[L17] Drug Repurposing: New Uses for Old Drugs or Systems Biomedicine?

Vladimir Poroikov

Institute of Biomedical Chemistry, Pogodinskaya Str. 10, Bldg.8, 119121, Moscow, Russia
E-mail: vladimir.poroikov@ibmc.msk.ru

Biological activity is one of the most important properties of chemical compounds, which provides the possibility of their use as medicines. At the same time, due to the biological activity, chemical compounds may cause toxic effects in the human body or the environment, which significantly restrict opportunities for their practical exploitation.

The intrinsic reason for biological activity is the interaction of chemical compounds with the biological system at the molecular level. The estimated number of molecular targets for the approved drugs is about 500 while the number of the currently investigated individual targets is estimated as several thousand. Despite the difficulties in finding of inhibitors of protein-protein interactions caused by relatively weak “druggability” for this type of pharmacological targets, it is vigorously investigated nowadays. Taking into account an enormous amount of macromolecular complexes that are involved in the function of biological systems, the number of potential pharmacological targets may reach 105. The number of already synthesized commercially available unique small organic compounds, which are available for experimental testing, is more than 60 million. The number of virtual structures of organic compounds exceeded 166 billion molecules. Therefore, the dimensionality of the currently available chemical-biological space for chemical compounds available as samples and known pharmacological targets is about 1010, while for virtual compounds and potential targets it is about 1016. It is clear that experimental study of the interaction of all drug-like structures with each known pharmacological target is an enormous task, which could not be accomplished from both economical and practical point of view. As a result, all existing information about biologically active compounds is incomplete.

The challenge to investigate all possible biological activities for the compound under study was never aimed at the pharmaceutical industry, which was mostly focused on the “one disease – one target” (magic bullet) concept introduced by Paul Ehrlich more than a hundred years ago. However, in recent years, it has become apparent that all pharmacological agents interact with many molecular targets in human body causing pleiotropic effects. This realization led to the idea that some existing drugs may be used for medical indications different from those restricted by the original prescriptions. Some existing examples of new pharmacotherapeutic applications for the launched medicines discovered due to the serendipity in clinical trials or pre-clinical studies have supported this idea.

Due to the current knowledge about pharmacodynamics and pharmacokinetics of the launched drugs, their repurposing may significantly reduce the time & financial expenses and risks of the development. Thus, it looks rather attractive to perform a systematic virtual screening of new pharmacotherapeutic effects of the launched drugs additionally to the occasional findings. Both ligand-based and target-based cheminformatics approaches are currently used for this purpose. Also, to identify new applications for the launched drugs, computational analysis of the complex “drug – disease - biological processes” networks is applied.

We will consider the both chemo- and bioinformatics methods employed for finding new uses for old drug, and present the examples of novel pharmacotherapeutic effects found based on the computational prediction. The possibilities and limitations of the currently available information that may be used for knowledge-based methods will be discussed. Both “known unknowns” and “unknown unknowns” influence on these studies; bearing in mind those issues one comes to the concept of Systems Biomedicine