

## Systems Biology: Taking a Big Picture

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“There are more things in heaven and earth, Horatio, than are dreamt of in your philosophy” (Shakespeare, Hamlet). This philosophical profundity of William Shakespeare may correctly represent the current status of our understanding of universe. In connection to this, life sciences including medicine are not an exception by any benchmark. Since the birth of science of omics, it has been envisioned that life as we know it, is far more complex than ever being anticipated. Sure enough, the data churned out by genomics, proteomics and other omics profoundly unravelled the mesmerizing complexity of life. Consequently, individual molecular components and their role in organisms have been catalogued and in order to develop an understanding of their inherent interactive biology, a new offshoot of molecular biology emerged about a decade ago referred to as Systems Biology.

Systems biology attempts to explain structural and functional organization of the biological systems in relation to interactions of their constituent bio-molecules. This consequently provides insights into the phenotypic behaviour of biological systems. Thus in contrast to the conventional reductionist approach which deals with the characterization of individual molecule, systems biology investigate the interaction of several molecular components leading to specific phenotypes. The data procured from this approach have provided profound insights into the molecular machinery of diseases with complex genetic basis such as diabetes mellitus, neurodegenerative diseases, autoimmune and inflammatory diseases, several types of cancers, molecular events involved in the pathogenesis of microbes and even delineated potential therapeutic targets.

With the advent of the technological novelties in the genomics, proteomics and metabolomics, the magnitude of data thus produced is astounding. To make the most out of this perpetually flooding data, computational biology (bioinformatics) works hand in the hand with the omic sciences. Bioinformatics practices are required to integrate bio-molecules on the basis of physical interactions, expression pattern and other regulatory associations (epistasis). In addition, computational molecular evolution analyses of genes, genomes and proteins could be merged to provide more resolution to the data. Further adding to the complexity, to explore the influence of environmental factors on genes expression and consequent association, such variables could be merged with the data. In total this results in an extensive network of radiating strings of connections linking one molecule to another. From this it could be traced which molecule(s) plays a central role, which components have auxiliary involvement in the process under examination. This in turn further lead to develop mathematical models to predict unknown associations thereby directing the empirical studies to fill the gaps in our understanding of molecular cascades involved in genotype-phenotype relationship in different pathological and normal processes. Furthermore, given the role of individual molecule in a network drug target could be pointed for subsequent in silico and empirical screening.

Molecular network of p53 gene. Protein interaction network of p53, one of the major protein involved in several cancers, is developed using STRING v9.05 limiting partner proteins to 100 and confidence score set at highest (0.90). The central red circle represents the p53 protein (TP53) showing several connections radiating to other partner molecules where direct physical binding, post translational modifications, activation, inhibition, phenotype, catalysis, reaction and co expression connection lines are coloured as blue, pink, green, red, cyan, purple, black and yellow respectively. Note the proteins connected with p53 (only 100 shown here) are also interconnected. This suggests that mutation or deregulation of p53 may interfere with the regulation of other small networks and associated functions.

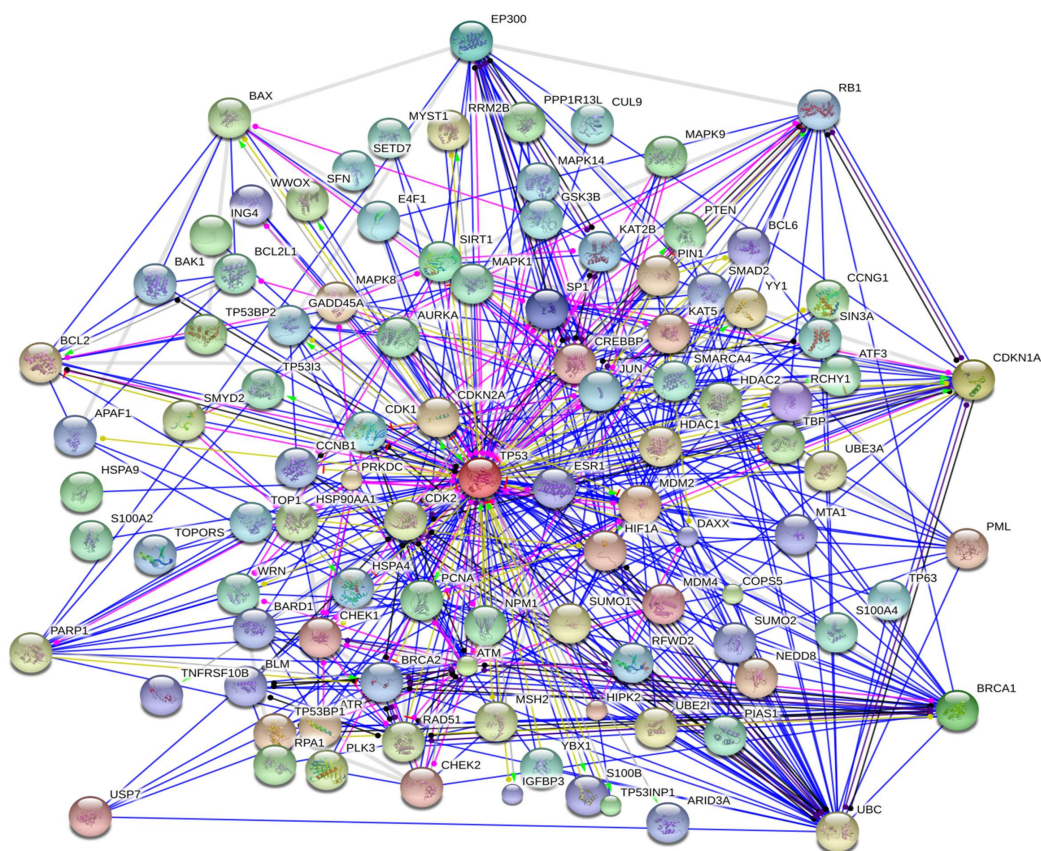
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Systems biology presents a paradigm where different branches of science interconnect for a common goal further suggesting the fading demarcation in the classical division of scientific knowledge. In addition, it clearly demonstrates the role of bioinformatics in both modern and futuristic understanding of molecular physiology and pathology at insightful resolution.

Owing to these observations, it is seemingly imperative for the young researcher in Pakistan especially in the

field of life sciences to align their breadth of knowledge with the current advances in bioinformatics, phylogenomics and molecular systems. A number of universities, institutions and laboratories have acquired the technologies or are in the process and scientists willing to accept the health challenges of current era will find a fertile ground to conduct research to solve mysteries of biology. We believe this will facilitate them to expand their vision and may enable them to develop a more generalized inference from their set of data.

