Role of Bioinformatics in Clinical Trials: An Overview

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Abstract—*Bioinformatics is the convergence of biotechnology, genomics and information technology that analyses data and even represent in statistical form. It even plays an important role in understanding the molecular works that is the basis of life. Bioinformatics associated with clinical trials are known as Clinical Bioinformatics. Understanding the relationship between clinical informatics and bioinformatics helps in discovering and developing the new diagnostics and therapies for diseases. The clinical application of bioinformatics associated with science and technology is to understand molecular mechanism and potential therapies for human diseases. Clinical bioinformatics is a new and important concept for the development of diseases-specific biomarkers, mechanism-oriented understanding and individualized medicine which provides biological and medical information to allow for individualized healthcare. In this review, we describe the clinical bioinformatics and its applications.*

Keywords*: Bioinformatics, Clinical bioinformatics, genomics, biotechnology*

1. INTRODUCTION

In the era of 1960s, computer science played an important role in the study of molecular biology. Bioinformatics uses biological information and mathematical, statistical and computing methods to research living things[1]. Bioinformatics has large impact on biological research in microarray technology, proteomics, pharmacogenomics, oncology and systems biology[2]. It is a thriving field that is the forefront of science and technology. As with the fast developing world humans have become the 'data-gatherers', whose every aspect of life has inferences based on these activities. In this new culture, everything will become data[3]. Everything can be measured and turned into collection of numbers that can be stored, archived in databases through cable or wireless conduits and analyzed[4].

The science relating to bioinformatics has many components. It usually refers to biological molecules and therefore requires knowledge in the field such as biochemistry, molecular biology, molecular evolution, thermodynamics, biophysics, molecular engineering and statistical mechanics. It requires use of computer science, mathematics and statistical approaches[5]. Bioinformatics is the juncture of experimental and theoretical science. It is also about understanding the molecular world that adds fuel to the life from evolutionary and mechanistic perspectives[6].

Bioinformatics was originally developed for the analysis of biological sequences. But now, it encompasses a wide range of subject areas like structural biology, gene expression and genomics studies (figure1). Bioinformatics associated with clinical trials has gone through much depth of the studies of different subjects and has provided number of ways that has never been imagined[5].

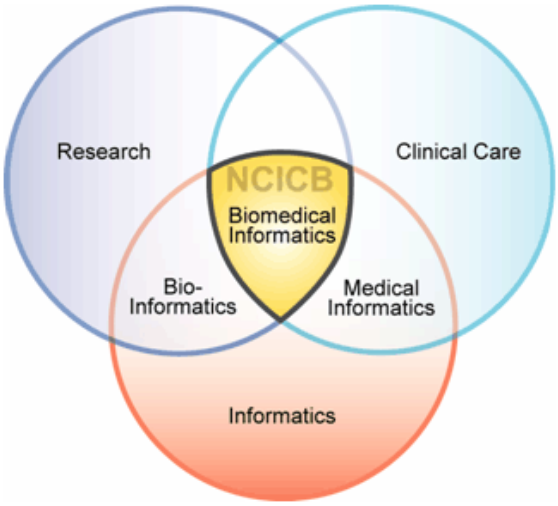

Fig. 1: Uses of biomedical informatics.

The term *'Clinical Bioinformatics'* is defined here as clinical application of bioinformatics-associated sciences and technologies to understand molecular mechanisms nd potential therapies for human diseases. Clinical bioinformatics is the developing science which consists of the combination of clinical informatics, bioinformatics, medical informatics, information technology, mathematics, and omics science[7] (Fig. 2). Clinical bioinformatics was initially proposed to provide biological and medical information for individualised healthcare. It enable researchers to search online biological databases and use bioinformatics in medical practice. It select

appropriate software to analyse the microarray data for medical analysis, for medical decision-making. It even optimize the development of disease-specific biomarkers, and identify drug target and clinical validation[8].

Understanding the interaction between clinical informatics and bioinformatics helps in discovering and developing the new diagnostics and therapies for diseases. Clinical bioinformatics is regarding the analysis and visualisation of complex medical datasets[9]. It focus more on clinical informatics, including patient complaints, history, therapies, clinical symptoms and signs, physician's examinations, biochemical analyses, imaging profiles, pathologies and other measurements[10]. In this field, computational and high experimental techniques are applied to identify agents in cancer diagnosis, treatment, prevention and control. It even encourages the development of chemical, structural and biochemical methods[11].The study of clinical bioinformatics tried to match disease complexity of patient information, clinical data, standard laboratory evaluations, brain imaging data and genetic data obtained from molecular profiling experiment. Clinical bioinformatics shows new path on the combination of clinical measurements.

