



# Open PHACTS

Open Pharmacological Space

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data integration

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# The Innovative Medicines Initiative

EC funded public-private partnership for pharmaceutical research

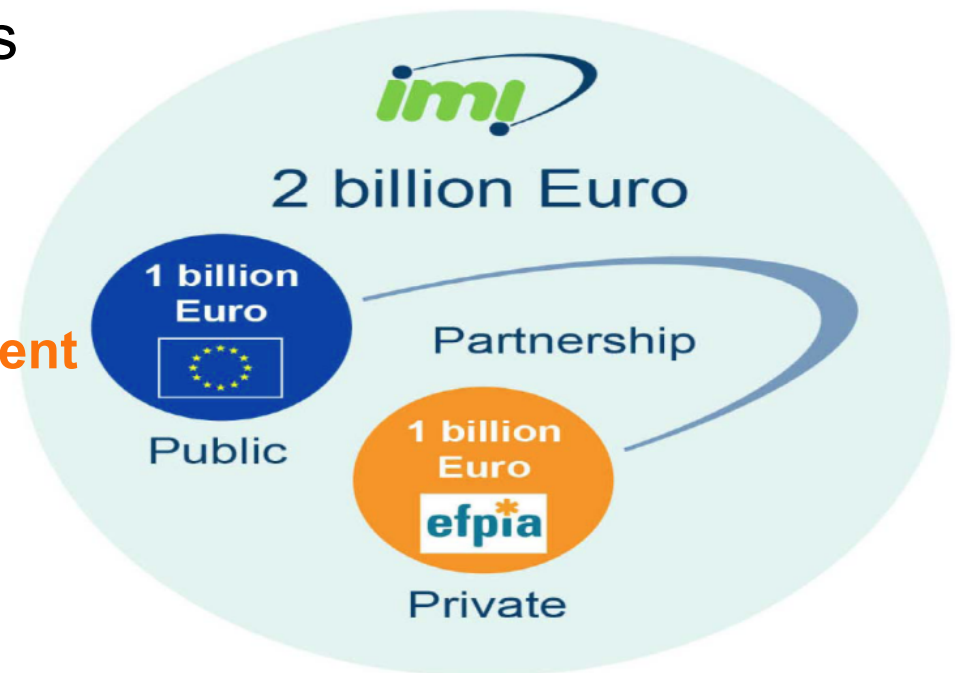
Focus on key problems

Efficacy

Safety

Education & Training

**Knowledge Management**



# Open PHACTS

## an infrastructure project

Develop / apply a set of robust **standards**...

Implementing the standards in a **semantic integration platform** (*“Open Pharmacological Space”*)...

Delivering **services** to support on-going drug discovery programs in pharma and public domain

