“Omics” research and systems medicine

“Omiks” araştırma ve sistemler tıbbı

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Abstract

Omics is an emerging area that has many aspects in the field of science and medicine. Several exiting developments have been achieved with omics including genomics, epigenomics, transcriptomics, proteomics, metabolomics, and bioinformatics. Systems biology is another emerging scientific area to develop new approaches for investigating complex interactions within biological systems.

Keywords: Omics, systems medicine

Özet

Omiks bilim ve tıp alanında önemli yönleri ile gelişmekte olan bir alandır. Omiks ile genomiks, epigenomiks, transkriptomiks, proteomiks, metabolomiks ve biyoinformatiksi içinde alan çeşitli heyecan verici gelişmeler sağlanmıştır. Sistemler tıbbı da biyolojik sistemlerdeki karmaşık ilişkileri araştırmak için yeni yaklaşımlar ortaya koyan yeni ortaya çıkmış bilimsel bir alandır.

Anahtar sözcükler: Omiks, sistem tıbbı

In the context of molecular systems biology [1, 2], genome medicine is described as the translation of genomic information to the benefit of patient (the system) during diagnosis and treatment of a disease, and it is almost named as bed-side experimenting or personalized medicine [3-5]. Here pharmacogenomics is becoming an important part of genome medicine. It already appears that many common diseases could be related to either many genetic polymorphisms with small effect or some polymorphisms with large effect. For example, it has been hinted that type 2 diabetes is relatively less genetically determined compared to rheumatoid arthritis or obesity.

The progress that systems biology has already made is enormous. Its subject resource ranges from molecules to organisms and ecosystems, and these have been investigated both...
in normal and in perturbed conditions to comprehend biological functioning of the respective system as a whole. Special biological hypothesis can also be scrutinized in perturbation experiments in which data-driven (bottom-up) and model-driven (top-down) strategies are combined [6]. Therefore utilization of system theory and engineering sciences has become an imperative. It also necessitates the recruitment of a new generation of scientists, who are expected to be equipped with knowledge and skills from many diverse branches of science [6].

It is already clear that systems biology has extended genetic engineering into synthetic biology by considering a cell or an organism to be made up of molecular modules interacting in a dynamic fashion. Therefore it considers a given diseased state as a perturbed global network. An example of such a synthetic study has been used for the development of better cancer therapeutics. For instance, synthetic lethality [7], in which mutations in two genes lead to death, has been exploited as a base for the development of better cancer therapeutics in a model organism. Synthetic lethality also appears to provide a versatile tool for targeting loss-of-function mutations, often leading to the inactivation of proteins.

Glycoproteins, in the context of an integrated proteomic and glycomic approach, have also been exploited in searching for cancer biomarkers. It has been well established that glycan modification of a protein often takes place either at asparagine or serine/threonine residues [8]. Decades of research efforts have established previously that such modifications are altered in a cancerous state to an extent that respective proteins could be exploited as tumor-associated antigens. Glycoproteins displayed on the cell surface or secreted, are involved in interactions with the cellular microenvironment. Glycoproteins have been the subject of some of the proteomics studies because of their potential to serve as a source of biomarkers. In the classification experiments glycoproteins have been enriched and analyzed by mass spectrometry (MS), their glycan structure have been characterized and glycopeptide backbone sequenced.

Studies in systems biology following the human genome project have lifted biomolecules, such as mRNA, microRNA, proteins, and single nucleotide polymorphism(s) (SNP) up to phenotype status. For example, a number of studies have used expression arrays to measure mRNA levels and considered them as quantitative phenotypes, and they have been further investigated for their association with genomic regions (expression quantitative trait loci, eQTLs). This approach also made possible the measurement of allelic mRNA expression. It has been realized that SNPs located within transcribed RNAs could affect the function of mRNA by changing their secondary structure. Such SNPs have been named as structural RNA SNPs (srSNPs) [9].

One interesting finding in the expression arrays has been that an allelic RNA expression imbalance (AEI) measured at an individual SNP arise mainly from cis-regulatory variants. As many genes have multiple transcription initiation sites, SNPs in the transcripts could represent multiple species of RNA, adopting distinct routes in processing, splicing, or cellular trafficking. Therefore, it has become obvious that the main RNA species must be determined at a given locus [9].

