

ORAL PRESENTATION

Open Access

Combining pharmacophore- and MD-based modelling for phase II metabolism prediction

Christin Rakers*, Gerhard Wolber

From 9th German Conference on Chemoinformatics
Fulda, Germany. 10-12 November 2013

As metabolism is considered a main cause for adverse drug reactions and failures of new drug candidates, our goal is to establish an *in silico* method to efficiently predict phase II metabolism – in particular sulfotransferase (SULT) activity. Since sulfotransferases exhibit low substrate specificities caused by their high degree of conformational freedom [1], activity prediction is a challenging task.

We therefore established a workflow based on molecular dynamics (MD) simulations to cover the whole spectrum of structural flexibility and incorporated it into multiple pharmacophores that represent specific modes of action. Using an ensemble of pharmacophores for virtual screening ensures accurate categorization of potential SULT ligands (e.g. substrates, inhibitors). Recent advances in MD technology [2] allowed for refinement of these pharmacophores by high-throughput MD simulations of ligand-target complexes. In addition, the initial binding process of a soluble ligand to the substrate-binding site of SULT was captured in unbiased 100 ns simulations using the software Desmond [3].

Published: 11 March 2014

References

1. Dong D, Ako R, Wu B: Crystal structures of human sulfotransferases: insights into the mechanisms of action and substrate selectivity. *Expert Opin Drug Metab Toxicol* 2012, **8**:635-646.
2. Dror RO, et al: Biomolecular simulation: a computational microscope for molecular biology. *Annu Rev Biophys* 2012, **41**:429-452.
3. Bowers KJ, et al: Scalable Algorithms for Molecular Dynamics Simulations on Commodity Clusters. *SC 2006 Conference, Proceedings of the ACM/IEEE* 2006.

* Correspondence: christin.rakers@fu-berlin.de
Computer-Aided Drug Design, Pharmaceutical and Medicinal Chemistry,
Institute of Pharmacy, Freie Universität Berlin, 14195 Berlin, Germany

doi:10.1186/1758-2946-6-S1-O15

Cite this article as: Rakers and Wolber: Combining pharmacophore- and MD-based modelling for phase II metabolism prediction. *Journal of Cheminformatics* 2014 **6**(Suppl 1):O15.



© 2014 Rakers and Wolber; licensee Chemistry Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/2.0/>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. The Creative Commons Public Domain Dedication waiver (<http://creativecommons.org/publicdomain/zero/1.0/>) applies to the data made available in this article, unless otherwise stated.

Publish with **ChemistryCentral** and every scientist can read your work free of charge

“Open access provides opportunities to our colleagues in other parts of the globe, by allowing anyone to view the content free of charge.”

W. Jeffery Hurst, The Hershey Company.

- available free of charge to the entire scientific community
- peer reviewed and published immediately upon acceptance
- cited in PubMed and archived on PubMed Central
- yours — you keep the copyright

Submit your manuscript here:
<http://www.chemistrycentral.com/manuscript/>