**Mix ideal with the pragmatic.** Build open that can accommodate non-open components in the real world.

23 partners

9 pharma

14 academic/SME/society

5 new partners in the process



# Pharma bring...

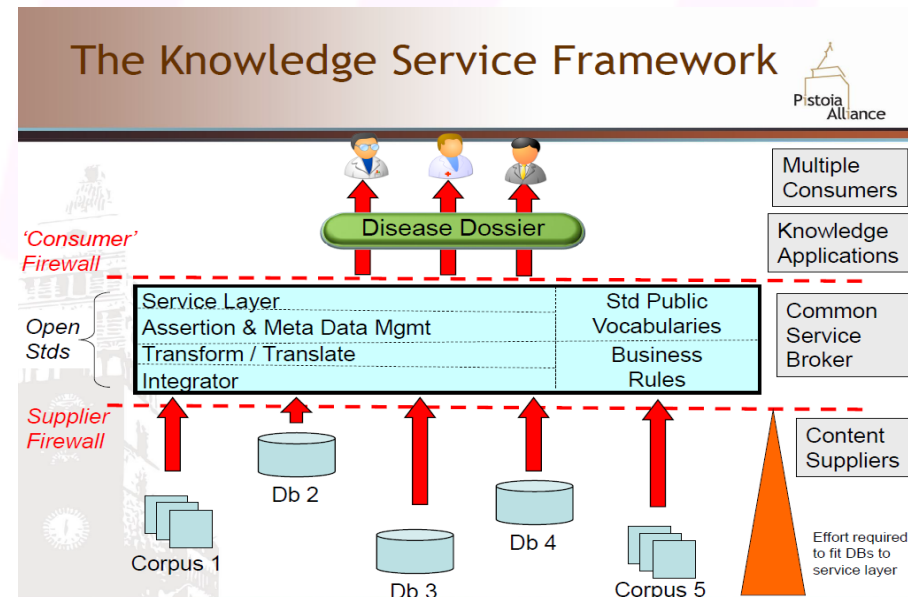
Pre-competitive collaboration

Agreement on standards, approaches

Research questions drive development

Clear use cases

Drive and direction





# Example research questions

Give all compounds with  $IC_{50} < xxx$  for target Y in species W and Z plus assay data

What substructures are associated with readout X (target, pathway, disease, ...)

Give all experimental and clinical data for compound X

Give all targets for compound X or a compound with a similarity  $> y\%$

73 questions identified across consortium

# What does 'Open' mean?

**OPS Open** - open access to all

**OPS Consortia** - data sets licensed just to the consortia

**OPS Academia** - fully open to academia

**"My OPS"**

**Open Source**

**Open Access Infrastructure.** GUI and back-end platform, online or download both + data for local setup

**Open Services:** for example, RSC services

**Open Data + Private Data:** licensing fun for all the family

**Commercial providers:** abstract service interface to swap in commercial and open source platforms

# Agile Development: 6 month 'lash up'

- Produce a working 'lash up' system
- Constrained to technologies in consortium + a few data sources
- Focused on 2 prioritized research questions
  - All oxidoreductase inhibitors active  $<100\text{nM}$  in both human and mouse
  - For a given compound [clozapine], give me the interaction profile with [human or mouse] targets
- Minimum requirements: two data sources (one targets, one compounds) and able to produce answers in 'manual time'.

# 'lash-up': youtube.com/openphacts

The screenshot displays the OpenPHACTS web application interface. The top navigation bar includes the OpenPHACTS logo, a 'Log in' button, and a 'Create account' button. The main content area is titled 'Compounds active against enzyme family' and 'Similarity Search'. The search criteria are set to 'Enzyme family class: 1.10.1.- : With NAD(+) or NADP(+) as acceptor'. The search results are displayed in a table with columns for 'Ic50', 'Species', and 'Inhibitor'. The results are grouped into several categories, each with a 'Group' label and a count of items. The first group is '3-(3,5-dimethyladamantyl)methyl-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a]azepine (2 Items)', with two entries: 169 (0.004, Mus+musculus) and 170 (0.0176, Homo+sapiens). The second group is '3-(3,5-dimethyladamantyl)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a]azepine (3 Items)', with three entries: 171 (0.000104, Mus+musculus), 172 (0.00225, Homo+sapiens), and 173 (0.01, Mus+musculus). The third group is '3-(3,5,7-trimethyladamantyl)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a]azepine (2 Items)', with two entries: 174 (0.000118, Mus+musculus) and 175 (0.00018, Homo+sapiens). The fourth group is '3-(2-(2,4-dihydroxyphenyl)-1-[hydroxy(4-hydroxyphenyl)methyl]-2-oxoethyl)-5,7-dihydroxy-2-(4-hydroxyphenyl)-4H-chromene (1 Item)', with one entry: 176 (0.0036, Homo+sapiens). The fifth group is '3,4,5-trimethoxycinnamic acid (1 Item)', with one entry: 177 (0.049, Homo+sapiens). The sixth group is '3,3',4,4'-tetrahydroxy-7,7'-dimethyl-5,5'-bis(1-methylethyl)-2H,2'H-8,8'-binaphtho[1,8-bc]furan-2,2'-dione (1 Item)', with one entry: 178 (0.0022, Homo+sapiens). The left sidebar contains a navigation menu with categories like OPS, Compound, Similarity Search, X-Substructure Search, Target, Pathway, Pharmacology, X-By Compound, X-By Assay, By Enzyme Family, Exemplars, Concept, and Searching. The bottom of the interface has a 'Settings' button.

