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Adressing Research Questions by Integration of Open PHACTS with Pipeline Pilot

Accelrys Seminar, Mainz, 14th May 2013

Christian Herhaus, Global Computational Chemistry

Innovative Medicines Initiative

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

The Open PHACTS Project

- Runs 2011-2014
- *Create a semantic integration hub ("Open Pharmacological Space")*
- Deliver services to support on-going drug discovery programs in pharma and public domain
- Leading academics in semantics, pharmacology and informatics,
- Driven by solid industry business requirements

http://www.openphacts.org/

Open PHACTS Partners

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Associate Partners

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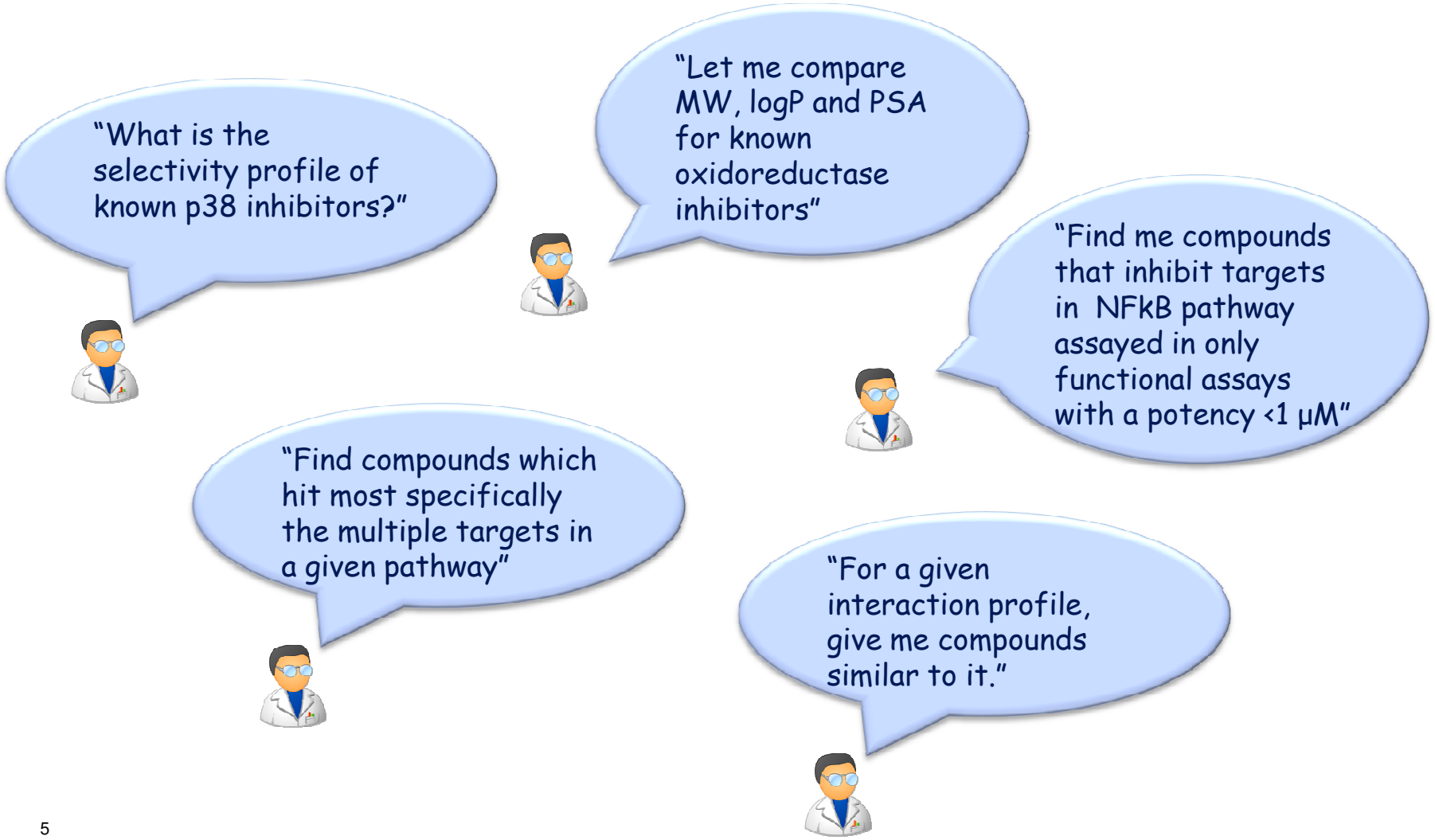
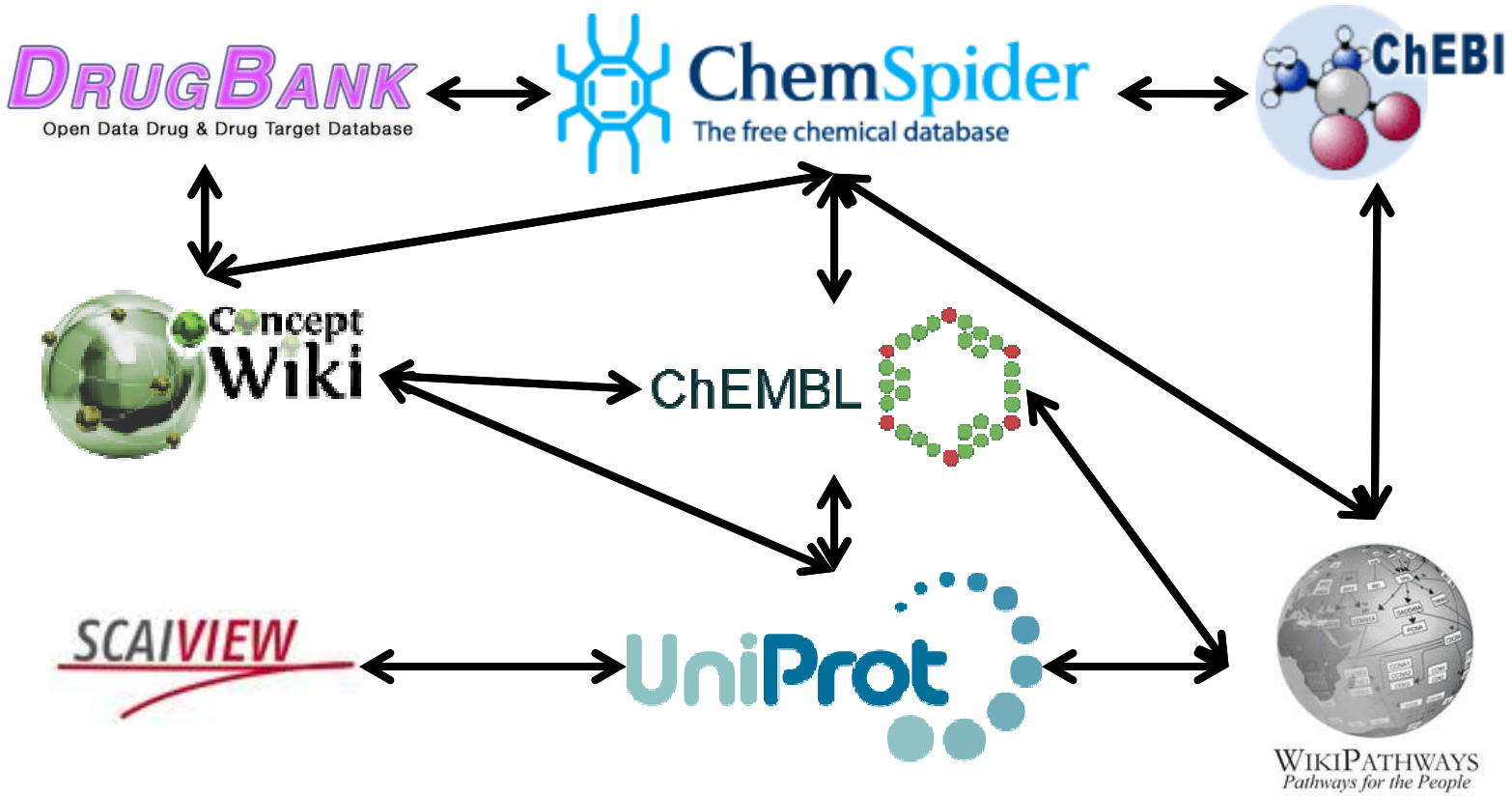
Focused on Answering Business Questions

