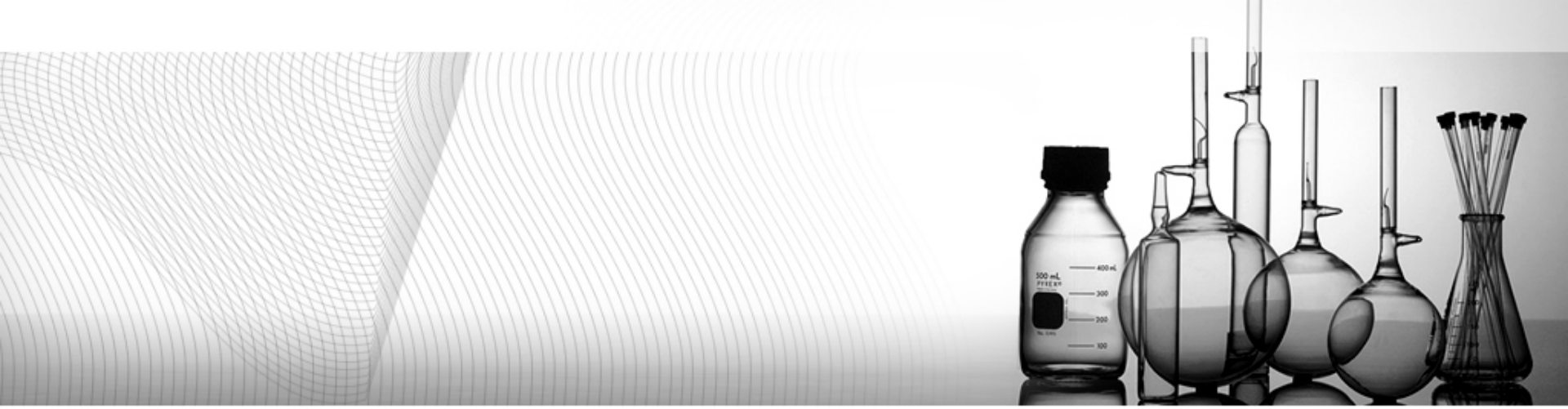


Open PHACTS
Open Pharmacological Space

Accessing OpenPHACTS:

Interactive exploration of compounds and targets from the semantic web

Katrin Stierand

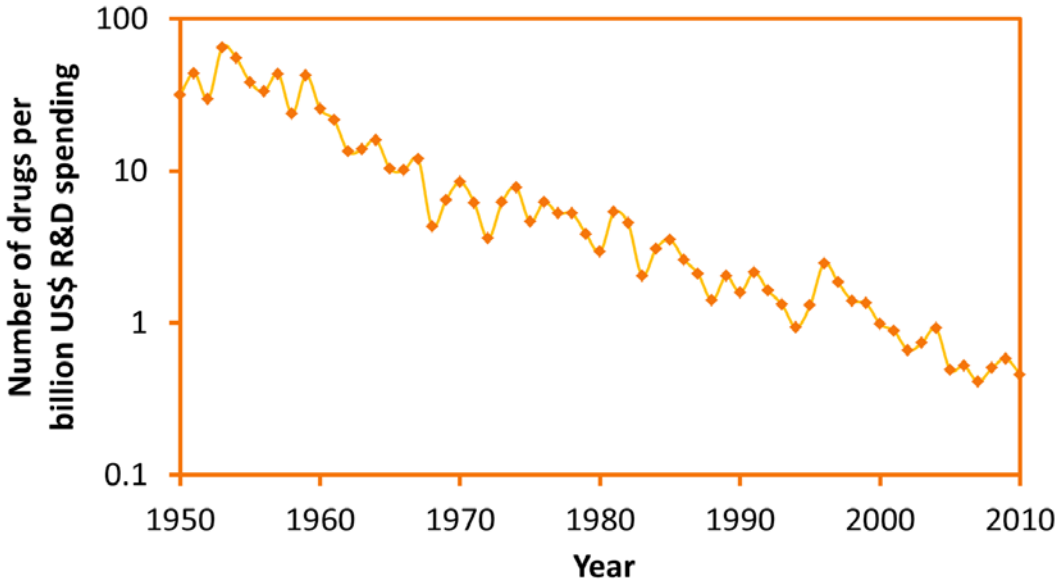
ZBH Center for Bioinformatics Hamburg

Outline

- OpenPHACTS
  - What is OpenPHACTS and why do we need it?
  - Use case driven development
  - Technical structure, eApps
- ChemBioNavigator
  - GUI and technical structure
  - Workflows

Why do we need Open PHACTS?