OpenPHACTS

Log in Create account

Compounds active against enzyme family Similarity Search

Enzyme family class: 1.10.1.- : With NAD(+) or NADP(+) as acceptor Browse EC codes

Variables

Filter by activity (nM): exclude below (<): 0 exclude above (>): 1000000

Species:  Human  Mouse  Rat  Pink Unicorn

Start search

Inhibitors for enzymes in class: 1.10.1.- => With NAD(+) or NADP(+) as acceptor - Records found: 250

Download to Excel

	Ic50	Species	Inhibitor
<b>Group: 3-(3,5-dimethyladamantyl)methyl-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a]azepine (2 Items)</b>			
169	0.004	Mus+musculus	3-(3,5-dimethyladamantyl)methyl-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a]azepine
170	0.0176	Homo+sapiens	3-(3,5-dimethyladamantyl)methyl-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a]azepine
<b>Group: 3-(3,5-dimethyladamantyl)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a]azepine (3 Items)</b>			
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173	0.01	Mus+musculus	3-(3,5-dimethyladamantyl)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a]azepine
<b>Group: 3-(3,5,7-trimethyladamantyl)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a]azepine (2 Items)</b>			
174	0.000118	Mus+musculus	3-(3,5,7-trimethyladamantyl)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a]azepine
175	0.00018	Homo+sapiens	3-(3,5,7-trimethyladamantyl)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a]azepine
<b>Group: 3-(2-(2,4-dihydroxyphenyl)-1-[hydroxy(4-hydroxyphenyl)methyl]-2-oxoethyl)-5,7-dihydroxy-2-(4-hydroxyphenyl)-4H-chromene (1 Item)</b>			
176	0.0036	Homo+sapiens	3-(2-(2,4-dihydroxyphenyl)-1-[hydroxy(4-hydroxyphenyl)methyl]-2-oxoethyl)-5,7-dihydroxy-2-(4-hydroxyphenyl)-4H-chromene
<b>Group: 3,4,5-trimethoxycinnamic acid (1 Item)</b>			
177	0.049	Homo+sapiens	3,4,5-trimethoxycinnamic acid
<b>Group: 3,3',4,4'-tetrahydroxy-7,7'-dimethyl-5,5'-bis(1-methylethyl)-2H,2'H-8,8'-binaphtho[1,8-bc]furan-2,2'-dione (1 Item)</b>			
178	0.0022	Homo+sapiens	3,3',4,4'-tetrahydroxy-7,7'-dimethyl-5,5'-bis(1-methylethyl)-2H,2'H-8,8'-binaphtho[1,8-bc]furan-2,2'-dione

Settings

# UTOPIA Documents (U Manchester)

Bioorganic &amp; Medicinal Chemistry Letters 19 (2009) 4183–4190



Contents lists available at ScienceDirect

## Bioorganic & Medicinal Chemistry Letters

journal homepage: [www.elsevier.com/locate/bmcl](http://www.elsevier.com/locate/bmcl)

### Discovery and functional evaluation of diverse novel human CB<sub>1</sub> receptor ligands

Nicolas Foloppe<sup>a,\*</sup>, Karen Benwell<sup>a</sup>, Teresa D. Brooks<sup>a</sup>, Guy Kennett<sup>b</sup>, Antony R. Knight<sup>b</sup>, Anil Misra<sup>b</sup>, Nathaniel J. T. Monck<sup>b</sup>

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#### ARTICLE INFO

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##### Keywords:

Cannabinoids

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Obesity

Pharmacophore

Virtual screening

#### ABSTRACT

Ligand-based virtual screening with a 3D pharmacophore led to the discovery of 30 novel, diverse and drug-like ligands of the human cannabinoid receptor 1 (hCB<sub>1</sub>). The pharmacophore was validated with a hit rate of 16%, binding selectivity versus hCB<sub>2</sub>, and expected functional profiles. The discovered compounds provide new tools for exploring cannabinoid pharmacology.