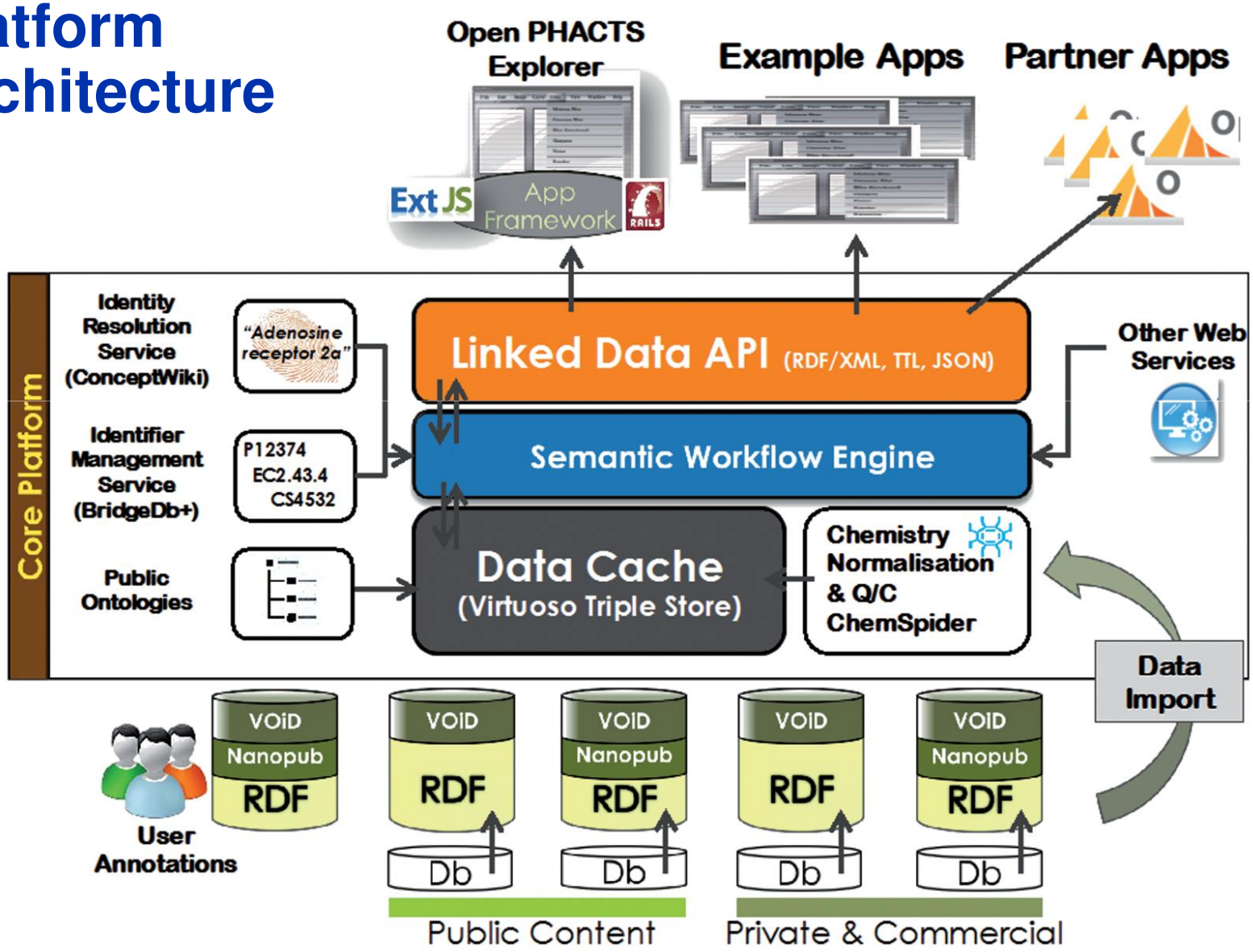


Datasets and Links

815 millions of Data triples, 18 millions of Mapping triples



Platform Architecture



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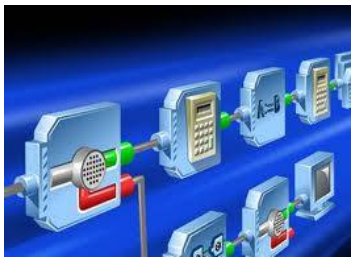
The Open PHACTS Linked Data API

