Open PHACTS

Deliverable 6.22

Report on results of case studies and scientific publications achieved with the Open PHACTS Discovery Platform

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Approved by UNIVIE, GSK, Janssen, PSMAR, AstraZeneca

February 2015
Version 1.0

Project title: An open, integrated and sustainable chemistry, biology and pharmacology knowledge resource for drug discovery
Instrument: IMI JU
Contract no: 115191

Start date: 01 March 2011
Duration: 60 months

Nature of the Deliverable	
Report	**x**
Prototype	
Other	
Dissemination level	
Public dissemination level	**x**
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5 - BIT – BioSolveIT GmbH
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602 - UPF – Universitat Pompeu Fabra
7 - LUMC – Leiden University Medical Centre
8 - RSC – Royal Society of Chemistry
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16 - AZ – AstraZeneca AB
17 - Pfizer – Pfizer Limited
18 - Esteve – Laboratorios del Dr. Esteve, S.A.
19 - Novartis – Novartis Pharma AG
20 - ME – Merck
21 - HLU – H. Lundbeck A/S
22 - Lilly – Eli Lilly and Company Limited
23 - NBIC – Stichting Netherlands Bioinformatics Centre
24 - SIB – Swiss Institute of Bioinformatics
25 - CD – ConnectedDiscovery
26 - EMBL-EBI – European Molecular Biology Laboratory
27 - Janssen – Janssen Pharmaceutica NV
28 - OGL – OpenLink Group Ltd
29 - OPF – The Open PHACTS Foundation
30 - ALM – Laboratorios Almirall S.A.
31 - SciBite – SciBite Limited

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1 Introduction

This deliverable follows up on D 6.18 (Interim report on results of case studies), providing an update on publications on use-cases solved with the Open PHACTS Discovery Platform by members of the consortium. This provides an overview on published work created with the help of the platform, but does not claim to be an exhaustive list. A full list of publications from within the consortium is available from http://www.openphacts.org/news-and-events/publications.

2 The scientific competency questions

D 6.1 introduced 20 research questions published by Azzaoui et al. [1], which were driving the development of the Open PHACTS Discovery Platform. Recently, KNIME workflows which are able to answer 16 of these 20 questions by using Open PHACTS API calls were published. [2] All workflows were made available on myexperiment.org (see http://www.myexperiment.org/workflows?filter=TAG_ID%28%224416%22%29), to allow users outside of the consortium access to an easy possibility to answer those questions. The still missing questions depend on datasets which are not yet included, but planned for the near future, such as patent and adverse events data.

3 Results of Ongoing Case Studies mentioned in D 6.18

TRPV1

A study on the usability of open data for the creation of classification models was performed with inhibitors of TRPV1. [3] Since the interim report, another study using this dataset was published, showing results of a pharmacophore screening using the data retrieved from open datasources, leading to the identification of compounds with a different type of scaffold (Figure 1). [4]

A perspective on the use of open data, including Open PHACTS, was given in [5]. This paper discusses the usability of open data for pharmacoinformatics, and states requirements needed for data quality.