The role of microRNA (miRNA) in cancer was first discovered in leukemia [10]. miRNA profiling studies have demonstrated differences between acute lymphoblastic leukemia
(ALL) and acute myeloid leukemia (AML), and specific miRNA signatures have been correlated with karyotype alterations in AML. Later on it has been demonstrated that miRNAs could also play a role in solid cancers because it has been found that they are differentially expressed in normal and tumor tissues. Furthermore, a number of studies on pancreatic cancer have indicated significant differences between tumors and chronic pancreatitis, normal pancreas and pancreatic cell lines. In some studies it has also been reported that specific miRNAs are upregulated in hepatocellular carcinoma [10].

Studies of small molecules in the context of human health have been performed since the ancient times. Nevertheless, information accumulated was insufficient to link metabolite measurements to the human genome or physiology. The recent metabolomics strategies essentially involve non-targeted and targeted methods. The targeted methods are similar to those employed in clinical chemistry laboratories. The non-targeted route, on the other hand, tries to include the metabolome as broadly as possible [11].

The term proteome has been invented to describe the entire protein complement of a genome [1]. The proteome of a genome changes in response to external stimuli, types of protein modifications in a spatial and temporal fashion. Therefore a given state of proteome can only be measured under differential experimental conditions. The measurements include three main steps: separation, quantification, and identification of distinct proteins. Data obtained would then be stored. Proteins often act within macromolecules connected by complex networks. It has been shown in model organisms that the networks reflect biological phenomena by employing inherent topological and dynamic features. Therefore, the interactome network specifies all the physical protein-protein interactions, occurring within a cell. Construction of the maps for global protein–protein interactions, interactomes, uses cloned open reading frames (ORFeomes) at the genome-scale. ORFeomes represent the encoded proteome in a given system (cell, tissue, organ or organism), and are used as the starting material in interactome mapping studies. Such maps are then compared with other methods, such as orthogonal interaction, to create a framework for information. To generate reliable biological models other functional genomic and proteomic data sets are integrated with this information. Initial interactome mapping studies have used simpler biological systems such as *Saccharomyces cerevisiae*, *Caenorhabditis elegans*, and fly. The present estimates implicated that the yeast interactome comprises approximately 28,000 potential protein-protein interactions. Likewise, to comprehend molecular basis of diseases, such as cancer, human interactome itself has to be characterized. Proteome-scale information is also required at structural, functional and dynamic levels. This information should also cover regulatory or biochemical interaction networks [1].

The present meaning of the term phenome implies the global phenotype at organism scale [12]. Its characterization is much more difficult than that of genomes because phenotype varies among cells or within a cell in a temporal dimension. It will always be incomplete and necessitate a conceptual framework created by integrating data from epidemiology, evolutionary biology physiology, and quantitative genetics. Phenomics studies are important because they map the causal links between genotype, environment, and phenotype. So far, genome-wide association (GWA) studies have revealed a small proportion of phenotypic variance [12]. For the human height phenotype for example only 10% of the genetic variation has been accounted for. Similar findings have been reported for some of the human diseases, such as breast, colorectal, and prostate cancers, diabetes,
and heart attack. Here it has been thought that to cope with phenotype variation, phenotypes had to be studied directly, although no strategy has been worked out as yet.

A fine roofing on top of above-summarized omics heavens is perhaps the studies of the global modifiers of chromatin. Function of chromatin modification enzymes comprising DNA methyl transferases and histone acetylase/deacetylases appears to be modulated by some elements such as Nickel and Arsenic [13]. The outcome is often inactivation or reactivation of some promoter elements, or redistribution of condensed/decondensed chromatin regions along the genome, and nucleotide transitions.

**Conclusion**

Post-genomic research has initiated the construction of a “little house” of systematic information that expands from within. Progress made so far has already been sufficiently perplexing to pre-genome scientists as they see galaxies of interactome have invaded the colorful pages of most cited journals. Aging in knowledge and well-established personal skills seem to be increasingly disturbing in medical profession. Everything we already have and every one of us is either going to be metamorphosized or transformed into the structures of that little house, or else. But, for the time being, Mendel himself would be exempted from the treat, as the pairwise interactions are still highly esteemed.

**References**