Chemical Structure Exact Search	/structure/exact GET	Compound Pharmacology Complete (DEPRECATED)	/compound/pharmacology GET
InchiKey to URL	/structure GET	Compound Pharmacology Paginated	/compound/pharmacology/pages GET
Inchi to URL	/structure GET	Data Sources	/sources GET
Chemical Structure Similarity Search	/structure/similarity GET	Get Enzyme Classification Root Classes	/target/enzyme/root GET
SMILES to URL	/structure GET	Get Enzyme Classification Class	/target/enzyme/node GET
Chemical Structure Substructure Search	/structure/substructure GET	Get Enzyme Classification Class Members	/target/enzyme/members GET
Get concept description	/getConceptDescription GET	Enzyme Pharmacology Count	/target/enzyme/pharmacology/count GET
Map free text to a concept URL based on semantic tag	/search/byTag GET	Enzyme Pharmacology Complete (DEPRECATED)	/target/enzyme/pharmacology GET
Map free text to a concept URL	/search/freetext GET	Enzyme Pharmacology Paginated	/target/enzyme/pharmacology/pages GET
Map URLs	/mapURL GET	Pathway Information	/pathway GET
Get ChEBI Ontology Class Members	/compound/chebi/members GET	Activity types	/pharmacology/filters/activities GET
Get ChEBI Ontology Root Classes	/compound/chebi/root GET	Units for activity type	/pharmacology/filters/units/ GET
Get ChEBI Ontology Class	/compound/chebi/node GET	Target Information	/target GET
ChEBI Class Pharmacology Count	/compound/chebi/pharmacology/count GET	Target Pharmacology Count	/target/pharmacology/count GET
ChEBI Class Pharmacology Complete (DEPRECATED)	/compound/chebi/pharmacology GET	Target Pharmacology Complete (DEPRECATED)	/target/pharmacology GET
ChEBI Ontology Class Pharmacology Paginated	/compound/chebi/pharmacology/pages GET	Target Pharmacology Paginated	/target/pharmacology/pages GET
Compound Information	/compound GET		
Compound Pharmacology Count	/compound/pharmacology/count GET		

https://dev.openphacts.org/

Pipeline Pilot Hackathon

Cambridge, 20th Feb 2013



- Demonstrate that the integration of the Open PHACTS API and Pipeline Pilot (PP) is possible
- Create a library of PP components for the Open PHACTS API
- Enable:
  - Easy querying of the Open PHACTS API
  - “Drag and drop” creation of useful PP workflows
  - Customisation of PP components
  - PP component transparency

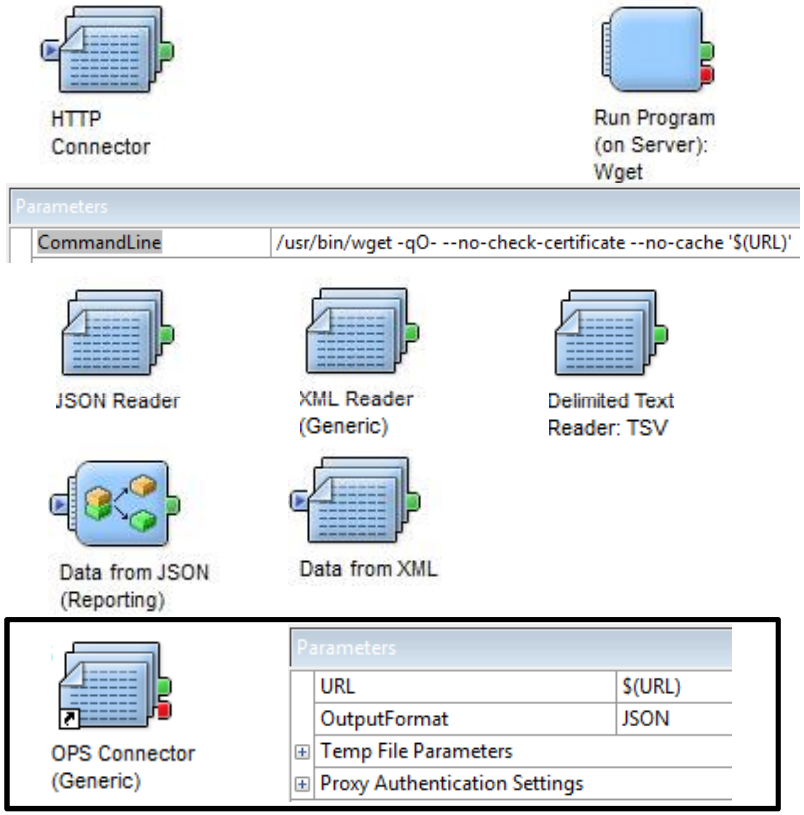
Connecting to Open PHACTS with PPilot

Chemical Structure Similarity Search `/structure/similarity` GET

Description

Returns a set of ChemSpider compound URLs, similar to the input molecule according to the specified algorithm and threshold. Driven by ChemSpider.

PARAMETER	VALUE	DESCRIPTION
app_id		Your access application id
app_key		Your access application key
searchOptions.Molecule	(required)	A SMILES string. E.g. CC(=O)Oc1ccccc1C(=O)O
searchOptions.SimilarityType		0: Tanimoto ; 1: Tversky ; 2: Euclidian
searchOptions.Threshold		Double <= 1.0
resultOptions.Limit		Integer. Search limit. Specefy how many results return back during the search. Default value: -1 .
resultOptions.Start		Integer. Return results starting the index. Default value: 0
resultOptions.Length		Integer. How many results should be returned starting from Start index. Default value: -1.
_format		The desired result format.