- Pharmaceutical companies currently expend significant effort integrating the vast amount of data publicly available into internal architectures.



Overall trend in R&D efficiency, inflation-adjusted (J. W. Scannel, A. Blanckley, H. Boldon and B. Warrington, *Nat. Rev. Drug Discov.*, 2012, **11**, 191-200, (doi:10.1038/nrd3681))

Currently, pharmaceutical companies assemble their own in-house databases of pharmacological and physicochemical data.

Drug discovery process is hindered by repetition of:

- Data extraction
- Transformation
- Loading stage

What is OpenPHACTS?

- OpenPHACTS Discovery Platform
  - an online platform with a set of integrated publicly available pharmacological data
- Open Pharmacological Space
- Intended to facilitate improvements in drug discovery in academia and industry
- Use and enhance semantic web standards

Open PHACTS
Open Pharmacological Space

Open PHACTS Project Partners

www.openphacts.org

Project Contacts: Pfizer – Coordinator (Bryn Williams-Jones), Universität Wien – Managing entity (Gerhard Ecker)

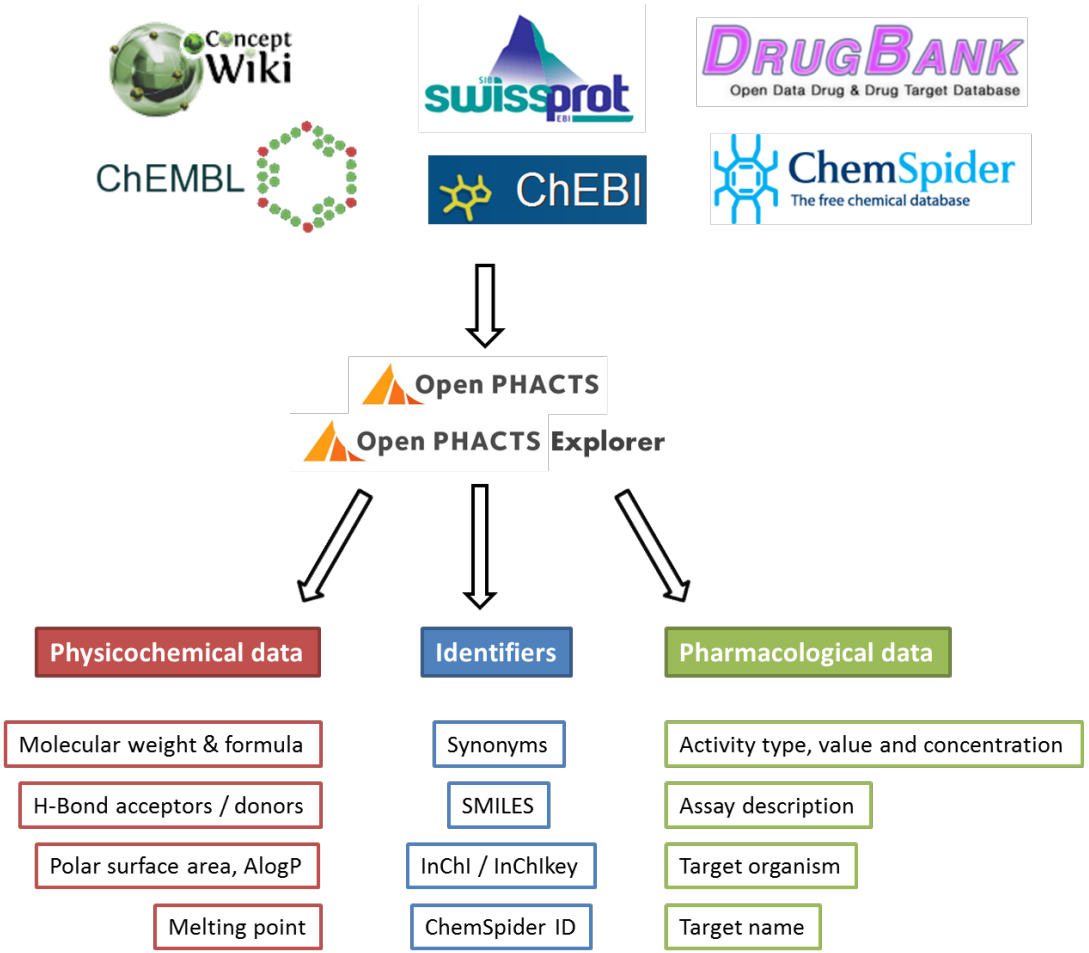
Pharmacology within Open PHACTS

The number of pharmacological questions that could be useful to answer is large, and Open PHACTS concentrates on answering the **top 20 ranked research questions** from a list of 83 proposed by consortium members.

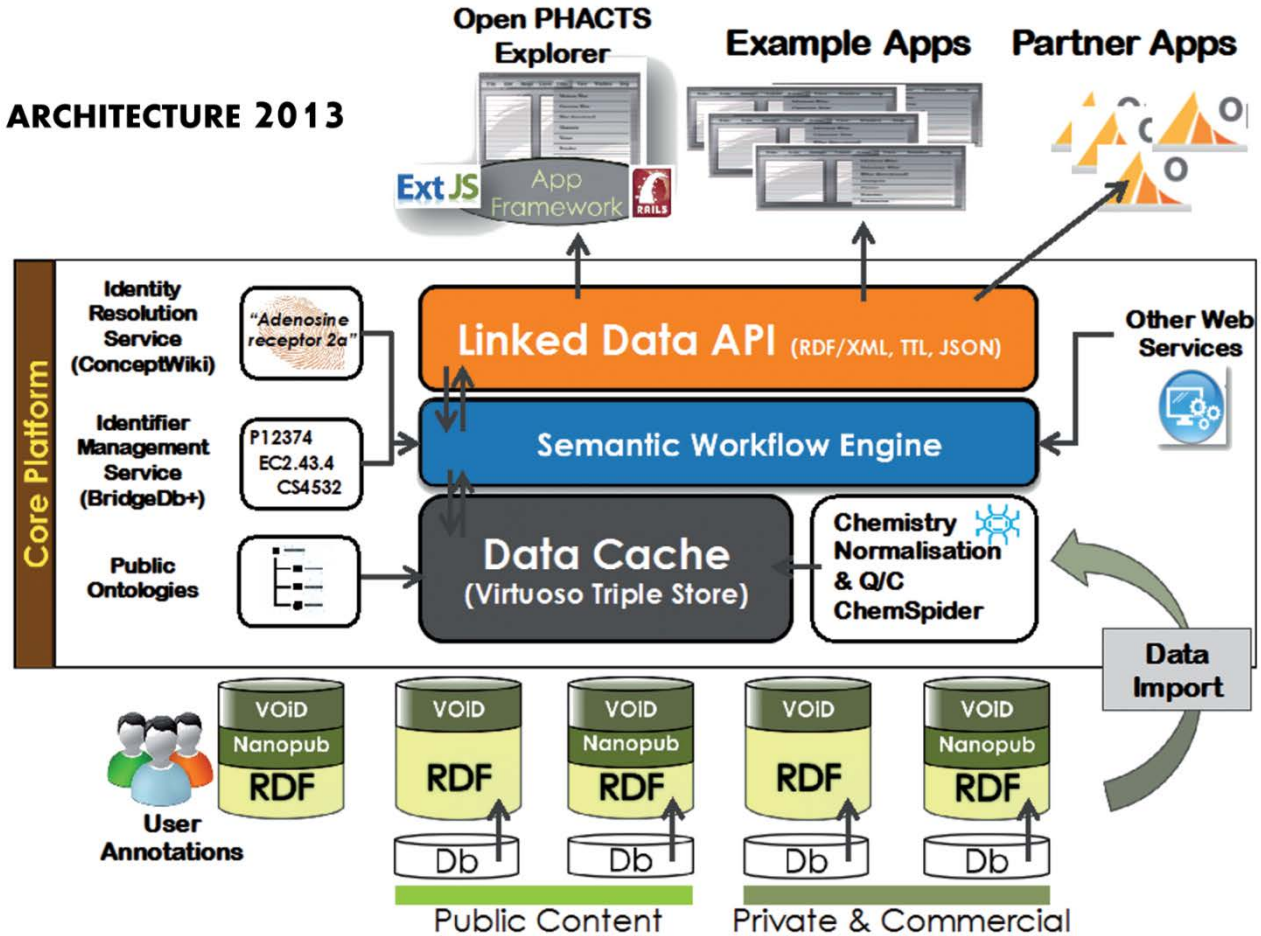
#1. All oxidoreductase inhibitors active at <100 nM in both human and mouse.

