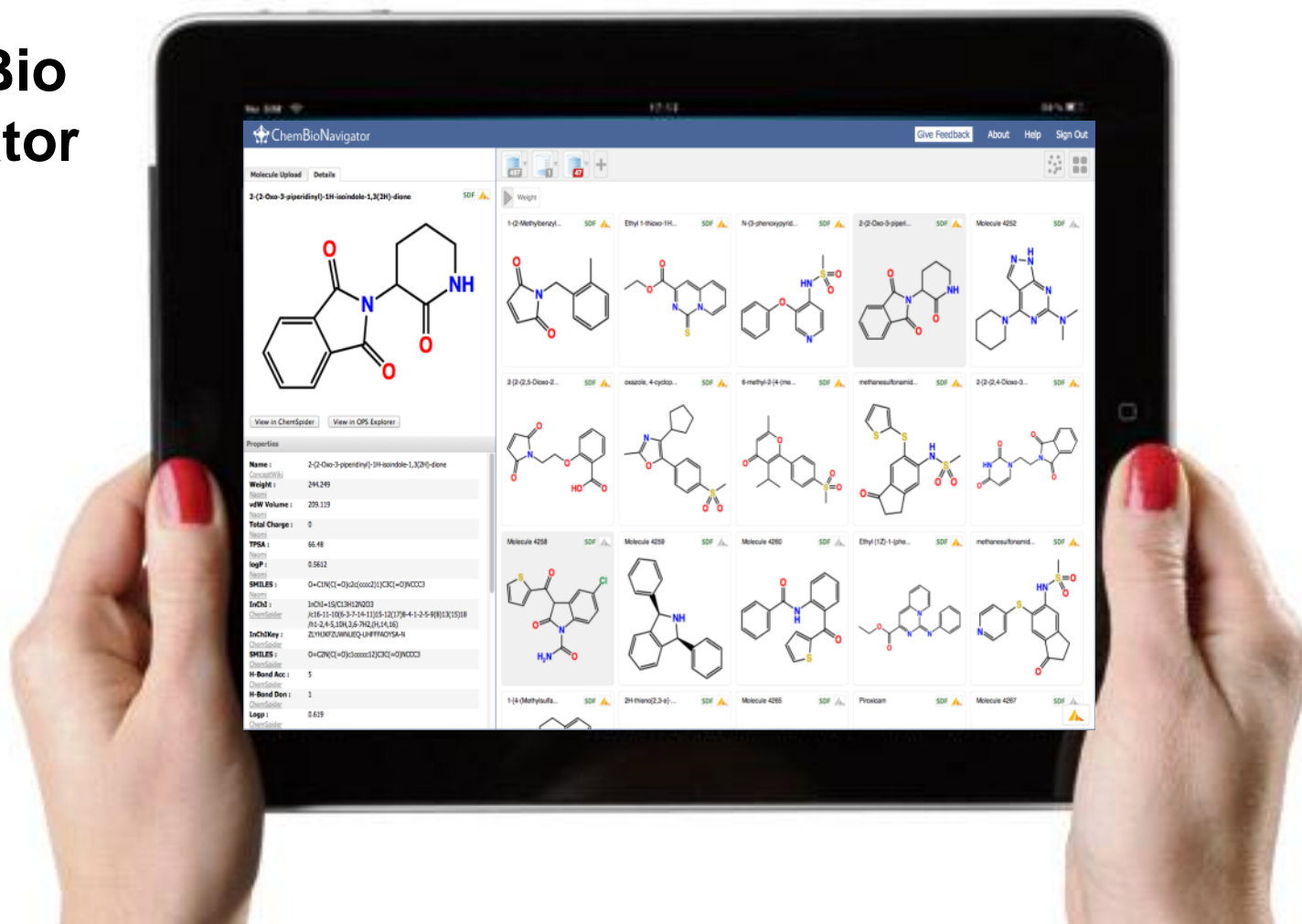
Taverna



<http://www.openphactsfoundation.org/apps.html>



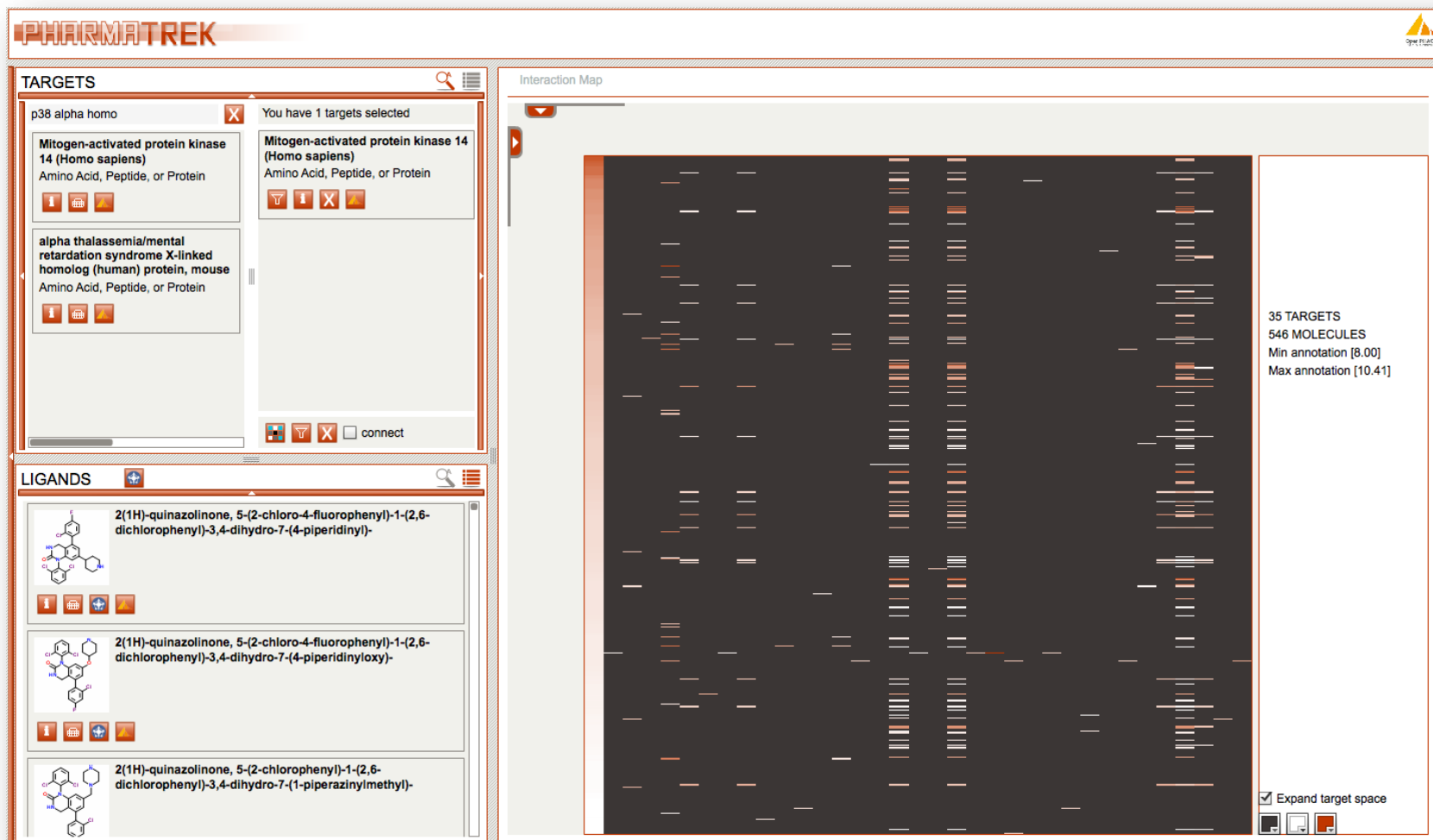
ChemBio Navigator



<http://chembionavigator.com>



Pharmatrek (<http://pharmatrek.org>)



PHARMATREK

TARGETS

p38 alpha homo

Mitogen-activated protein kinase 14 (Homo sapiens)
Amino Acid, Peptide, or Protein

Mitogen-activated protein kinase 14 (Homo sapiens)
Amino Acid, Peptide, or Protein

alpha thalassemia/mental retardation syndrome X-linked homolog (human) protein, mouse
Amino Acid, Peptide, or Protein

You have 1 targets selected

LIGANDS

2(1H)-quinazolinone, 5-(2-chloro-4-fluorophenyl)-1-(2,6-dichlorophenyl)-3,4-dihydro-7-(4-piperidiny)-

2(1H)-quinazolinone, 5-(2-chloro-4-fluorophenyl)-1-(2,6-dichlorophenyl)-3,4-dihydro-7-(4-piperidinoyloxy)-

2(1H)-quinazolinone, 5-(2-chlorophenyl)-1-(2,6-dichlorophenyl)-3,4-dihydro-7-(1-piperazinylmethyl)-