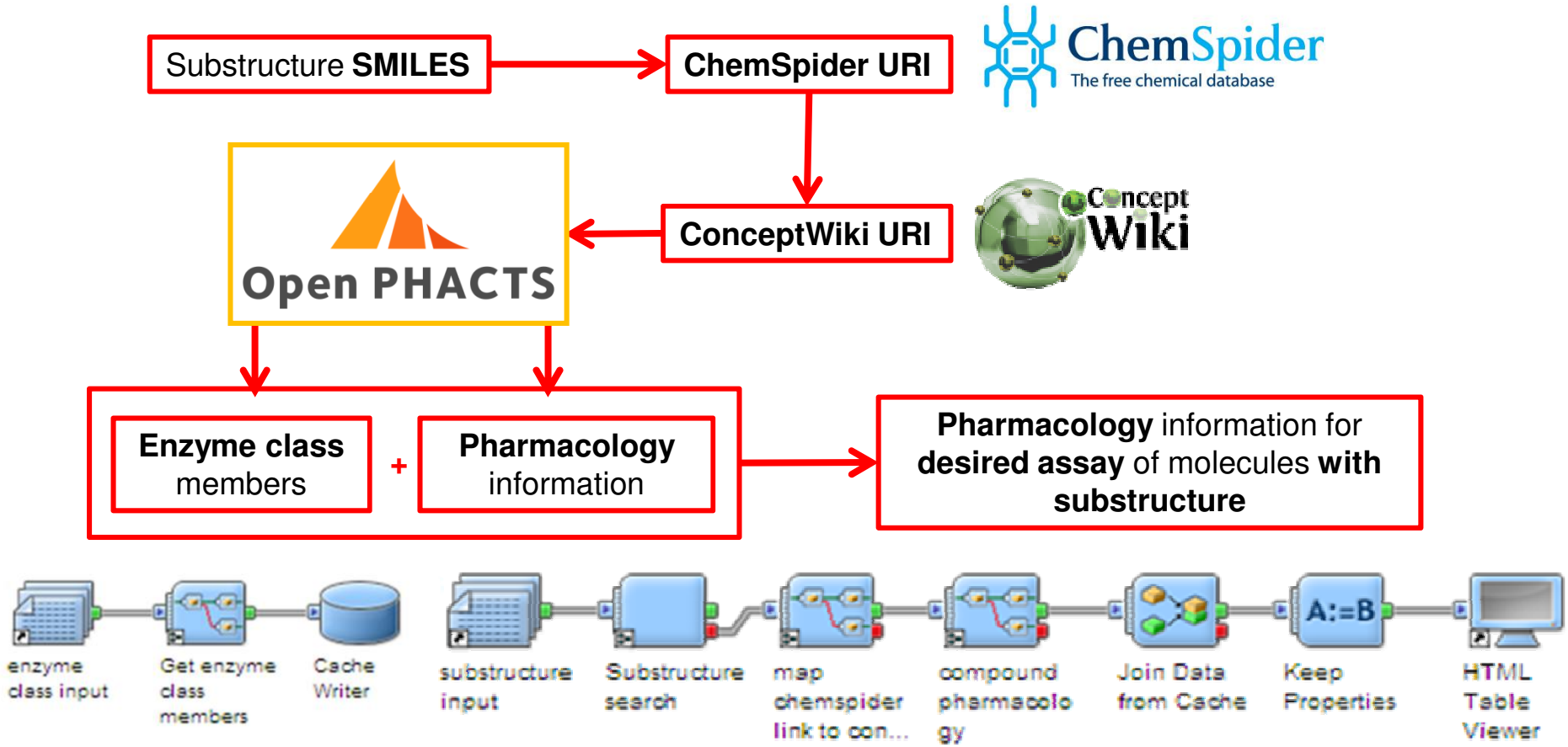


Example URL:

```
https://$(ops_server)/structure/similarity?app_id=$(app_id)&app_key=$(app_key)
&searchOptions.Molecule=c1ccccn1&searchOptions.SimilarityType=0
&searchOptions.Threshold=0.7&_format=json
```

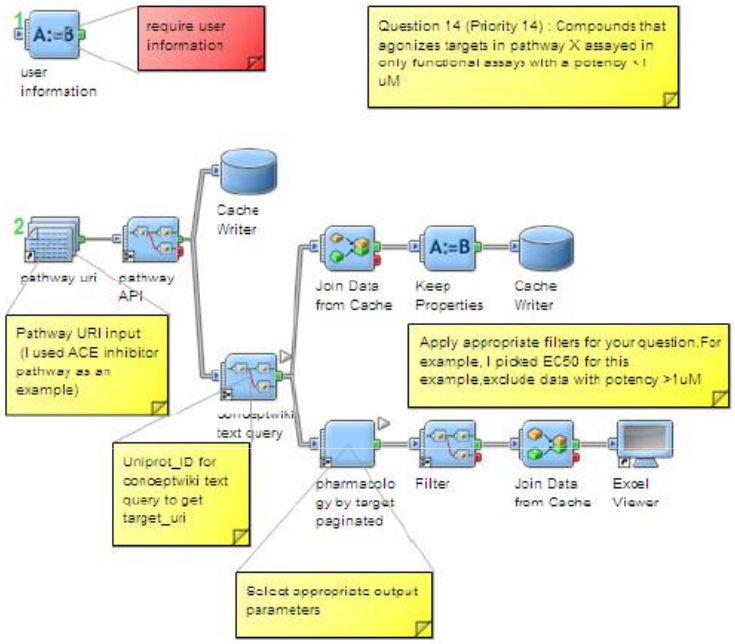
Answering Questions: Hackathon Example

*"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".*



Question 14 : Compounds that agonizes targets in pathway X assayed in only functional assays with a potency <1 uM

Pathway information	• Use pathway URI(s) as input e.g. http://rdf.wikipathways.org/WP1019_r48131 • Obtain all genes in that pathway as a result
Biomart web service	• Gene IDs provided in OPS pathway query are in form of Entrez. It needs to be converted into Uniprot IDs for further Conceptiwiki query
Conceptwiki mapping	• Text query of Uniprot IDs to get target URIs.
Target by pharmacology	• Retrieved pharmacology information for all targets in our desire pathway(s) using Conceptwiki target URIs • Option to select your output information
Filter	• Apply suitable filter(tailor made for your question.)