#1. For my given compound, which targets have been patented in the context of Alzheimer's disease?

Open PHACTS
Open Pharmacological Space



How does Open PHACTS work?



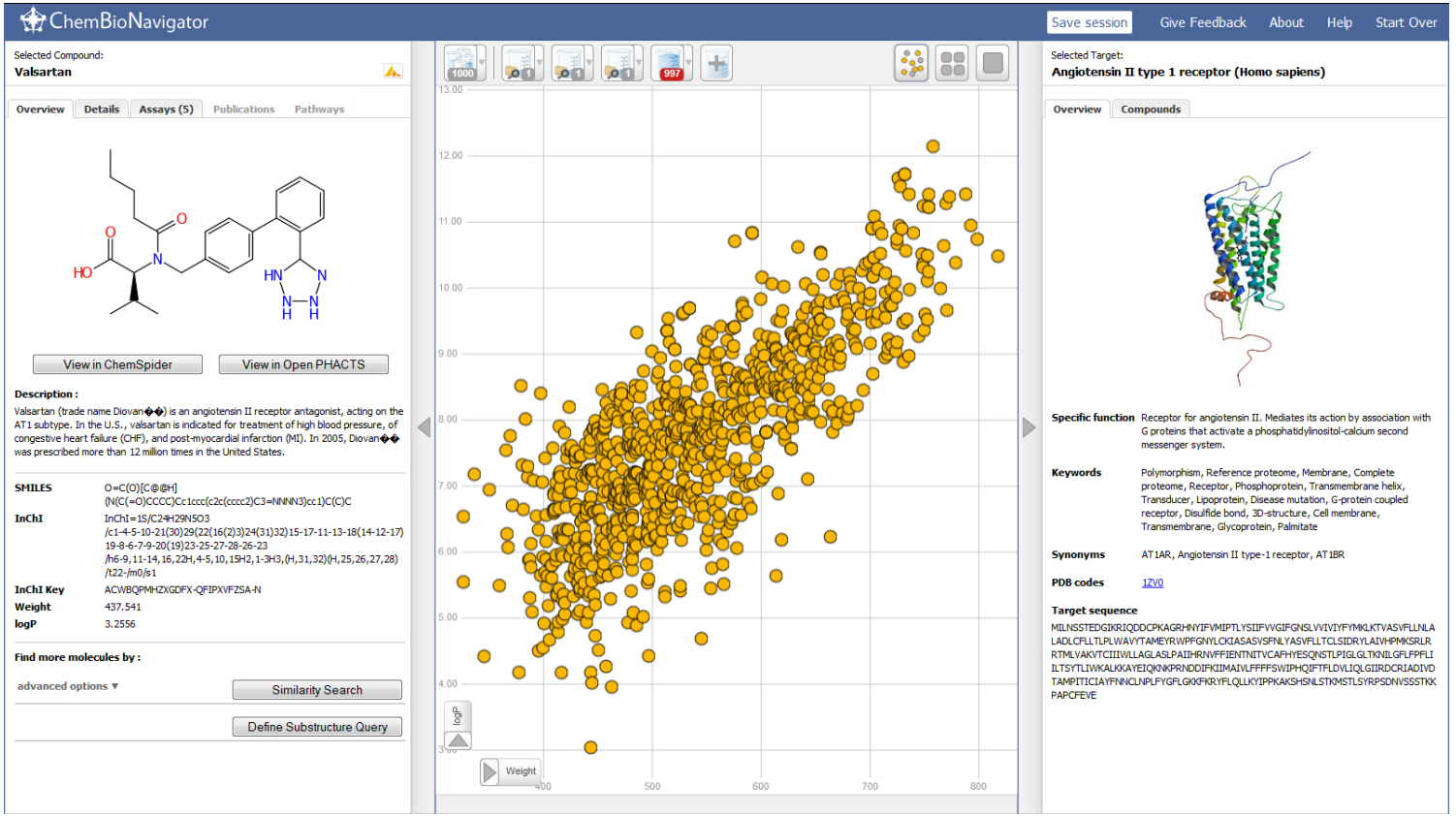
The ChemBioNavigator (CBN)

