WEB-SERVICES FOR PREDICTION OF BIOLOGICAL ACTIVITY VIA INTERNET

[1,2]Vladimir Poroikov, [1]Olga Tarasova, [1]Dmitry Druzhilovsky, [1]Anastassia Rudik, [1]Tatyana Gloriozova, [2]Alexandra Varenitsa, [2]Vera Lisitsyna, [2]Marina Shatskaya, [1]Dmitry Filimonov

[1]Orekhovich Institute of Biomedical Chemistry of Russian Academy of Medical Sciences, Pogodinskaya Str., 10, Moscow, 119121, Russia; [2]The N.I. Pirogov Russian National Research Medical University, Ostrovitianov Str., 1, Moscow, 117997, Russia

Based on the freely available information about biologically active compounds (PubChem, ChEBI, ChemSpider, DrugBank, etc.) new computational tools for biological activity estimation have been developed. The applied methods vary widely from the relatively simple pairwise chemical similarity assessment to more sophisticated ligand-based or target-based approaches.

Our group published the first study describing an approach to provide chemists with the information about the most relevant targets/assays for their compounds [1, 2], and additional computational tools with similar functionality have been developed in other labs more recently as well.

Open access web-services for biological activity profiling (e.g., http://sea.bkslab.org/, http://cpi.bio-x.cn/drar/, http://pharmaexpert.ru/passonline, etc.) employ both target-based and ligand-based drug design approaches; they use different mathematical algorithms and chemical structure description; prediction is provided for various biological end-points. No systematic comparison of the accuracy and predictivity of these web-services has been performed yet. Therefore, we have analyzed the relative predictive power of the available services to predict the biological activity profiles using new pharmaceuticals approved by US FDA in 2011 [3] as a case study.

Accuracy of prediction for both known main & side pharmacological effects and interaction with molecular targets will be reviewed. Possibilities for increasing the accuracy and predictivity using consensus prediction with several computational methods will be explored. Applications of successful *in silico* bioactivity prediction in collaborative drug discovery projects will be discussed in detail. This will include the authors' own experience [4-6] as well as some important examples taken from literature. Finally, we will discuss the prospects and limitations of using web-services for bioactivity prediction in pharmaceutical research and development.

Acknowledgements. The work is partially supported by RFBR grants 12-07-00597 and 12-04-91445-NIH_a.

References

1. Lagunin A. et al. *Bioinformatics*, 2000, **16**: 747-748.
2. Filimonov D.A., Poroikov V.V. In: *Chemoinformatics Approaches to Virtual Screening*. Eds. A. Varnek and A. Tropsha. Cambridge : RSC Publishing, 2008, 182-216.
3. Mullard A. *Nature Reviews Drug Discovery*, 2012, 11: 91-94.
4. Eleftheriou P. et al. *Eur. J. Med. Chem.*, 2011, **47**: 111-124.
5. Geronikaki A. et al. *J. Med. Chem*., 2008, **51**: 1601-1609.
6. Kryzhanovskii S.A. et al. *Pharmaceut. Chem. J.*, 2012, **45**: 605-611.