Filter for this specific question:

1. Select EC50 bioactivity data entry
2. Relation not equal to >
3. Convert activity unit from nM/-LogEC50 to uM
4. Assay with potency <1uM

Chris Chau (GSK)

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Question 14 : Compounds that agonizes targets in pathway X assayed in only functional assays with a potency <1 uM

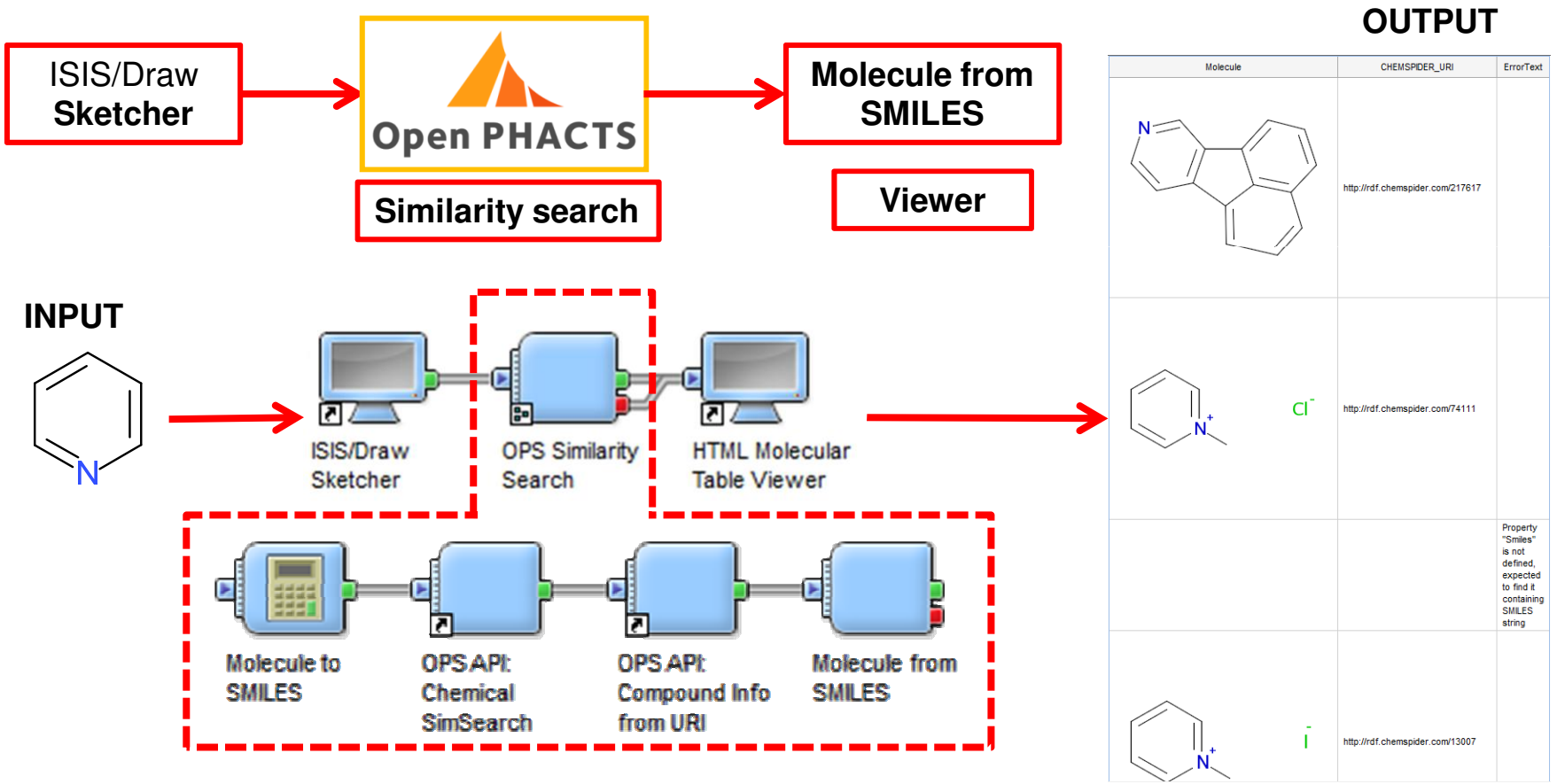
Example Results:

	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R	S	T	U	V	W	X
1	target_title	activity_ID	pmid	activity_type	relation	standardValue	standardUnits	chembl_assay_id	description	assay_organism	chembl_target_id	target_organism	chembl_compound_id	chemspider_uri	compound_uri	prefLabel	inchi	inchikey	full_mwt	smiles	ro5_violations	uM	pathway
2	Cathepsin	http://dati	2.1E+07	EC50	=	13.5	nM	http://dati	Inhibition	Homo sap	http://dati	Homo sap	http://dati	http://rdf.	http://ww	delanzomi	InChI=1S/(	SJFBTAPEP	413.275	B([C@H](C	1	1.35E-02	ACE Inh
3	Nitric oxi	http://dati	1.9E+07	EC50	=	420	nM	http://dati	Inhibition	Homo sap	http://dati	Homo sap	http://dati	http://rdf.	http://ww	N-(3-chlor	InChI=1S/(	VDKGHNO	428.819	Cn1cncc1C(=O)N(Cc2		0.42	ACE Inh
4	Mineraloc	http://dati	2E+07	EC50	=	3.8	nM	http://dati	Agonist activity at m	http://dati	Homo sap	http://dati	http://rdf.	http://ww	Aldosteroi	InChI=1S/(	PQSUYGKT	360.444	O=C(CO)[C@@H]4[C(		3.80E-03	ACE Inh
5	Mineraloc	http://dati	2.1E+07	-Log EC50	=	9.471		http://dati	Agonist ac	Homo sap	http://dati	Homo sap	http://dati	http://rdf.	http://ww	Aldosteroi	InChI=1S/(	PQSUYGKT	360.444	O=C(CO)[C@@H]4[C(		3.38E-04	ACE Inh
6	Mineraloc	http://data.kasabi.cc		EC50	=	2	nM	http://dati	Agonist ac	Homo sap	http://dati	Homo sap	http://dati	http://rdf.	http://ww	Prednisol	InChI=1S/(	OIGNJSKKI	360.444	O=C\1\C=C/[C@]4(/C		2.00E-03	ACE Inh
7	B2 bradyk	http://dati	1E+07	EC50	=	290	nM	http://dati	Inhibition	Cavia por	http://dati	Homo sap	http://dati	http://rdf.	http://ww	N-(4-chlor	InChI=1S/(	KTAARZWL	465.932	O=C(NCC)NCC(=O)N(c		0.29	ACE Inh
8	B2 bradyk	http://dati	1E+07	EC50	=	400	nM	http://dati	Inhibition	Cavia por	http://dati	Homo sap	http://dati	http://rdf.	http://ww	4-[({2-[(4-	InChI=1S/(	YAOHXRHI	523.968	Cc1ccc2cc	2	0.4	ACE Inh
9	B2 bradyk	http://dati	1E+07	EC50	=	56	nM	http://dati	Inhibition	Cavia por	http://dati	Homo sap	http://dati	http://rdf.	http://ww	(2E)-N-{2-[	InChI=1S/(	HRMANUL	592.995	FC(F)(F)c1	2	5.60E-02	ACE Inh
10	B2 bradyk	http://dati	1E+07	EC50	=	450	nM	http://dati	Inhibition	Cavia por	http://dati	Homo sap	http://dati	http://rdf.	http://ww	N-(2-cyan	InChI=1S/(	GSMWKYC	461.513	CCNC(=O)NCC(=O)N(C		0.45	ACE Inh
11	B2 bradyk	http://dati	1E+07	EC50	=	220	nM	http://dati	Inhibition	Cavia por	http://dati	Homo sap	http://dati	http://rdf.	http://ww	(2E)-N-{2-[	InChI=1S/(	QHVBUVLI	621.646	CCCOc1c((	1	0.22	ACE Inh
12	B2 bradyk	http://dati	1E+07	EC50	=	480	nM	http://dati	Inhibition	Cavia por	http://dati	Homo sap	http://dati	http://rdf.	http://ww	methyl 6-[	InChI=1S/(	DWSHMW	553.67	Cc1ccc2cc	1	0.48	ACE Inh
13	B2 bradyk	http://dati	1E+07	EC50	=	59	nM	http://dati	Inhibition	Cavia por	http://dati	Homo sap	http://dati	http://rdf.	http://ww	2-propena	InChI=1S/(	LQLXUORF	599.7	Cc1ccc2cc	2	5.90E-02	ACE Inh
14	B2 bradyk	http://dati	1E+07	EC50	=	54	nM	http://dati	Inhibition	Cavia por	http://dati	Homo sap	http://dati	http://rdf.	http://ww	2-propena	InChI=1S/(	AEFMWUU	570.487	COc1cccc(	2	5.40E-02	ACE Inh
15	B2 bradyk	http://dati	1E+07	EC50	=	350	nM	http://dati	Inhibition	Cavia por	http://dati	Homo sap	http://dati	http://rdf.	http://ww	N~2~-[(4-a	InChI=1S/(	ISROIASQI	509	O=C(NCCC	1	0.35	ACE Inh
16	B2 bradyk	http://dati	1E+07	EC50	=	660	nM	http://dati	Inhibition	Cavia por	http://dati	Homo sap	http://dati	http://rdf.	http://ww	(2E)-3-(4-r	InChI=1S/(	YMXBZVM	587.752	Cc1ccc2cc	1	0.66	ACE Inh
17	B2 bradyk	http://dati	1E+07	EC50	=	23	nM	http://dati	Inhibition	Cavia por	http://dati	Homo sap	http://dati	http://rdf.	http://ww	2-propena	InChI=1S/(	VUYAWMA	554.487	Cc1ccc(cc	2	2.30E-02	ACE Inh
18	B2 bradyk	http://dati	1E+07	EC50	=	260	nM	http://dati	Inhibition	Cavia por	http://dati	Homo sap	http://dati	http://rdf.	http://ww	2,4-penta	InChI=1S/(	RGYRXPGC	490.402	Cc1nc2c(cccc2s1)OC		0.26	ACE Inh
19	B2 bradyk	http://dati	1E+07	EC50	=	55	nM	http://dati	Inhibition	Cavia por	http://dati	Homo sap	http://dati	http://rdf.	http://ww	(2E)-N-{2-[	InChI=1S/(	TTZDPFYXI	598.012	FC(F)(F)c1	2	5.50E-02	ACE Inh
20	B2 bradyk	http://dati	1E+07	EC50	=	4.1	nM	http://dati	Inhibition	Cavia por	http://dati	Homo sap	http://dati	http://rdf.	http://ww	(2E)-N-{2-[	InChI=1S/(	LRFPQMIX	555.023	O=C(\C=C\	1	4.10E-03	ACE Inh
21	B2 bradyk	http://dati	1E+07	EC50	=	130	nM	http://dati	Inhibition	Cavia por	http://dati	Homo sap	http://dati	http://rdf.	http://ww	(2E)-N-{2-[	InChI=1S/(	MBVMOW	598.012	Cc1ccc2cc	1	0.13	ACE Inh
22	B2 bradyk	http://dati	1E+07	EC50	=	100	nM	http://dati	Inhibition	Cavia por	http://dati	Homo sap	http://dati	http://rdf.	http://ww	2-propena	InChI=1S/(	ACAUQEGI	608.459	FC(F)(F)c1	2	0.1	ACE Inh
23	B2 bradyk	http://dati	1.9E+07	-Log EC50	=	10.47		http://dati	Antagonis	Homo sap	http://dati	Homo sap	http://dati	http://rdf.	http://ww	L-Seryl-L-p	InChI=1S/(	WFRTYDJN	2243.59	C[C@H]([C	3	3.39E-05	ACE Inh
24	B2 bradyk	http://dati	1.9E+07	-Log EC50	=	10.31		http://dati	Antagonis	Homo sap	http://dati	Homo sap	http://dati	http://rdf.	http://ww	Bradykini	InChI=1S/(	QXZGBUJJ	1060.21	O=C(N[C@	3	4.90E-05	ACE Inh