www.chembionavigator.org

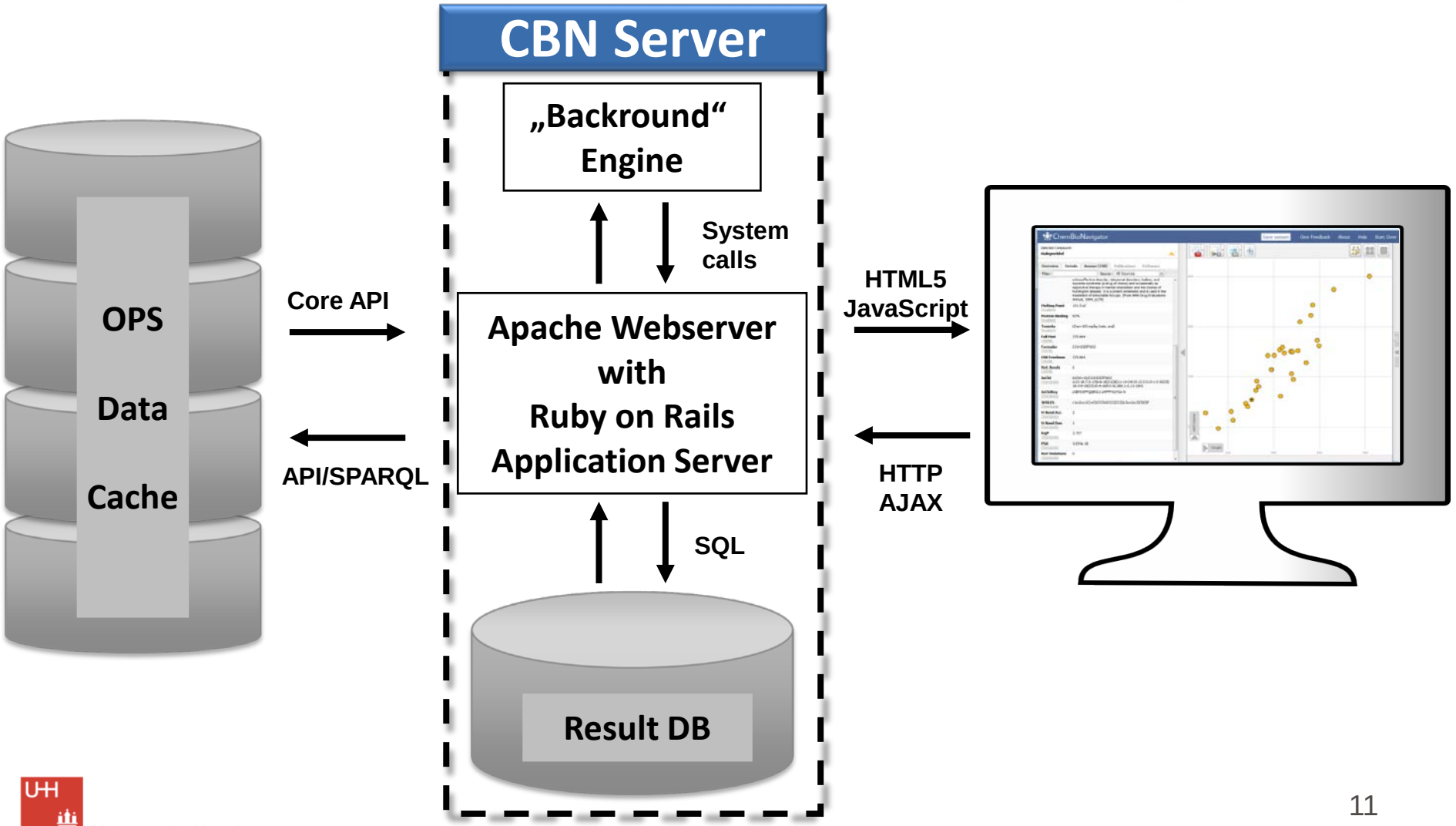
Google style: Interactive – Simplicity rules

Stierand K., Harder T., Marek T., et al. Molecular Informatics, Volume 31, Issue 8, p. 543–546, August 2012