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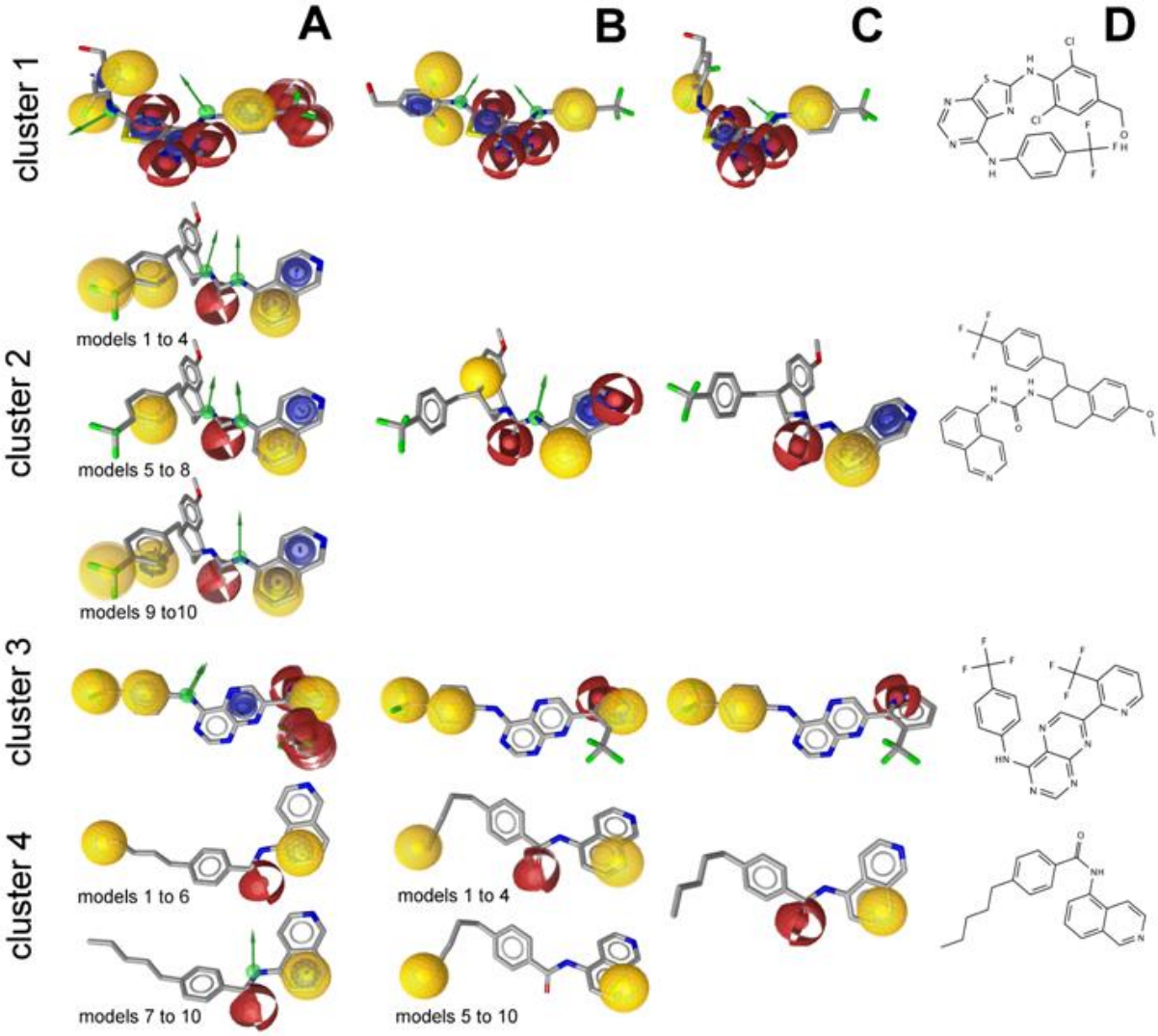

Figure 1: Pharmacophore models for TRPV1 antagonists derived from public sources

STF Use-Cases

The results from the use-cases selected by the scientific task force (STF) at the first Researchathon in London were published in the open access journal Plos ONE [6]. These use cases cover 1) the comprehensive identification of chemical matter for a dopamine receptor drug discovery program 2) the identification of compounds active against all targets in the Epidermal growth factor receptor (ErbB) signaling pathway that have a relevance to disease and 3) the evaluation of established targets in the Vitamin D metabolism pathway to aid novel Vitamin D analogue design.

Use case 1 shows the integration of Open PHACTS data with in-house data in a pharmaceutical company using Pipeline Pilot, while use cases 2 and 3 focus on academic research questions which are solved using KNIME workflows.

The following picture shows an overview of the use case 2 workflow:

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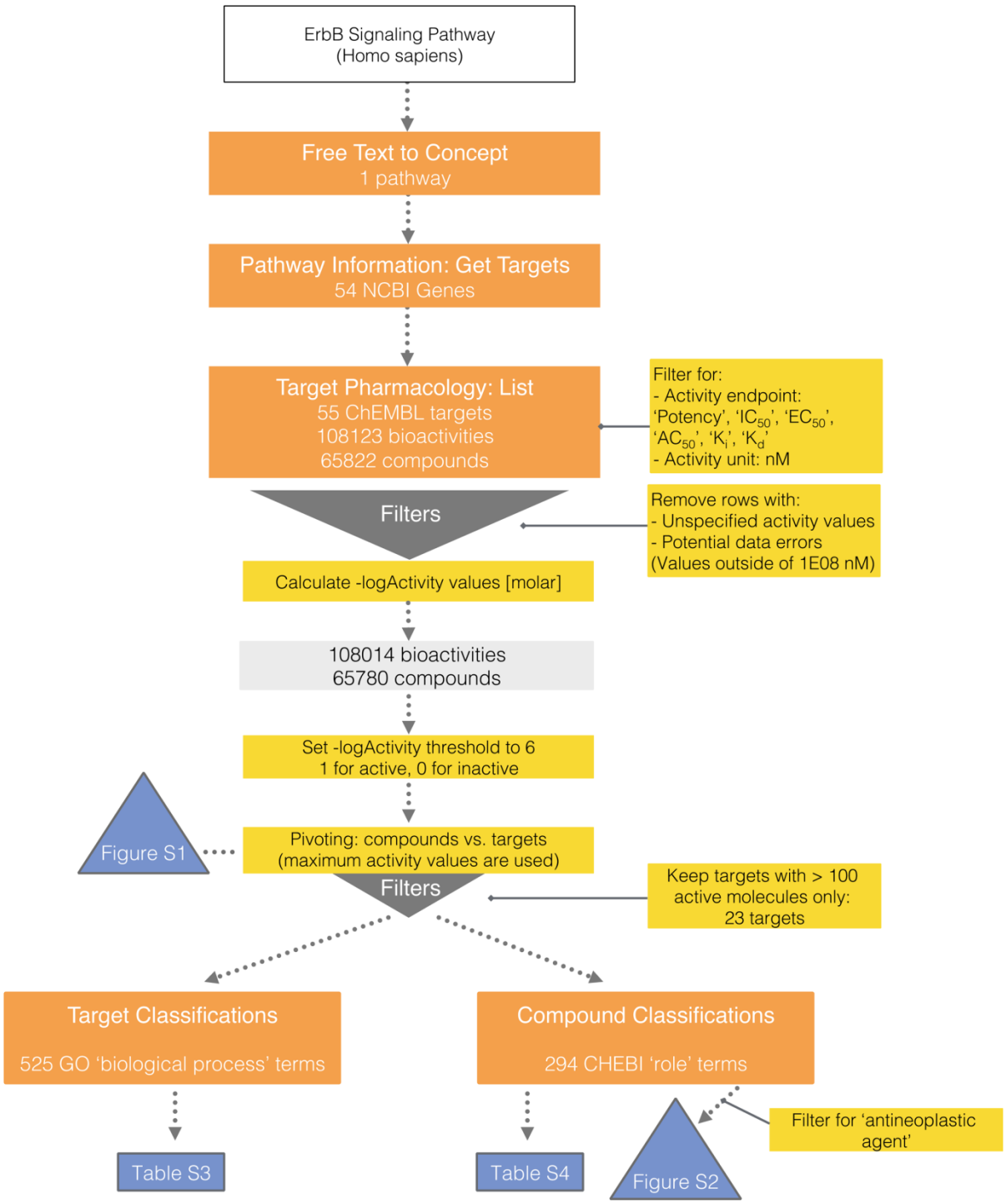

In addition, there are ongoing studies on inhibitors of ABC-transporter, such as MDR1, BSEP, BCRP, and MRP2.

Finally, it should be mentioned that these are only studies conducted by members of the consortium and where the results justified publication. There are numerous hits via the Open

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PHACTS Explorer and selected Example Applications such as the ChemBioNavigator, which are used in the daily work, but finally are not explicitly mentioned in publications.

4 References

[1] Kamal Azzaoui, Edgar Jacoby, Stefan Senger, Emiliano Cuadrado Rodríguez, Mabel Loza, Barbara Zdrazil, Marta Pinto, Antony J. Williams, Victor de la Torre, Jordi Mestres, Manuel Pastor, Olivier Taboureau, Matthias Rarey, Christine Chichester, Steve Pettifer, Niklas Blomberg, Lee Harland, Bryn Williams-Jones, Gerhard F. Ecker (2013). Scientific competency questions as the basis for semantically enriched open pharmacological space development**.** *Drug Discov Today* **18**: 843-852.
http://www.sciencedirect.com/science/article/pii/S1359644613001542

[2] Christine Chichester, Daniela Digles, Ronald Siebes, Antonis Loizou, Paul Groth, Lee Harland, Drug discovery FAQs: workflows for answering multidomain drug discovery questions, *Drug Discov Today*, Available online 20 November 2014. http://dx.doi.org/10.1016/j.drudis.2014.11.006.

[3] Tsareva D, Ecker GF (2013). How far could we go with Open Data - A case study for TRPV1 antagonists. *Mol Inf* **32**: 555–562. DOI: 10.1002/minf.201300019

[4] Daria Goldmann, Peter Pakfeifer, Steffen Hering, Gerhard F. Ecker. Novell Scaffolds for Modulation of TRPV1 Identified with Pharmacophore Modeling and Virtual Screening, *Future Med Chem*, in print

[5] Daria Goldmann, Floriane Montanari, Lars Richter, Barbara Zdrazil, and Gerhard F Ecker (2014). Exploiting open data: a new era in pharmacoinformatics. *Future Med Chem* **6**: 503-514. DOI: 10.4155/FMC.14.13

[6] Ratnam J, Zdrazil B, Digles D, Cuadrado-Rodriguez E, Neefs J-M, et al. (2014) The Application of the Open Pharmacological Concepts Triple Store (Open PHACTS) to Support Drug Discovery Research. *PLoS ONE* **9**(12): e115460. doi:10.1371/journal.pone.0115460

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