Biomarkers: state of the art and perspectives

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Recent years saw an explosive increase of biochemical markers in medicine, mainly due to the translational research on the molecular basis of human diseases and to the technological research that resulted in efficient procedures for the analysis of such molecules. For example, high throughput gene sequencing analyzes a complete genome in a few days, and microchip based technologies permit the study of hundreds of gene variants in a single run in large series of subjects.

Every day a new gene responsible for a human disease is identified and it is becoming clear that "modifier" genes, inherited independently of the disease-gene, influence the phenotype of each patient and helps to predict the outcome. A large group of diseases (diabetes, cardiovascular diseases and obesity) are associated with complex interactions between several (some still unknown), genes and are influenced by environmental factors.

This complex interaction, which seems to vary from patient to patient, has led to the concept of "personalized medicine".

Studies on xenobiotics metabolism revealed a myriad of gene and gene variants that modulate the individual's sensitivity to drugs, thus leading to the concepts of pharmacogenomics and pharmacogenetics. Similarly, genetic variants may influence the nutrient's absorption, pathway and nutritional effects (nutrigenomics). All these genetic variants are biomarkers that may be easily analyzed.

The Human Genome Project showed that the human genome is constituted by 20,000-30,000 genes (a surprisingly low number when compared to other species). Therefore, a number of mechanisms that regulate gene expression may be active in humans. Some of these mechanisms have been studied and have already been related to human diseases. For example, the altered methylation of some genes is related to various human neoplasia. Similarly, microRNAs are involved in the regulation of the expression of a several human genes, and mounting evidence indicates that also this mechanism may be impaired in human diseases.

mRNA sequences are currently analyzed also by RT-PCR technology. These molecules may be markers of specific retroviral infection (i.e., HCV, HIV), or represent a signal of neoplastic cells (minimal residual disease), or help to predict micrometastases in neoplastic patients. In addition to specific mRNA molecules, the chip technology permits today to assess the expression profile of cells and tissue testing hundreds of mRNA molecules together.

After the era of "genomics", the interest of researchers refocused on proteins and more specifically on "protein-protein" interactions, a complex network that further regulates the differential expression and activity of gene products. Such complex interactions may be impaired in human diseases and can be analyzed by "proteomics" methodologies.

Finally, the relationships between genetics and human behaviour are beginning to be elucidated. Aggressive or depressive behaviour is under the control of a genetic network; suicide may be related to alterations of the epigenetic regulation of specific genes. Also partner selection may be related to DNA, and in some species the specific genes have been identified - another example of "personalized biomarkers".

Conclusions. The technology and the study of biomarkers is becoming easyer, but the deep understanding of clinical biochemistry and molecular genetics confirmed the real "uniqueness" of each individual. This may be an excellent opportunity for laboratory medicine to reposition the patient at the heart of the medical process.

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