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

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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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## References

- [1] Kingston W. Antibiotics, invention and innovation. *Research Policy*. 2000;**29**:679-710. Available from: <http://www.sciencedirect.com/science/article/pii/S0048733399000451> [Accessed: Nov 12, 2013]
- [2] Hagen JB. The origins of bioinformatics. *Nature Reviews. Genetics*. 2000;**1**:231-236. DOI: 10.1038/35042090
- [3] Shoichet BK, McGovern SL, Wei B, Irwin JJ. Lead discovery using molecular docking. *Current Opinion in Chemical Biology*. 2002;**6**:439-446. DOI: 10.1016/S1367-5931(02)00339-3
- [4] Karplus M, McCammon JA. Molecular dynamics simulations of biomolecules. *Nature Structural Biology*. 2002;**35**:646-652. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/12198485>
- [5] van de Waterbeemd H, Gifford E. ADMET in silico modelling: Towards prediction paradise?, *Nature Reviews. Drug Discovery*. 2003;**2**:192-204. DOI: 10.1038/nrd1032
- [6] Lionta E, Spyrou G, Vassilatis DK, Cournia Z. Structure-based virtual screening for drug discovery: Principles, applications and recent advances. *Current Topics in Medicinal Chemistry*. 2014;**14**:1923-1938. DOI: 10.2174/1568026614666140929124445
- [7] Tambunan USF, Alkaff AH, Nasution MAF, Parikesit AA, Kerami D. Screening of commercial cyclic peptide conjugated to HIV-1 Tat peptide as inhibitor of N-terminal heptad repeat glycoprotein-2 ectodomain Ebola virus through in silico analysis. *Journal of Molecular Graphics & Modelling*. 2017;**74**:366-378. DOI: 10.1016/j.jmgm.2017.04.001
- [8] Parikesit AA, Kinanty USFT. Screening of commercial cyclic peptides as inhibitor envelope protein dengue virus (DENV) through molecular docking and molecular dynamics. *Pakistan Journal of Biological Sciences*. 2013;**16**:1836-1848. DOI: 10.3923/pjbs.2013.1836.1848
- [9] Tambunan USF, Parikesit A, Nasution MAF, Hapsari A, Kerami D. Exposing the molecular screening method of Indonesian natural products derivate as drug candidates for cervical cancer (summer 2017). *Iranian Journal of Pharmaceutical Research*. 2017;**16**:1113-1127. Available form: [http://ijpr.sbm.ac.ir/article\\_2088.html](http://ijpr.sbm.ac.ir/article_2088.html)
- [10] Tambunan USF, Parikesit AA, Ghifari AS, Satriyanto CP. In silico identification of 2-oxo-1,3-thiazolidine derivatives as novel inhibitors candidate of class II histone deacetylase

- (HDAC) in cervical cancer treatment. *Arabian Journal of Chemistry*. 2015;**1**:1-6. DOI: 10.1016/j.arabjc.2015.07.010
- [11] Prasasty VD, Tambunan USF, Siahaan TJ. Homology modeling and molecular dynamics studies of EC1 domain of VE-cadherin to elucidate docking interaction with cadherin-derived peptide. *OnLine Journal of Biological Sciences*. 2014;**14**:155. DOI: 10.3844/ojbsci.2014.155.162
- [12] Lengauer T, Sing T. Bioinformatics-assisted anti-HIV therapy. *Nature Reviews. Microbiology*. 2006;**4**:790-797. DOI: 10.1038/nrmicro1477
- [13] Spicer J. Technology evaluation: Nimotuzumab, the Center of Molecular Immunology/YM BioSciences/Oncoscience. *Current Opinion in Molecular Therapeutics*. 2005;**7**: 182-191. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/15844627> [Accessed: May 4, 2018]
- [14] Chen Y, Shoichet BK. Molecular docking and ligand specificity in fragment-based inhibitor discovery. *Nature Chemical Biology*. 2009;**5**:358-364. DOI: 10.1038/nchembio.155
- [15] Lee A, Lee K, Kim D. Using reverse docking for target identification and its applications for drug discovery. *Expert Opinion on Drug Discovery*. 2016;**11**:707-715. DOI: 10.1080/17460441.2016.1190706
- [16] Lee M, Kim D. Large-scale reverse docking profiles and their applications, *BMC Bioinformatics*. 2012;**13**(Suppl 1):S6. DOI: 10.1186/1471-2105-13-s17-s6
- [17] Kharkar PS, Warriar S, Gaud RS. Reverse docking: A powerful tool for drug repositioning and drug rescue. *Future Medicinal Chemistry*. 2014;**6**:333-342. DOI: 10.4155/fmc.13.207
- [18] Tafer H, Ameres SL, Obernosterer G, Gebeshuber CA, Schroeder R, Martinez J, Hofacker IL. The impact of target site accessibility on the design of effective siRNAs. *Nature Biotechnology*. 2008;**26**:578-583. DOI: 10.1038/nbt1404
- [19] Prasasty VD, Krause ME, Tambunan USF, Anbanandam A, Laurence JS, Siahaan TJ. <sup>1</sup>H, <sup>13</sup>C and <sup>15</sup>N backbone assignment of the EC-1 domain of human E-cadherin. *Biomolecular NMR Assignments*. 2015;**9**:31-35. DOI: 10.1007/s12104-013-9539-6
- [20] Blondelle SE, Lohner K. Optimization and high-throughput screening of antimicrobial peptides. *Current Pharmaceutical Design*. 2010;**16**:3204-3211. Available form: <http://www.ncbi.nlm.nih.gov/pubmed/20687884> [Accessed: Mar 8, 2013]
- [21] Ferreon JC, Volk DE, Luxon BA, Gorenstein DG, Hilser VJ. Solution structure, dynamics, and thermodynamics of the native state ensemble of the Sem-5 C-terminal SH3 domain. *Biochemistry*. 2003;**42**:5582-5591. DOI: 10.1021/bi030005j
- [22] Coimbatore Narayanan B, Westbrook J, Ghosh S, Petrov AI, Sweeney B, Zirbel CL, Leontis NB, Berman HM. The nucleic acid database: New features and capabilities. *Nucleic Acids Research*. 2014;**42**:D114-D122. DOI: 10.1093/nar/gkt980

- [23] Fachrul M, Utomo DH, Parikesit AA. lncRNA-based study of epigenetic regulations in diabetic peripheral neuropathy. *Silico Pharmacology*. 2018;**6**:7. DOI: 10.1007/s40203-018-0042-8
- [24] Parikesit AA, Utomo DH, Karimah N. Determination of secondary and tertiary structures of cervical cancer lncRNA diagnostic and siRNA therapeutic biomarkers. *Indian Journal of Biotechnology*. 2018;**23**:1. DOI: 10.22146/ijbiotech.28508
- [25] Youngblood MW, Erson-Omay EZ, Günel M. Personalized medicine through advanced genomics. In: *Malig. Brain Tumors*. Cham: Springer International Publishing; 2017. pp. 31-48. DOI: 10.1007/978-3-319-49864-5\_3
- [26] Pi C, Zhang M, Peng X, Zhang Y, Xu C, Zhou Q. Liquid biopsy in non-small cell lung cancer: A key role in the future of personalized medicine? *Expert Review of Molecular Diagnostics*. 2017;**17**:1089-1096. DOI: 10.1080/14737159.2017.1395701
- [27] Tsimberidou A-M. Initiative for molecular profiling and advanced cancer therapy and challenges in the implementation of precision medicine. *Current Problems in Cancer*. 2017;**41**:176-181. DOI: 10.1016/j.currproblcancer.2017.02.002

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