It is a new and important concept for the development of disease-specific biomarkers, mechanism-oriented understanding and individualized medicine. The generation has much changed and genomic, transcriptomic and proteomic data from human studies have expanded due to high throughput biotechnologies. Alongwith, clinical measurements and examined informations have risen due to the development of advanced clinical devices[12]. As clinical bioinformatics is particularly focused on clinical context, it is characterized by the challenge of integrating molecular and clinical data to accelerate the translation of knowledge discovery into effective treatment and personalised medicine.

Due to the ambitious nature of clinical bioinformatics, variety of factors support research in this direction. Firstly, in last few years new genome sequencing and other high throughput experimental techniques have generated a large amount of data. When these data are merged with clinical data, it may lead to major biomedical discoveries[13]. Secondly, the new diagnostic tests based on molecular biomarkers are available to clinicians, thus making new advancements in curing diseases. Thirdly, with advancement in technology there has been increase in online availability of the biomedical text corpus, which had been made through published manuscripts, abstracts, textual comments and reports, as well as direct-to-web publication, led to the development of new algorithms. Such algorithms have been proved to be able to effectively combine the information of text with that of in biological knowledge[14]. Finally, the consistent growth of publicly available data and the possibility to access low-cost, high-throughput molecular technologies has meant that computational technologies and bioinformatics prove to play a central role in genomic medicine[15].

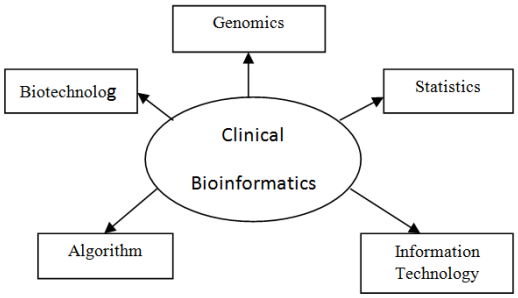

Fig. 2: Constituents of clinical bioinformatics

2. CLINICAL BIOINFORMATICS DATABASES

Online Mendelian Inheritance in Man (OMIM)- It is a comprehensive, authoritative and timely knowledge base of human genes and genetic disorders. These are compiled to support human genetics research and education and the practice of clinical genetics. It was started by Dr Victor A. McKusick as the definitive reference Mendelian Inheritance in Man. It is now distributed electronically by the National Center for Biotechnology Information. Here it is integrated with the Entrez suite of databases. Entrez is a client-server system for retrieval of information related to molecular biology.

OMIM is the derivation of biomedical literature. It is written and edited at Johns Hopkins University. The inputs are taken from scientists and physicians around the world. Each OMIM entry has a full-text summary of a genetically determined phenotype and/or gene. It has numerous links to other genetic databases such as DNA and protein sequence. OMIM is an easy and straightforward platform to the developing information in human genetics[16].

3D Tooth Atlas- It refers to the dental anatomy and interactive 3D tooth atlas. Users have to sign in with a username and a password. Then click on “My Subscriptions” on the right and then select “3D Tooth Atlas 7-Dental Edition” on the left.

Cardiosource Plus- It is an educational resource from American College of Cardiology. It covers cardiac information and the clinical trials databases [17].

Florinash- Florinash is a 5 year EC-funded FP7 project investigating the role of intestinal microflora in non-alcoholic fatty liver disease (NAFLD) which assimilate metabolomic, transcriptomic and proteomic profiles with patient metadata to enable the exploration of clinical hypotheses. http://www.florinash.org/

EVIMalaR- EVIMalaR is a 5 year joint research FP7 Network of Excellence, funded by the European Commission and currently involving 42 partners from 34 institutes in Europe, Africa, India and Australia. It work for malaria research that is directed towards a better understanding of the basic knowledge of the parasite, its vector and of the biology of the interactions between the parasite and both its mammalian host and vectors. http://www.evimalar.org/

Chernobyl Tissue Bank- The Chernobyl Tissue Bank (CTB) is an international cooperation that collects, stores and disseminates biological samples from tumours and normal tissues from patients for whom the aetiology of their disease is known - exposure to radioiodine in childhood following the accident at the Chernobyl power plant. http://www.chernobyltissuebank.com/

RD-CONNECT- It is an integrated platform connecting databases, registries, biobanks and clinical bioinformatics for rare disease research. Funded by the European Union's Seventh Framework Programme under the International Rare Diseases Research Consortium (IRDiRC), RD-Connect is a global infrastructure project initiated in November 2012 that links genomic data with registries, biobanks, and clinical bioinformatics tools to produce a central research resource for rare diseases [18].

