Genomes to Hit Molecules In Silico: A country path today, a highway tomorrow- An update

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The advent of information rich era grants us the opportunity to sketch a pathway from Genome → Gene → Protein → Drug to develop personalized medicine almost in an automated way. Currently however, without the help of any database, an inspection of a DNA sequence does not tell us whether it is likely to be a gene and if it is a gene for mRNA, what the likely three dimensional structure of its protein product is. Also drug design softwares fall short of expectations even if the structures of drug targets are known.

Addressing these issues from a physico-chemical perspective, we have developed all atom energy based methodologies for whole genome analysis (1) (ChemGenome), tertiary structure prediction of proteins (2) (Bhageerath and Bhageerath-H) and protein/DNA targeted lead molecule design (3) (Sanjeevini). During the process, we discovered that physico-chemical properties such as hydrogen bonding, stacking and solvation energies convey the functional destiny of DNA sequences. Bhageerath-H crossed 60% accuracy in predicting tertiary structures of soluble proteins to medium resolution, the world’s best server’s performance in CASP10 (2012) being at 55%. Sanjeevini in collaboration with experimental groups delivered a micromolar compound against breast cancer and a sub-micromolar compound against malaria. The presentation will highlight as to how these can be configured into (Dhanvantari) an assembly line to deliver hit molecules from genomic information.

Related References