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Bioinformatics: A bridge between Genetics and Chemistry

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During the last few decades, when the molecular biology evolves and matures, the biological data is increasing at an astronomical pace. The existing information is itself mind-boggling. While keeping in mind the size and complexity of biological information, creating and maintaining databases for storing and organizing such information is a prerequisite. Moreover, bioinformatics play a vital role in processing this information. Now, the question arises that what exactly is 'Bioinformatics'? Although, bioinformatics is a popular term in science and technology but its definition is not universally agreed upon. Generally speaking, bioinformatics is the field of science in which biology, computer science, and information technology merge to form a single discipline. Furthermore, bioinformatics is inextricably intertwined with chemistry, biophysics, pharmacology, mathematics and statistics.

The major portion of research in chemistry is involved in betterment of human health with drug development being key player performing this task. Drug development is an iterative, complex, expensive and time-consuming process which comprises of several discrete stages:-

- Selection of disease
- Validation of the target where the potential new drugs might be able to affect
- Discovery of lead compound i.e. a chemical compound that has pharmacological or biological activity that can serve as potential drug
- Lead optimization which aims at refining the chemical structure of the lead compound to improve its ADMET profile (Absorption, Distribution, Metabolism, Excretion and Toxicity) to enhance the effectiveness of the drug.
- Pre-clinical trials: laboratory tests of a new drug, usually done on culture of cells or organs or a whole animal, to see if the hoped-for treatment really works and if it is safe to test on humans.
- Clinical trials
- Manufacturing of drug

Traditionally, scientists usually turned to nature in search of compounds that can act as therapeutic agent. The main bottlenecks in such methods were the cost and time required to identify, synthesize and test such compounds. Most of the compounds were rejected during testing phase owing to the poor pharmacokinetics, absence of required biological activity or existence of toxicity. By the 1990s the pharmaceutical industry focused upon the new great hope for drug discovery—modern high-throughput screening (HTS) of compounds produced by combinatorial chemistry. It takes around 12-15 years and a huge amount of 800 million dollars approximately to create a new drug. Intervention of bioinformatics at some plausible steps can be hailed as potential turning point to bring down the cost and time required in the drug discovery process.

In silico methods can help in identifying 'druggable' gene or protein or metabolites targets via whole-genome gene expression data, proteomic data or metabolomic data. Databases like National Center for Biotechnology Information (NCBI)

GenBank, EBI-EMBL and DNA Databank of JAPAN (DDBJ) have primary genomic data. Swiss-PROT, TrEMBL and Protein Information Resource (PIR) are databases of annotated protein sequences. GeneCards is a database of human genes, their products and their involvement in diseases. KEGG and PathDB are the databases on metabolic and regulatory pathways. Protein Databank (PDB) has three-dimensional structures of proteins.

Bioinformatics tools can also be used to analyze the target structures for possible binding or active sites. Using the three-dimensional structure of the target site, ligands can be selected from the virtual library and fitted into the target site. This process is also known as docking stimulation. The drug compound can be designed by incremental construction of a ligand model within the model of the target site i.e. de novo designing. The designed compound can then be checked for their drug likeness, dock these molecules with the target, rank them according to their binding affinities, further optimize the molecules to improve binding characteristics using the in silico techniques. Although HTS is useful in the hunt for novel leads, screening of small subsets chosen by virtual screening can be very useful when the structure of the target is available.

Future of drug discovery is dependent on the fruits of intricately entwined research in chemistry and bioinformatics, which play a critical role in improving our quality of life.

Table: Structure based design technologies (Davis et. al. 2003)

Objective	Technology	Bioinformatics tools
3D structure generation of biomolecular target	X-ray crystallography, cryo electron microscopy and NMR	O, MODELLER
Prediction of bound ligand conformation	Ligand docking	AUTODOCK, GOLD
Ligand optimization	Receptor interaction mapping	GRID, MCSS, SUPERSTAR
Affinity prediction	Structure-activity relationship (3D-QSAR) Scoring	CATALYST, GOLPE GOLD, GLIDE
Automated Ligand design	*de novo* design	LEAPFROG, SPROUT

The intimate interplay between bioinformatics, genetics and chemistry has driven innovation through the roof. Bioinformatics aid in deciphering the code hidden under the veil of genetics and transform it into useful resources to promote human health with the help of chemistry.

Certain websites having bioinformatic tools related to drug discovery:

1. Computational Resources for Drug Discovery (CSIR)
   http://crdd.osdd.net/index.php
2. Supercomputing Facility for Bioinformatics & Computational Biology (IIT Delhi)
   http://www.scfbio-iitd.res.in/tutorial/drugdiscovery.htm

References:

- "Bioinformatics and Drug Discovery"; Ivanov, A.S., Veselovsky, A.V., Dubanov, A.V. and Skvortsov, V.S. (2006) Methods in Molecular Biology, 316, 389-431.
- "Application and Limitations of X-ray Crystallographic Data in Structure-Based

Ligand and Drug Design"; Davis, A.M., Teague, S.J. and Kleywegt, G.J. (2003) Angewandte Chemie International Edition, 42, 2718-2736.

- "Drugs: From discovery to Approval"; Rick Ng (2008) Wiley-Blackwell; 2nd edition

Swati Mahendru has earned her Masters degree in Chemistry from University of Delhi and is currently pursuing her Ph.D. from University of Delhi, Delhi, India. She has been working on structural polymorphism exhibited by short oligodeoxynucleotide sequences and their interaction with various ligands.