

Editorial

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Translational Bioinformatics Support for Personalized and Systems Medicine: Tasks and Challenges

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The Scientific Bases of Personalized and Systems Medicine

The current challenges in healthcare including the high costs and high rates of Adverse Drug Reactions (ADRs) call for fundamental changes in both drug development and clinical practice [1,2]. The "onesize-fits-all" drugs ignoring individual differences are often the causes of the ADRs. Paper-based and non-standardized clinical systems have also contributed to errors and adverse events. At the same time, the fast development in biomedical science has not been translated into better clinical outcomes [3].

Personalized medicine may provide promising solutions for these predicaments. Based on the development of pharmacogenomics and systems biology, personalized medicine may help change the gear from reductionism-based and disease-centered medical practice toward a systems-based, integrative, and human-centered care [1,4]. Pharmacogenomics and systems biology are emerging fields that may provide systemic insights into health, diseases, and medicine [1]. Focusing on the individual differences in therapeutic responses, pharmacogenomics may help elucidate the molecular mechanisms for the prediction of disease progression and treatment outcomes [5]. Such understanding may provide the scientific basis of personalized medicine.

Because genes interact with other molecules and the environment, pharmacogenomics needs to be integrated with systems biology to have a holistic understanding of health and wellness [6]. Systems biology provides novel perspectives for studying biological systems at various levels of information [7]. The integration of pharmacogenomics and systems biology would promote the transformation from diseases and single drug targets to the whole humans and integrative therapies to achieve personalized and systems medicine.

For instance, the malfunction of metabolism is the risk factor of many complex diseases. By integrating experimental and computational methods, systems biology may help establish the foundation of systems medicine for understanding the occurrence and progression of complex metabolic diseases [8]. The elucidation of the function of enzymes in the metabolic network can help with the reconstruction of genome-scale metabolic models toward the development of personalized medicine.

Translational Bioinformatics: The Informatics Bases of Personalized and Systems Medicine

The translation of pharmacogenomics and systems biology into personalized and systems medicine relies on the effective support from information technologies [9]. With the fast development of these emerging fields and the exponential growth of both experimental and clinical data, it is necessary to solve the "lost in translation" problem by analyzing data across various domains [10]. Issues of inaccessible data, disparate data sources, inefficient workflow, and ineffective communication call for better informatics tools to provide more efficient data and knowledge management, decision support, and knowledge discovery [7,11].

Combining computational technologies and biomedical knowledge, translational bioinformatics may provide the solutions to promote the management, analysis, and sharing of biomedical data and information by both scientists and clinicians [7]. As a subdivision of translational medicine, translational bioinformatics may help establish a powerful platform to bridge the gap among various knowledge domains for the translation of the voluminous biomedical data into predictive and preventive medicine [12].

Specifically, genomic analysis methods in bioinformatics can improve the understanding of the connection between genotypes and phenotypes [3]. Data integration methods can help connect clinical and laboratory data streams to enable more efficient workflow and better communication in both clinical and research settings [13]. Techniques including data mining, knowledge discovery, and Electronic Health Records (EHRs) would allow clinical decision support for better diagnosis and treatment selections to bring the right interventions to the right people [3]. Ultimately, such translational informatics support would help save costs, avoid errors and risks, reduce adverse drug reactions, and overcome therapeutic resistance [3]. These are the essential elements for the accomplishment of personalized medicine.

Translational Bioinformatics Support for Personalized Medicine: The Tasks and Challenges

One of the most important tasks of translational bioinformatics is to bridge the gaps among various knowledge domains, from the basic studies of genomics, proteomics, disease pathogenesis, pharmacology, and toxicology, to clinical investigations including internal medicine [7]. Often used together with High-Throughput (HTP) studies, translational bioinformatics is indispensable for establishing patient's unique profiles and patient subgroups, the critical steps for the practice of personalized medicine [1]. In addition, translational bioinformatics needs to be combined with systems biology approaches to enable the simulation of systems networks and the predictive modeling for better preventive and therapeutic strategies.

Specifically, translational bioinformatics should play a critical role in the studies of the structure-function relationships and genotypephenotype associations for elucidating the mechanisms of health and diseases [3]. Furthermore, translational bioinformatics is needed for the modeling of systemic interactions among genes, drugs, tissues,

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systems, and the environment at different levels [14]. These associations are essential for finding systems-based biomarkers for better diagnosis and treatment outcomes. A feedback loop can connect the interactive concepts of the structures, functions, genes, drugs, environment, genotypes, and phenotypes.

For example, the structural and functional changes and the interactions between drugs and genes at the molecular level can influence the downstream networks, while the overall changes ultimately show as clinical phenotypic manifestations and treatment results [1]. The understanding of such genotype-phenotype correlations may help change the focus of medical practice from single targets to the whole systems, from isolated diseases to the whole humans [14].

In conclusion, translational bioinformatics methods based on data integration, data mining, and knowledge discovery can help translate scientific discoveries into efficient decision support for both scientists and clinicians. With the integration of bioinformatics and health informatics, better EHRs and Clinical Decision Support Systems (CDSSs) can be designed to analyze both genotypic and clinical phenotypic data for better therapeutic results [15]. Although up to now no generally accepted EHR tools have been developed for such purposes, such a challenge provides opportunities for further development while emphasizing the roles of translational biomedical informatics in personalized and systems medicine.

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