Chapter 1

Introductory Chapter: The Contribution of Bioinformatics as Blueprint Lead for Drug Design

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Additional information is available at the end of the chapter

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1. Bioinformatics and drug design

Drugs are the most utilized pharmacobiochemicals for sustaining human's health. Previously, the drug was designed unintentionally and mostly with trial and error. The well-known example is the discovery of antibiotics by Alexander Fleming which was found unintentionally [1]. However, as pharmaceutical technology is gaining momentum with the advance of molecular biology, the genome technology was applied as well to assist the development of the novel drugs. It has given a way for the development of the new kind of science, bioinformatics, which is a multidisciplinary study to integrate molecular biology and information technology [2]. There are some methods in bioinformatics that provided assistance to drug design. They are, namely, sequence alignment for determining the conservation of genome and proteome; homology modeling for determining the protein model; molecular docking method to enable high-performance screening of large amounts of lead compound [3]; molecular dynamics to set the standard to comprehend the trajectory of lead compound, as well as its interaction [4]; and ADME-TOX method to enable fine-grained detection of pharmacological and toxicological properties of lead compounds [5]. Those methods are eventually used as blueprint lead for molecular cloning or genetic engineering experiment to generate high throughput molecular profiling of the drug leads, as a means of rational drug design approach [6].

2. Rational design of drugs

The implementations of rational drug design made it possible to customize drugs at the molecular and structural level. The possibilities are enormous as the molecular design is only limited by the extent of the available computational power. The availability of commercial

cyclic peptide database has made possible to design drugs in various molecular configurations of peptide sequences [7, 8]. However, the classical approach of the isolation of natural product-based is still in use due to the availability of its respective database [9]. Moreover, due to the influence of natural product chemistry, the design of semisynthetic or synthetic-based compounds is still on demands [10]. Researchers also look for a smarter pathway to deliver drug such as utilizing E-cadherin-based drug design [11].

Although the rational drug design approach has provided groundbreaking innovations such as the development of antiretroviral/HIV drugs and smart anticancer chemotherapy agent such as nimotuzumab, it does not mean that the progression of life-threatening diseases has been halted [12, 13]. The complexity of disease's molecular mechanism has long baffled the biomedical researchers. The threat of multidrug antibiotic resistance bugs, pandemic viral infections (Ebola, avian influenza, MERS-CO, etc.), and civilization disease such as aging is pushing the researchers to develop much more advanced drug designs. In this end, the intelligence modifications of existing bioinformatics methods are devised to propose the novel way of developing drugs. The fragment-based docking method was utilized in order to construct drugs based upon the molecular fragment database [14]. Moreover, the reverse docking method was devised to optimize the lead compounds based on the proteomics library [15–17]. Finally, the development of transcriptomics approach enables researchers to develop the new breed of drugs, such as silencing(si)RNA-based lead compounds [18]. In this end, the smart design enables novel wet laboratory experimental methods such as the blood-brain barrier drug design method [19] and high throughput screening [20]. Thus, the molecular elucidation of the drug could be elucidated in a fine-grained manner using the NMR and crystallography instruments that are already commonly utilized in the field of protein crystallography [21]. Based on the advanced crystallography techniques, more proteins structure is already elucidated. This could be a great help in providing fine-grained receptor structures for rational drug design. Moreover, although crystallizing RNA molecules are tougher than protein, more RNA structures are already elucidated and deposited in the online database [22].

3. Outlook

As bioinformatics and protein crystallography are getting their momentum to contribute greatly in the study of rational drug design, it is found that the molecular mechanism of diseases is possible should be revealed based upon post genomics and proteomics approaches especially transcriptomics and epigenetics-based ones. The interplay of transcriptomics and epigenetics in the molecular mechanism of disease should be considered as primary information in the biomedical research [23]. Moreover, due to the influx of transcriptomics data, RNA structure elucidation is getting a momentum to be considered as a blueprint in drug design [24]. In this end, due to the specificity of the human genetic fingerprint, personalized medicine was developed where each patient got different medication depending on their genomics fingerprint [25–27]. The role of big data and artificial intelligence methods will be crucial in screening the influx of omics data in order to generate useful information to be revealed as the blueprint of drug design.

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