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The cannabinoid system was initially identified as mediating the effects of the major psychoactive components of *Cannabis sativa*, Δ<sup>9</sup>-tetrahydrocannabinol. To date, this system includes at least two receptors, CB<sub>1</sub> and CB<sub>2</sub>, the biology of which has been extensively reviewed.<sup>1–3</sup> CB<sub>1</sub>, a GPCR coupled to inhibitory G-proteins G<sub>i/o</sub>, is expressed in the central nervous system where it is found on presynaptic terminals, serving to modulate neurotransmitter release. It is also found in peripheral tissue. CB<sub>1</sub> is primarily found

Endocannabinoids like anandamide and 2-arachidonoyl glycerol are elevated in the plasma, adipose tissue and pancreas of obese humans and animals.<sup>10</sup> In genetically obese rodents endocannabinoid levels are elevated in the hypothalamus, an area of the brain that modulates feeding behavior.<sup>11</sup> Centrally, endocannabinoids elicit feeding behavior via activation of CB<sub>1</sub> receptors.<sup>7</sup> Peripheral CB<sub>1</sub> activation causes lipogenesis in adipose tissue and liver, and reduces the oxidation of free fatty acids (FFA).<sup>12</sup> Also

[Back to overview](#)

10.1016/j.bmcl.2009.05.114

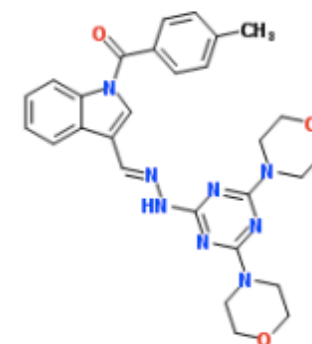


3-((2-(4,6-...y))methanone

3-((2-(4,6-dimorpholino-1,3,5-triazin-2-yl)hydrazono)methyl)-1H-indol-1-yl)(p-tolyl)methanone

[\[More...\]](#)

Ki Value : 2299

Ki of 2299 in [19520572](#)

1-(4-(3-(2,4...-yl)ethanone

1-(4-(3-(2,4-dimethoxyphenyl)-1-m-tolyl-1H-pyrazole-5-carbonyl)piperazin-1-yl)ethanone

[\[More...\]](#)

Ki Value : 1943

Ki of 1943 in [19520572](#)
[Look up](#)

# Sustainability and community

Data in and data out

Consortium (pharma) members

Public and commercial  
databases

Publishers

Services built on OPS

# Sustainability \$

After 3 years?

Pharma customers

Public funders

Services built on top

Publishing data in

# Focus and future

One area - **pharmacology**

“Production Level” software

Semantic pragmatics: everyday use  
by scientists not informaticians

An **infrastructure** that can be built  
upon, to provide a stable foundation  
for further pre-competitive informatics  
collaboration



Developers  
(Builders)



End users  
(Drivers)



# Nanopublications

## Capturing scientific information in the Triple Store



[nature.com](#) ▶ [journal home](#) ▶ [archive](#) ▶ [issue](#) ▶ [commentary](#) ▶ [full text](#)

