Combinatorial Chemistry & High Throughput Screening, 2008, *11*, 583-586

Chemogenomics: A Discipline at the Crossroad of High Throughput Technologies, Biomarker Research, Combinatorial Chemistry, Genomics, Cheminformatics, Bioinformatics and Artificial Intelligence

Eric Maréchal*

Unité mixte de recherche 5168 CNRS-CEA-INRA-Université Joseph Fourier, Institut de Recherches en Technologies et Sciences pour le Vivant, 17 avenue des Martyrs, 38058 Grenoble, France

Abstract: Chemogenomics is the study of the interaction of functional biological systems with exogenous small molecules, or in broader sense the study of the intersection of biological and chemical spaces. Chemogenomics requires expertises in biology, chemistry and computational sciences (bioinformatics, cheminformatics, large scale statistics and machine learning methods) but it is more than the simple apposition of each of these disciplines. Biological entities interacting with small molecules can be isolated proteins or more elaborate systems, from single cells to complete organisms. The biological space is therefore analyzed at various postgenomic levels (genomic, transcriptomic, proteomic or any phenotypic level). The space of small molecules is partially real, corresponding to commercial and academic collections of compounds, and partially virtual, corresponding to the chemical space possibly synthesizable. Synthetic chemistry has developed novel strategies allowing a physical exploration of this universe of possibilities. A major challenge of cheminformatics is to charter the virtual space of small molecules using realistic biological constraints (bioavailability, druggability, structural biological information). Chemogenomics is a descendent of conventional pharmaceutical approaches, since it involves the screening of chemolibraries for their effect on biological targets, and benefits from the advances in the corresponding enabling technologies and the introduction of new biological markers. Screening was originally motivated by the rigorous discovery of new drugs, neglecting and throwing away any molecule that would fail to meet the standards required for a therapeutic treatment. It is now the basis for the discovery of small molecules that might or might not be directly used as drugs, but which have an immense potential for basic research, as probes to explore an increasing number of biological phenomena. Concerns about the environmental impact of chemical industry open new fields of research for chemogenomics.

Keywords: Chemogenomics, chemical genetics, bioinformatics, cheminformatics, biomarker, machine learning.

INTRODUCTION

The simple (and expensive) view of pharmacological screening aiming to the selection of novel drug candidates by large scale serendipity has moved forward following the spectacular progresses in genomics and chemistry. Millions of gene and protein sequences are now stored in public databases and can be structurally and functionally studied with high throughput genetic engineering and recombinant expression methods, meta-genomic large scale approaches (genomics, transcriptomics, proteomics, metabolomics), biomarker-based phenotypic analyses, etc. The structures of millions of chemical compounds can be easily generated, and are now physically and / or electronically stored in real and virtual chemolibraries. Automatic instruments, handling thousands to millions of biological and chemical samples, which were originally developed for the pharmaceutical industry, are now available in academic laboratories, still at a modest scale but allowing the screening for molecules having an effect on original targets or targets neglected by industry. Virtual screening approaches, using structural docking algorithms, grow exponentially.

*Address correspondence to this author at the Unité mixte de recherche 5168 CNRS-CEA-INRA-Université Joseph Fourier, Institut de Recherches en Technologies et Sciences pour le Vivant, 17 avenue des Martyrs, 38058 Grenoble, France; E-mail: eric.marechal@cea.fr

Chemogenomics is the study of the interaction of functional biological systems with exogenous small molecules [1], or in broader sense the study of the structural and functional intersections of biological and chemical spaces. Chemogenomics can be considered as a descendent of conventional pharmaceutical approaches, since it involves the screening of chemolibraries for their effect on biological targets. It requires therefore expertises in biology, chemistry and computational sciences (bioinformatics, cheminformatics, machine learning methods) but it is more than the simple apposition of each of these disciplines. It is interesting to note that cheminformatics studies the space of small molecules in the context of their interactions with biological objects, and is therefore clearly a subspecialty of chemogenomics. Other subspecialties emerged from the combination of biological and chemical strategies, such as forward and reverse chemical genetics. Combining biological, chemical and mathematical approaches is expected to allow the emergence of a flourishing research, and the definition of new fields of knowledge [2]. In this special issue, current advances in various aspects of chemogenomics are illustrated.

1. Diversity Oriented Chemical Synthesis and Diversity Oriented Biomarker Development: Enabling Strategies and Tools for Chemogenomics

In its most naïve understanding, the story begins when a collection of small molecules has been screened for its effect

1386-2073/08 $55.00+.00