ChemBioNavigator GUI



Compound panel | Drawing area | Target panel


CBN Server
„Backround“ Engine
System calls
Apache Webserver with Ruby on Rails Application Server
SQL
Result DB
OPS
Data
Cache
Core API
API/SPARQL
HTML5 JavaScript
HTTP AJAX

Features

- Provenance: all data is interlinked with the original source
- Drill-down: interactive sorting based on public and private properties
- Housekeeping: put compounds in „buckets“ to retain an overview
- Searching: based on similarity, substructure or related target
- Persistence: store a session and resume work later

Development strategies

- Several interviews with people from pharmaceutical industry
- Knowledge of valuable features and deficiencies
- Extract trends from all interviews

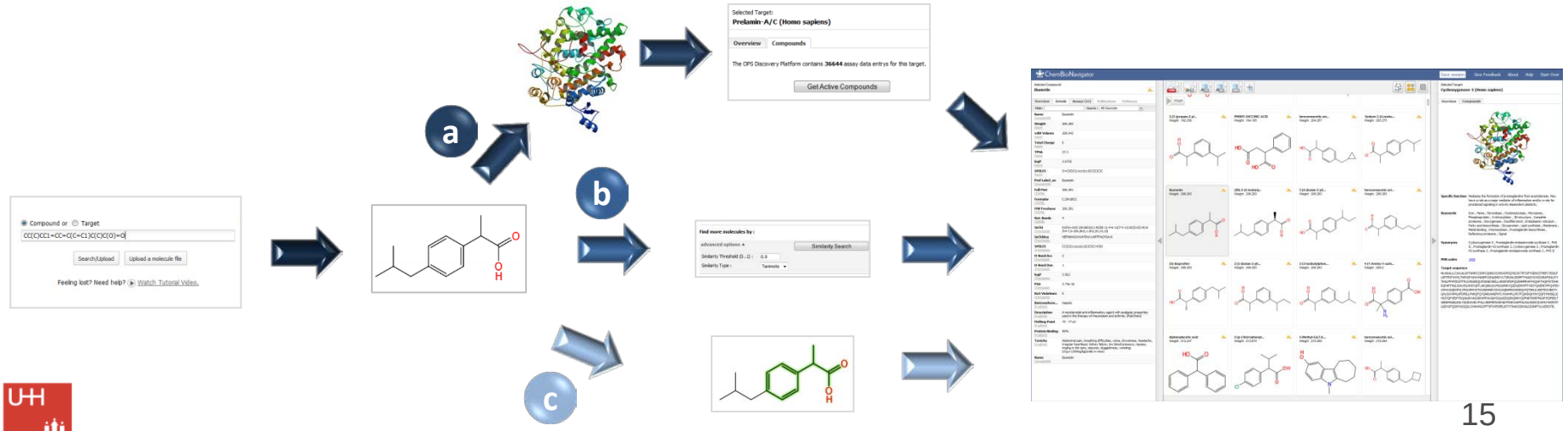
=> agile and target-oriented development

Workflows

- Compound centric <-> target centric
- Extension and drill-down of data
- Three main workflows (following slides)
  - two compound centric
  - one target centric
- Workflows can be combined

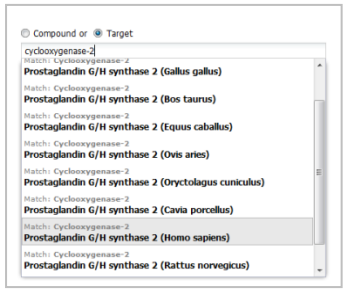
Workflow I

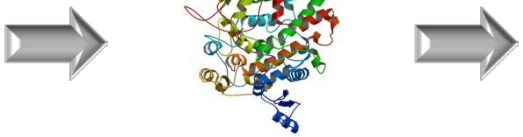
- Start with a single compound name or a SMILES and extend the molecule set by related compounds:
  a) Find target via assay data and load all compounds from OPS, which are active against this target
  b) Start a similarity search
  c) Define a substructure and start a substructure search