Interaction Map

35 TARGETS
546 MOLECULES
Min annotation [8.00]
Max annotation [10.41]

☒ Expand target space



Utopia <http://getutopia.org>

Utopia Documents - pcbl.1000976 1..16

Back to overview

acetylactate

2-acetylactate mutase

2-acetylactate mutase
In enzymology, a 2-acetylactate mutase is an enzyme that catalyzes the chemical reaction 2-acetylactate \rightleftharpoons 3-hydroxy-3-methyl-2-oxobutanoate. Hence, this enzyme has one substrate, 2-acetylactate, and one product, 3-hydroxy-3-methyl-2-oxobutanoate. This enzyme belongs to the family of isomerases, specifically those intramolecular transferases transferring other groups. The systematic name of this enzyme class is 2-acetylactate methylmutase.

[View Wikipedia web page...](#)

Acetylactate decarboxylase

Acetylactate decarboxylase
In enzymology, an acetylactate decarboxylase is an enzyme that catalyzes the chemical reaction (S)-2-hydroxy-2-methyl-3-oxobutanoate \rightleftharpoons (R)-2-acetoin + CO₂. Hence, this enzyme has one substrate, (S)-2-hydroxy-2-methyl-3-oxobutanoate, and two products, (R)-2-acetoin and CO₂. This enzyme belongs to the family of lyases, specifically the carboxy-lyases, which cleave carbon-carbon bonds.

[View Wikipedia web page...](#)

ACETOLACTSYNI-CPLX

ACETOLACTSYNI-CPLX
Bifunctional acetylactate decarboxylase / acetylactate synthase (livB/N) carries out both the first step in valine biosynthesis and the second step in isoleucine biosynthesis. The livB/N protein complex catalyzes the conversion of pyruvate and oxobutanoate into 2-acetylactate and the conversion of 2-acetylactate into 2-acetylactate. Both reactions generate carbon dioxide as a product (CITS: 146087001701047009233161817513011751116326011). This enzyme has a wide substrate range in vitro (CITS: 15558598). This bifunctional enzyme is a tetramer comprising two livB subunits and two livN subunits. Its apparent molecular weight rises above the expected weight for this configuration when pyruvate is added in vitro (CITS: 8360995). The livB large subunit can catalyze the reaction in isolation and is not inhibited by valine in the manner of the holoenzyme. However the Vmax for the reaction as catalyzed by only livB is

9 of 16 pages

[Look up](#)

www.chemspider.com

InChI=1S/C5H8O4/c1-3(6)5(2,9)...



Open PHACTS Associate Partner Community





Moving Forward

The Open PHACTS Foundation

OPF is a not-for-profit membership organisation, supporting the Open PHACTS Discovery Platform:

A sustainable, open, vibrant and interoperable information infrastructure for applied life science research and development.

To reduce the barriers to drug discovery in industry, academia and for small businesses, the **Open PHACTS Discovery Platform** provides tools and services to interact with multiple integrated and publicly available data sources. To integrate this data, extensive cross-referencing of scientific concepts is needed across all databases.

The Open PHACTS Foundation ensures the sustainability of the **Open PHACTS Discovery Platform** infrastructure and acts as a hub for relevant scientific research and development.



ChEMBL



The free chemical database

**DRUGBANK**
Open Data Drug & Drug Target DatabaseWikiPATHWAYS
Pathways for the People

Key Resources

 [Open PHACTS API](#) [Open PHACTS Repository](#)