3. APPLICATIONS OF CLINICAL BIOINFORMATICS

Clinical bioinformatics has various applications in various fields. Health care is becoming an increasingly data-intensive field as doctors and researchers invest a lot of medical data on patients and their illness [13]. Like, even health informatics spreads out in various branches like medical informatics, nursing informatics, dental informatics and public health informatics. Even spread out more among these branches (Fig. 3). The availability of large sets of digital medical information has made it possible to use the informatics to improve the health care and medical research. In today's world, informatics is being applied at every stage of health care from basic research to care delivery. It includes many specializations such as bioinformatics, medical informatics and biomedical informatics. The most famous example is, the Human Genome Project relied on informatics to analyse and sequence the 3 billion chemical base pairs[1].

Clinical bioinformatics even play major role in identifying agents in cancer diagnosis, treatment and control. It encourages the development of chemical, structural and biochemical methods to all basic and clinical cancer research[5]. In this field, biomarkers are used to detect different stages of cancer. Sequence alignment techniques are as a primary tool for research[19].

Diabetes is a devastating disease. It is characterized by high glucose levels in the blood. The primary treatment plan was controlling diet. Various methods are being applied for the treatment of diabetes through clinical bioinformatics. First, sequence alignment techniques. Second, gene expression techniques[20].

Thus, overall we can say that clinical bioinformatics play an important role in number of clinical applications including omics technology, metabolic and signalling pathways, biomarker discovery and development, computational biology, genomics, proteomics, metaboliomics, pharmacomics, transcriptomics, high-throughput image analysis, human molecular genetics, human tissue bank, mathematical medicine and biology, protein expression and profiling and system biology[21]. Understanding the relationship between clinical informatics and bioinformatics helps in discovering and developing the new diagnostics and therapies for diseases[22].

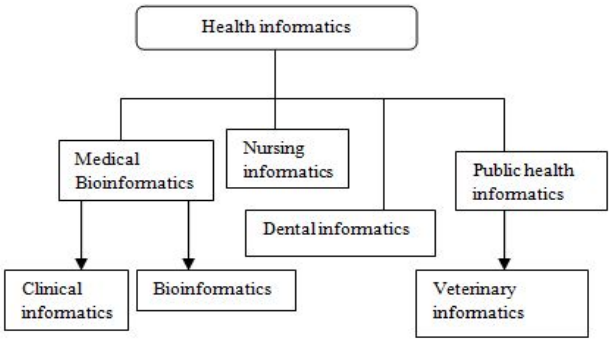

Fig. 3: Types of health informatics

4. CHALLENGES AND OPPORTUNITIES

In spite of being of much use, clinical bioinformatics has to face many challenges. Like, it is expensive. Even there is difficulty in controlling the exposure that is type and timing. It is a matter of great problem that there is cooperation among a diverse group of stakeholders which includes research sponsors, clinical investigators, patients, prayers, physicians and regulators are necessary in conducting a clinical trial. The following issues reflect the broad, systemic issues in clinical research. First is prioritizing of clinical research questions. Second is the divide between clinical research and clinical practice. And finally, the globalization of clinical trials.

The globalization of clinical research provides great opportunities for significantly improving the efficiency of the drug development process. Due to these trials, the pharmaceutical companies have a great benefit not only in North America and Western Europe but also in many developing regions such as Asia, South America and Eastern Europe. It results in lowering overall developmental cost and increased patient populations. Even it can lead to launching of new medical products in multiple regions all over the world. Clinical trials can be said to be a double-edged sword. Well designed and conducted studies can improve the efficiency of the drug[23,24].

5. CONCLUSION

Bioinformatics is the convergence of biotechnology, genomics and information technology that analyses data and even represent in statistical form. It even plays an important role in understanding the molecular works that is the basis of life. Bioinformatics associated with clinical trials are known as Clinical Bioinformatics. Basically, clinical bioinformatics is defined as the clinical application of bioinformatics associated with sciences and technologies. It helps in understanding the molecular mechanism and potential therapies for human diseases. It even provides biological and medical information to allow for individualized healthcare.

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