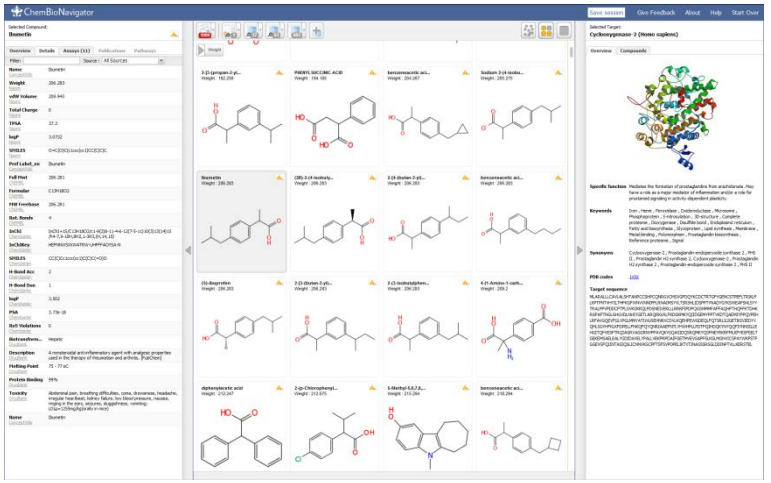


Workflow II

- Start with target name
- The CBN loads the target information from OPS.
- On mouse click, all active compounds are loaded in the CBN.



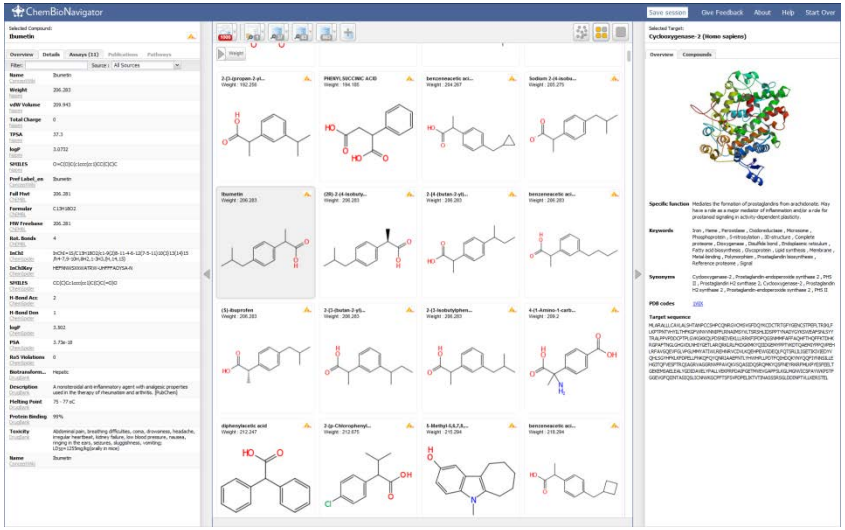




Workflow III

- Start with a set of SMILES or a SD file:
- The given compounds are initialized by NAOMI and annotated with data from the OPS.

O=C(O)C(c1ccc(cc1)CC(C)C)C
O=C(O)C(c1ccc(cc1)CC2CCC2)C
O=C(O)[C@@H](c1ccc(cc1)CC(C)C)C
O=C(O)C(c1ccc(cc1)CC2CC2)C
O=C(O)[C@@H](c1ccccc1)C
O=C(O)C(c1cc(ccc1)CC(c2ccccc2)C)C
O=C(O)C(c1ccc(cc1)CC2CCCCC2)C
O=C(O)C(c1ccccc1)C(c2ccccc2)c3ccccc3
O=C(O)C(c1cc(ccc1)CC)C
O=C(O)C(c1cc(ccc1)CCCC)C
O=C(O)C(c1ccc(cc1)C(CC)C)C
[O-]C(=O)C(c1ccccc1)CC([O-])=O
O=C(O)C(c1cc(ccc1)C(CC)CC)C
O=C(O)C(c1ccc(cc1)CC2CCCC2)C
O=C(O)C(c1ccc(cc1)C(C)C)C



Conclusion

- OpenPHACTS integrates data from different data sources and provides it via an API
- Design and choice of sources use-case driven
- CBN exemplarily uses the OPS
- Enables navigation through the chem-bio space
- Development of workflows based on interviews with scientists of pharmaceutical industry

Acknowledgement

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- **Lothar Wissler** – BioSolveIT GmbH
- Christian Lemmen – BioSolveIT GmbH
- Matthias Rarey – ZBH Center for Bioinformatics

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Thank you for your attention!