Subscribe to the Foundation Newsletter

Subscribe

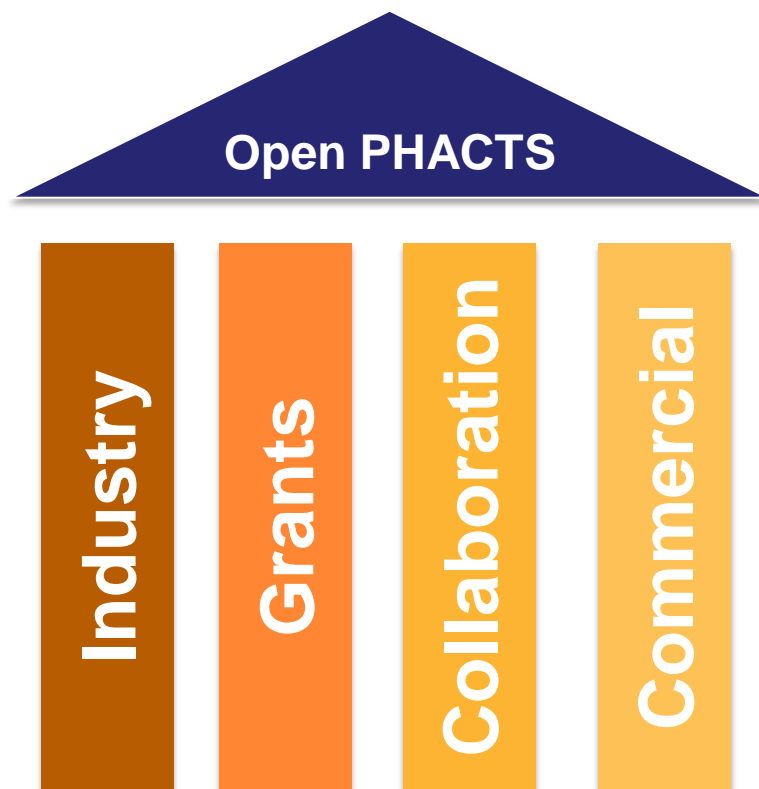
Contact us

Email:
info@openphactsfoundation.org

Twitter: [@Open PHACTS](#)