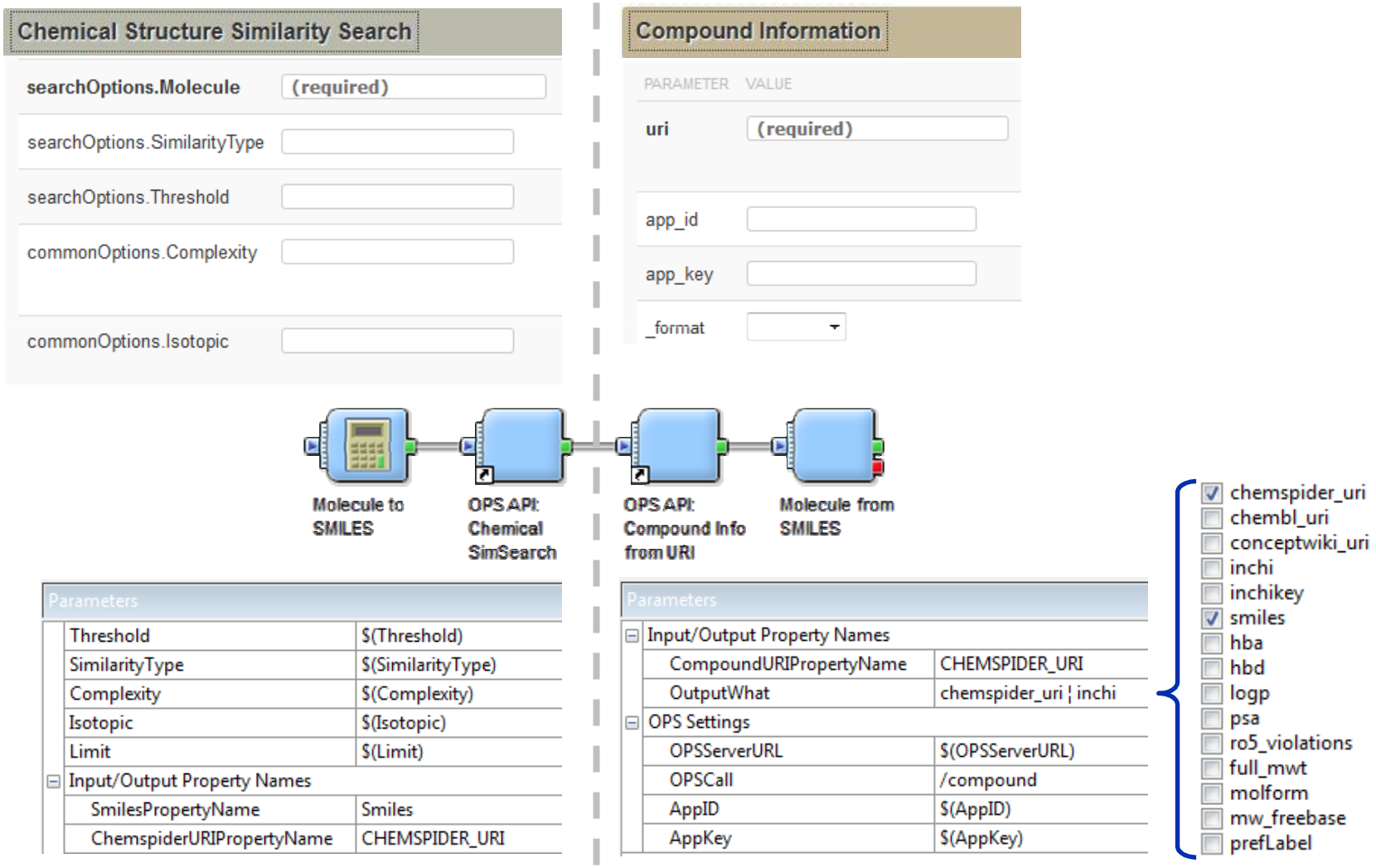
By Chris Chau (GSK)

From Tailored Prototyping to a Toolbox

Modularisation of partial solutions along Open PHACTS API calls



Mapping API Calls to Components



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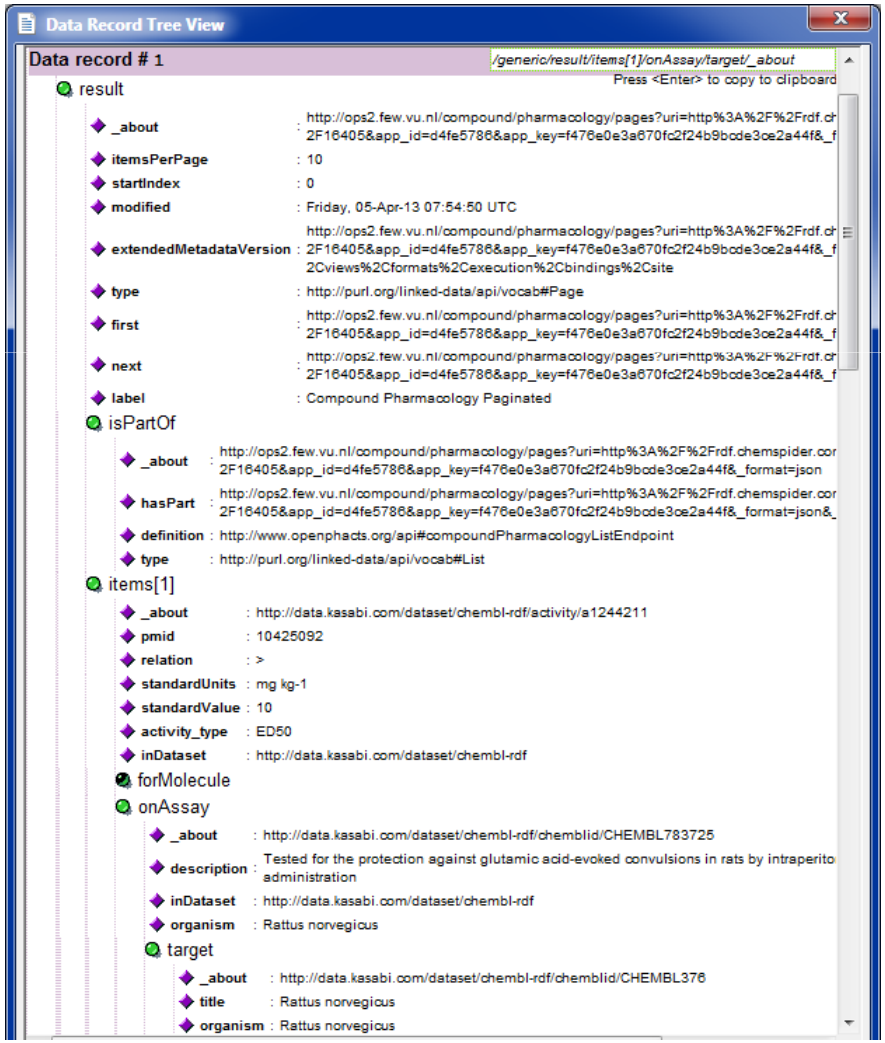
Open PHACTS Hierarchical Data Structure