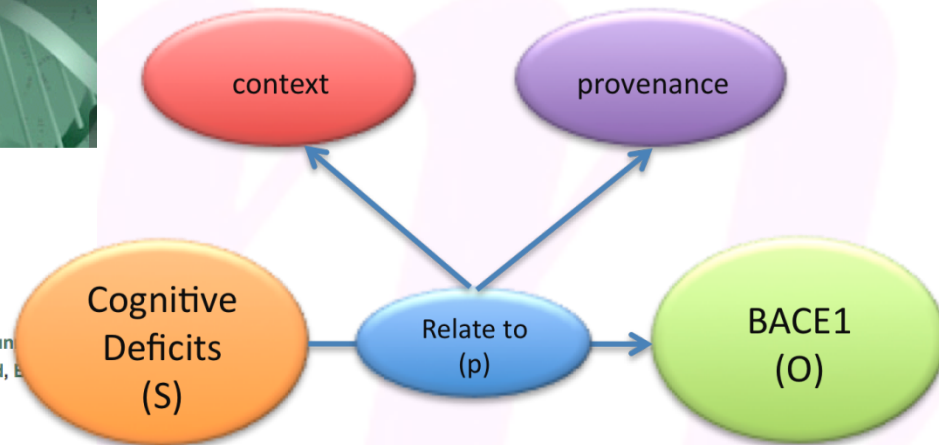
NATURE GENETICS | COMMENTARY

### The value of data

Barend Mons, Herman van Haagen, Christine Chichester, Peter-Bram 't Hoen, Johan T den Dunen, Gertjan van Ommen, Erik van Mulligen, Bharat Singh, Rob Hooft, Marco Roos, Joel Hammond, Eike Kiesel, Belinda Giardine, Jan Velterop, Paul Groth & Erik Schultes

[Affiliations](#) | [Contributions](#) | [Corresponding author](#)

*Nature Genetics* 43, 281–283 (2011) | doi:10.1038/ng0411-281  
Published online 29 March 2011



### Nano-Publication in the e-science era

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ABSTRACT

Newer standards like RDFa also facilitate this and integrate with

# Onwards and Upwards

Connection between developers and users

Architecture

Services: e.g. entity identification and resolution and representing similarity, ORCID, DataCite

Models: RDF / Nanopublication model spec and guidelines

## Prototype

March 2012: Internal Prototype Delivery

September 2012: Release 1<sup>st</sup> Prototype

# Why should you care?

Will be first real large scale semantic data integration project – a pilot that can be extended

Provides a single delivery format and pipeline to your customers?

# Find out more?

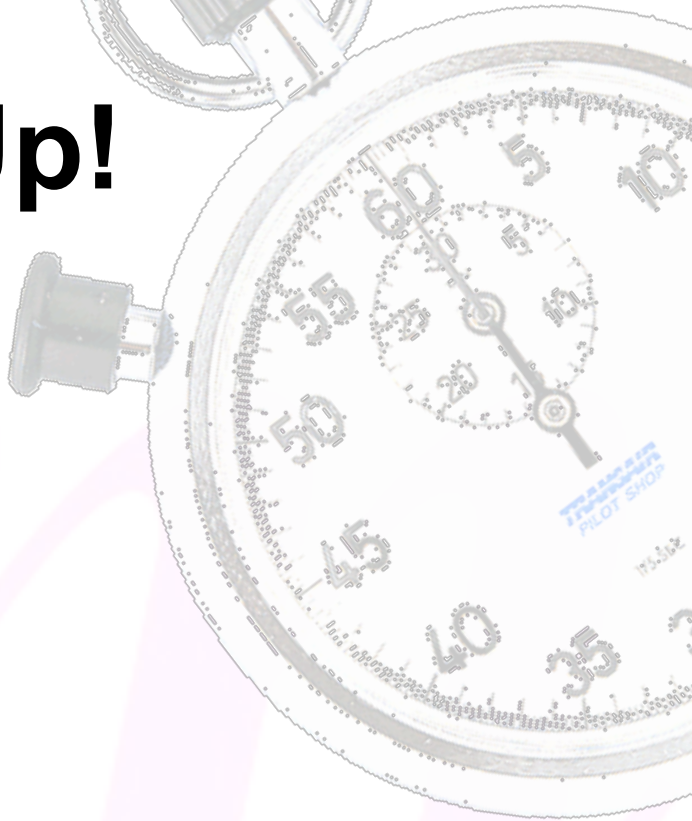
Email me



Apr/May 2012 - a workshop and intro  
for publishers

also for data providers/vendors

# Time's Up!



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**Lash-up: [youtube.com/openphacts](https://www.youtube.com/openphacts)**