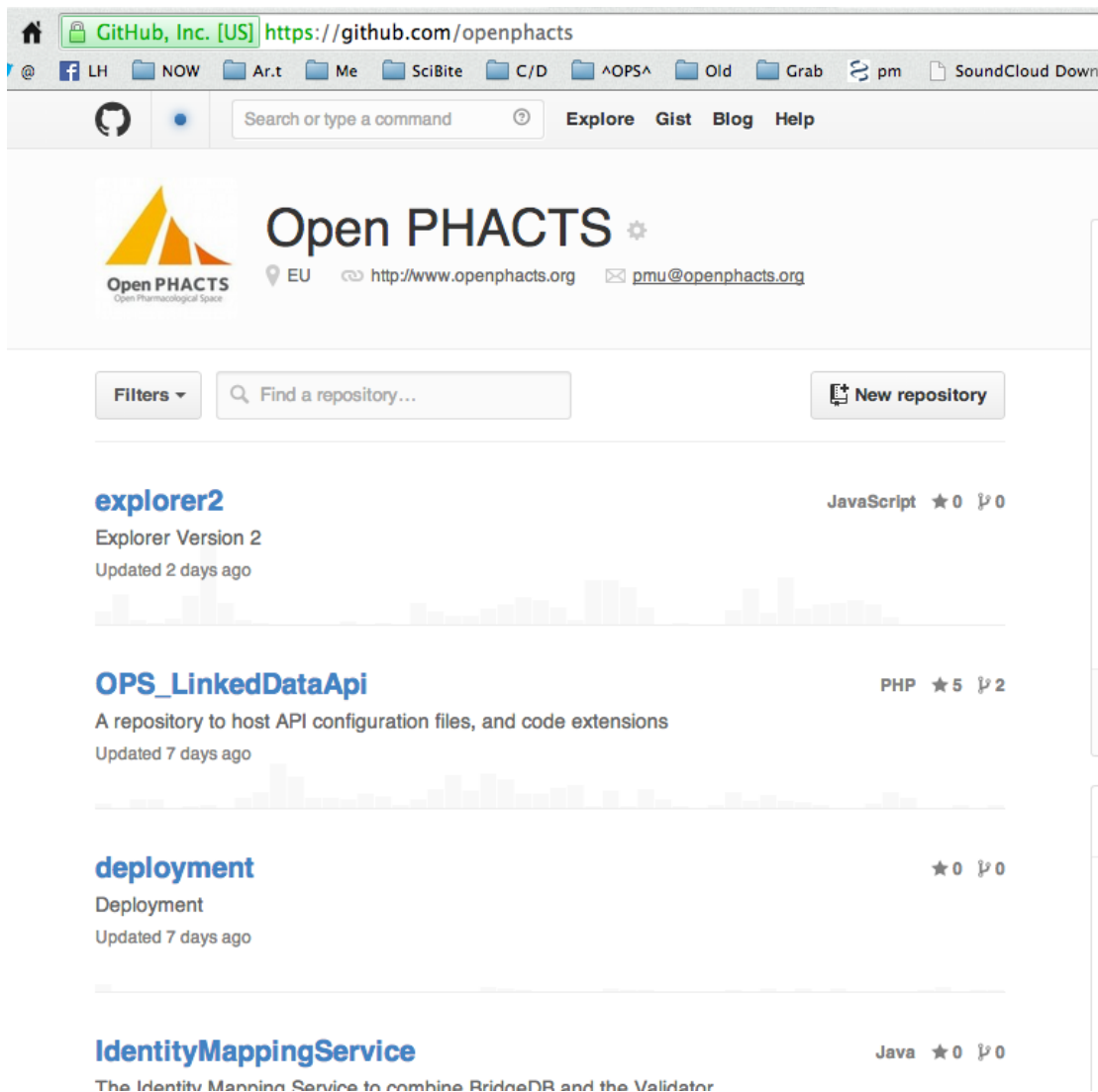


Sustainability





**Wait A Minute
Its Free – Why Pay?**



The screenshot shows the GitHub repository page for Open PHACTS. The browser address bar displays the URL <https://github.com/openphacts>. The repository page header includes the Open PHACTS logo, the name "Open PHACTS", and contact information: "EU", "http://www.openphacts.org", and "pmu@openphacts.org". Below the header, there is a search bar with the text "Find a repository..." and a "New repository" button. The repository list shows four repositories:

- explorer2** (JavaScript) with 0 stars and 0 forks. Description: "Explorer Version 2", updated 2 days ago.
- OPS_LinkedDataApi** (PHP) with 5 stars and 2 forks. Description: "A repository to host API configuration files, and code extensions", updated 7 days ago.
- deployment** with 0 stars and 0 forks. Description: "Deployment", updated 7 days ago.
- IdentityMappingService** (Java) with 0 stars and 0 forks. Description: "The Identity Mapping Service to combine BridgeDR and the Validator".

<https://github.com/openphacts>

Membership Benefits



The not-for-profit Foundation maintains the Open PHACTS Discovery Platform, a versatile infrastructure of integrated biomedical data, and actively engages an ecosystem of industry and academic semantic web experts.

Integrated data:

Pharmacological

Physicochemical

Disease

Gene

Pathways

Steer the direction

- Prioritise new projects
- Get involved with Foundation governance
- Identify development opportunities
- Propose new data sources to include
- Develop new use-cases and workflows
-

Training opportunities

Enjoy training opportunities by experts.

Early access to releases

Members have early access to infrastructure and platform updates and new releases, including a locally installable system

Engage a community of experts and peers

The Foundation serves a unique and vibrant scientific community, facilitating collaboration between the pharma industry, academia & SMEs.

Influence the security policy

Membership Levels

Full

Nominate and vote for the Board of Trustees

Contributing

Vote for the Board of Trustees

Individual

Non-voting

Get involved in projects and collaborate

turnover. Pay in cash or by donating people-hours to the Foundation.

www.openphactsfoundation.org

info@openphactsfoundation.org

Open PHACTS Foundation
c/o Royal Society of Chemistry,
Thomas Graham House,
Science Park, Cambridge, CB4 0WF





✦ The (Immediate) Future Of Open PHACTS

- Establish the Open PHACTS foundation
- Recruit members and partners
- Further develop scientific resources
 - Open chemical patent data (SureChEMBL)
 - Gene-Disease associations (DisGeNet)
 - Develop the Open PHACTS VM
- Connect with other projects (IMI+beyond)

Thanks!

lee@connecteddiscovery.co.uk | [@Scibitely](https://www.scibitely.com)

Acknowledgements



Pfizer Limited
Universität Wien
Technical University of Denmark
University of Hamburg, Center for
Bioinformatics
BioSolveIT GmbH
Consorci Mar Parc de Salut de Barcelona
Leiden University Medical Centre
Royal Society of Chemistry
Vrije Universiteit Amsterdam

Spanish National Cancer Research Centre
University of Manchester
Maastricht University
Aqnowledge
University of Santiago de Compostela
Rheinische Friedrich-Wilhelms-Universität
Bonn
AstraZeneca
GlaxoSmithKline
Esteve

Novartis
Merck Serono
H. Lundbeck A/S
Eli Lilly
Netherlands Bioinformatics Centre
Swiss Institute of Bioinformatics
ConnectedDiscovery
EMBL-European Bioinformatics Institute
Janssen
OpenLink



pmu@openphacts.org



@Open_PHACTS



Open PHACTS





Science-Driven Dynamic Integration



“What are the physiochemical properties of warfarin salts, tautomers or stereo-isomers?”



“What are the biological responses to warfarin?”

**Scientific Lenses over Linked Data: An approach
to support task specific views of the data.
A vision.**

Christian Brenninkmeijer¹, Chris Evelo², Carole Goble¹, Alasdair J G Gray¹,
Paul Groth³, Steve Pettifer¹, Robert Stevens¹, Antony J Williams⁴, and Egon
L Willighagen²

<http://bit.ly/1gzOhS2>