A Challenge for Pipeline Pilot Data Tree Functionality

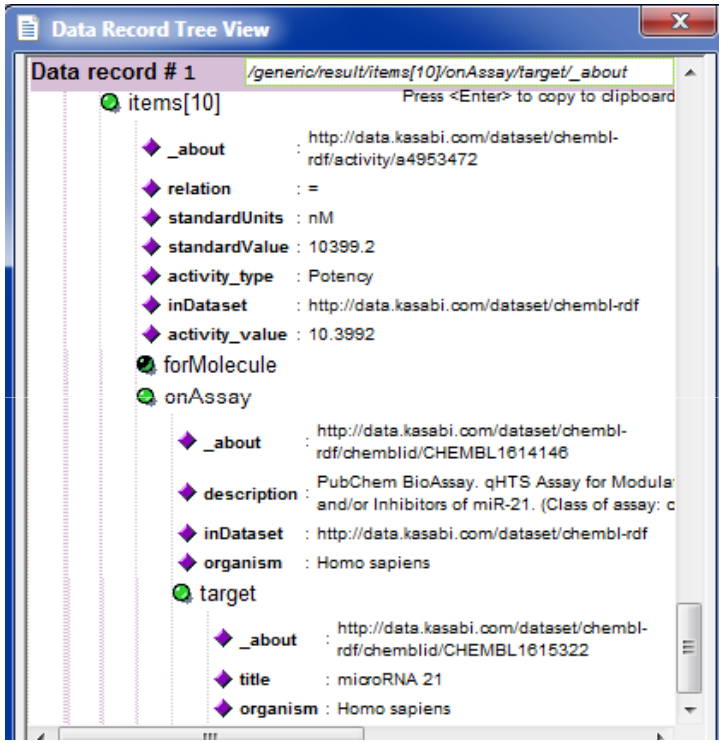


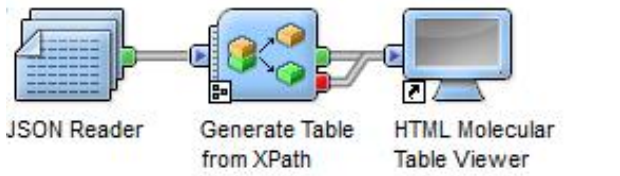
- Data Tree Manipulators
  - Copy Hierarchical Properties
  - Copy Nodes
  - Delete Hierarchical Properties
  - Delete Nodes
  - Detach Nodes
  - Flatten Hierarchy
  - Insert Nodes
  - Leaf Nodes to Properties
  - Move Hierarchical Properties
  - Move Nodes
  - Pad Properties
  - Properties to Leaf Nodes
  - Query Nodes
  - Reattach Nodes
  - Unflatten Hierarchy

Hierarchical Functions Index

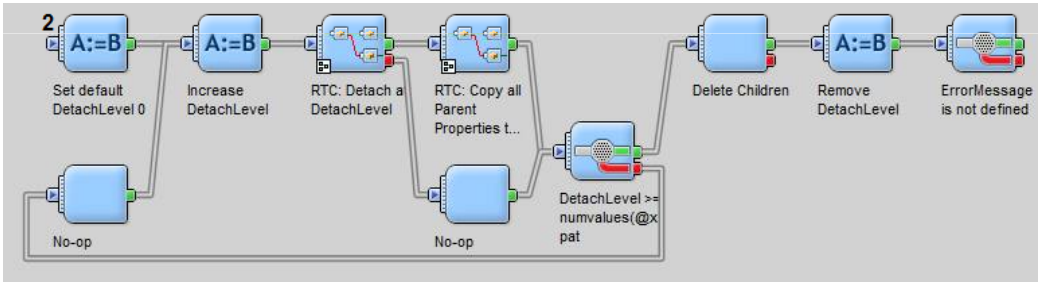
- AddChild
- DataRoot
- DataSetRoot
- GlobalRoot
- IsValidLocation
- NodeAppendChild
- NodeDeleteAllChildren
- NodeDeleteChild
- NodeGetFirstChild
- NodeHasChild
- NodeIsNull
- NodeIthChild
- NodeIthProperty
- NodeIthPropertyName
- NodeMetaDataProperty
- NodeNumChildren
- NodeNumProperties
- NodeParent
- NodePathLocation
- NodeProperty
- NodeQuery
- NodeRemoveMetaData
- NodeSerialize
- NodeSetType
- NodeType
- NodesEqual
- NumChildren

Unfolding the Open PHACTS Data Hierarchy





Parameters	
RootXPath	/generic/result
ExtractionXPath	/items/onAssay/target



_about	title	organism	description	inDataset	relation	standardUnits	standardValue	activity_type	activity_value
http://data.kasabi.com/dataset/chembl-rdf/chemblid/CHEMBL1615322 http://data.kasabi.com/dataset/chembl-rdf/chemblid/CHEMBL1614146 http://data.kasabi.com/dataset/chembl-rdf/activity/a4953472	microRNA 21	Homo sapiens Homo sapiens	PubChem BioAssay. qHTS Assay for Modulators of miRNAs and/or Inhibitors of miR-21. (Class of assay: confirmatory)	http://data.kasabi.com/dataset/chembl-rdf http://data.kasabi.com/dataset/chembl-rdf	=	nM	10399	Potency	10.399

Thank you!

Slides:

- Lee Harland (Connected Discovery Ltd.)
- Jack Gibb (Royal Society of Chemistry)
- Chris Chau (GlaxoSmithKline)
- … and many other authors from EFPIA and Open PHACTS

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