

12th World Congress on Pharmaceutical Sciences and Innovations in Pharma Industry

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In silico assessment of cardiovascular adverse effects of drug-drug interactions

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Statement of Problem: Adverse Drug Effects (ADEs) are one of the leading causes of death in developed countries and the main reason for drug recalls from the market. The ADEs associated with action on the cardiovascular system are the most dangerous and widespread. Treatment of human diseases often requires the intake of several drugs, which can lead to drug-drug interactions (DDIs) causing an increase in the frequency and severity of adverse effects. Evaluation of ADEs, as well as the effect of DDIs on their manifestation, is a non-trivial task and requires numerous experimental and clinical studies.

Methodology & Theoretical Orientation: To solve this problem, we developed a computational approach to assess the cardiovascular effects of DDIs. This approach includes: (I) prediction of interaction of individual drugs with human proteins and influence on expression of human genes based on structure-activity relationships implemented in PASS software; (II) selection of proteins and genes that are associated with cardiovascular diseases, participate in functioning of cardiovascular system and expressed in the heart or blood vessels; (III) integration of the resulted profiles and calculation of interaction scores for each cardiovascular effect; (IV) validation of developed approach based on the data on known DDIs.

Findings: The developed approach allows predicting the following adverse effects of DDIs: myocardial infarction, ischemic stroke, ventricular tachyarrhythmia, cardiac failure and arterial hypertension. Validation of the approach on known DDIs showed its acceptable accuracy for the studied effects.

Conclusion & Significance: The developed approach allows predicting cardiovascular adverse effects of DDIs for drug pairs and provides insights into their molecular mechanisms on the levels of proteins and genes. It can find practical application in the clinic for the selection of the safest combinations of drugs.

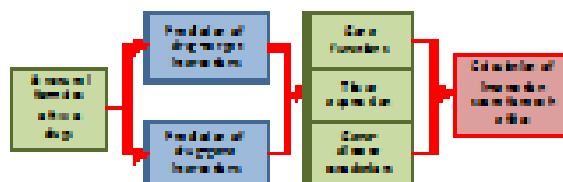


Figure 1: In silico approach for the prediction of cardiovascular adverse effects of drug-drug interactions.

Recent Publications

1. Ivanov S, Semin M, Lagunin A, Filimonov D, Poroikov V (2017) *In silico* identification of proteins associated with drug-induced liver injury based on the prediction of drug-target interactions. Mol Inform. 36(7) Doi:10.1002/minf.201600142.
2. Dmitriev A, Rudik A, Filimonov D, Lagunin A, Pogodin P et al. (2017) Integral estimation of xenobiotics toxicity with regard to their metabolism in human organism. Pure and Applied Chemistry. 89(10):1449-1458.
3. Ivanov SM, Lagunin AA, Poroikov VV (2016) *In silico* assessment of adverse drug reactions and associated mechanisms. Drug Discov. Today. 21(1):58-71.
4. Ivanov S M, Lagunin A A, Pogodin P V, Filimonov D A, Poroikov V V (2015) Identification of drug targets related to the induction of ventricular tachyarrhythmia through a systems chemical biology approach. Toxicol. Sci. 145(2):321-336.
5. Ivanov S M, Lagunin A A, Pogodin P V, Filimonov D A, Poroikov V V (2014) Identification of drug-induced myocardial infarction-related protein targets through the prediction of drug-target interactions and analysis of

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biological processes. Chem. Res. Toxicol. 27(7):1263-1281.

Biography

Sergey M Ivanov received his MS in Biochemistry, specializing in Medical Biochemistry from Russian State Medicinal University, Russia, in 2011, under the guidance of Dr. Alexey Lagunin; and his PhD in Mathematical Biology and Bioinformatics under the guidance of Dr. Alexey Lagunin at the Institute of Biomedical Chemistry, Russia, in 2014. Since 2012, he has been working as a Junior Researcher in the Department of Bioinformatics of the Institute of Biomedical Chemistry, Russia, and recently (2015) as a Lecturer in the Department of Bioinformatics of Medico-biological Faculty in Pirogov Russian National Research Medical University, Russia. His research interests include bioinformatics, chemoinformatics, systems biology, transcriptomics and *in silico* toxicology.

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