Glycomics and Lipidopics

Extended Abstract

Genomics versus metabolomics in disease diagnosis

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Abstract:

To study the genomics versus metabolomics in disease diagnosis. This study focuses on metabolomics in disease diagnosis and how a combined genotype-phenotype approach can help in accurate disease diagnosis, especially in the early stages of disease. Despite many technological advances, accurate diagnosis of diseases, it is a major stumbling block in the medical world for an effective precision care for the patient. Disease takes as many as two decades to be detected and the late stage diagnosis are left untreated with many billions of dollars are wasted in patient care. The primary reason is the biology of initiation and progression mechanisms of diseases are far too complex with silent cascade of events over two decades without any major symptoms and thus disease can escape from early diagnosis. Conventional late stage disease diagnosis is aided by MRI, CT scans, histopathologic analysis of biopsies combined with clinical chemistry but without any curable treatment options. Thus, unfortunately, many a time's only invasive surgical interventions are applied for the treatment, prolonging the life of the patient, with unaffordable treatment options. Discovery of novel medicines is also hampered by the complexity of biology of disease progression. In the last two decades, genomics centered diagnostics have become the major focus for identifying disease, but their applications in the medical world for accurate disease diagnosis is still far from reality. In addition, genetic diagnosis is identifying far many mutations in a disease, for example 800 plus mutations in autistic disorders leaving scientific communities perplexed. Discovering novel early targets of disease initiation process is very crucial and thus amenable for prophylactic treatments to prevent disease progression. Now that the scientific knowledge of the nutrients that are the basis of nutrient deficiency diseases is established,determining the role of diet in metabolic regulation has become a key scientific objective of nutrition research. The importance of diet to health has become even more obvious with the realization that many of life's modern diseases are the result of subtle but chronic metabolic imbalances related in part to diet. Although many of the diseases that medicine has dealt with successfully over the past century have been those caused by exogenous toxins or pathogenic organisms, the metabolic diseases including atherosclerosis, obesity, hypertension, type 2 diabetes, osteoporosis and various inflammatory diseases are caused by chronic imbalances of normal metabolic pathways . These diseases thus pose a great challenge for all aspects of traditional public health intervention, including nutrition. Diets are a part of the problem and nutrition should play a vital role in metabolic disease prevention. Metabolic balance is responsive to not simply the presence of essential nutrients at the limits of their adequacy, but also to the proportion of essential nutrients and to the abundance of nonessential components in the diet. As dietary strategies seek to modify metabolism for health benefits, the importance of understanding precisely how much of each nutrient is optimal leads to the necessity to redefine safety of nutrients consumed in amounts beyond those necessary for adequacy. New strategies, technologies and knowledge must be established to evaluate both the efficacy and the safety of diets designed specifically to chronically influence metabolism. Genomics technologiesInvestigators of diagnostics, pharmaceuticals and nutrition are developing new approaches to recognize, prevent and reverse metabolic imbalances. New weapons in the scientific arsenal to support these approaches are the tools emerging from genomics and the technologies of global gene expression. In addition to providing new knowledge of genes and their functions, genomics has propelled a change in the perspective of biological scientists: "the systems approach." Until recently, rigorous studies to understand the biological reactions, structures, catalysts and signals of life were largely reductionist. Scientists reduced their biological interests to increasingly narrow spheres to understand molecular mechanisms. Nutritionists also focused greater attention on molecular details to understand how nutrients in the diet exert their effects on biology. These approaches, although successful in understanding specific mechanisms, lose the ability to examine the larger behavior of entire biological organisms. Genomics technologies, however, change the strategy of nutrition research. It is now possible to measure simultaneously thousands of biological events in molecular detail. With these principles in place, scientists are extending the analysis of gene expression and its global perspective to examine the other layers of biological organization, proteins and metabolites. The massive increases in computer power are at the core of these scientific achievements.The expansion in the capabilities of computerized data

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management that has made genomics possible is also making it possible to see a new future for nutritional intervention: personalized health. Scientists of all biological disciplines are embracing computer-powered genomics as the ultimate key to understanding biodiversity. The differences between pathogenic and benign viruses and bacteria are emerging from genomic research . Interestingly, the field of nutrition is moving toward the complex issue of biodiversity, and the variation between individual humans. Genomics will not be the only, and probably not the most important, platform for nutrition. Nutrition scientists will use the downstream products of genes with -omic detail, proteomics and metabolomics. Assessing efficacy and safety in the postgenomic eraIn traditional public health, healthy is defined by the lack of disease. In effect, individuals are "diagnosed" for the presence of various diseases using a large battery of biomarkers whose presence reflect the explicit presence or consequences of pathogens, toxins, dysregulated cells or nutrient deficiencies. These diagnostics simultaneously identify the presence and physiological basis of disease. Individuals are judged to be healthy if they emerge from a complete battery of diagnostics without demonstrating the presence of any biomarkers of disease. This strategy has been very effective for decades, if not centuries. But as medical science has become successful in dealing with certain diseases, the remaining health issues have proven to be distinct in their properties, and to therefore require distinctly different strategies for detection, prevention and cure. Diseases that result after long-term chronic imbalances in metabolism do not necessarily produce biomarkers of damage until the disease is well established. Even more ominously, it is not possible to reverse chronic diseases by simply restoring normal balance to specific aspects of metabolism. Clearly, prevention is necessary as the restoration of optimal metabolism before damage has occurred. However, if imbalances in metabolism are to be reversed before explicit damage has occurred, it is necessary to be able to detect the metabolic imbalance itself, i.e., by requiring metabolic assessment. Furthermore, metabolic assessment must be relatively global to determine potential imbalances in any pathways that could lead to disease. Atherosclerosis is an example of a disease afflicting a large proportion of the population that is caused not by an acute exogenous agent, but by a chronic imbalance of the endogenous metabolism of cholesterol. Lessons learned from the battle against atherosclerosis are proving to be valuable in developing strategies to combat other metabolic problems with a significant nutritional component. Cholesterol is a very difficult molecule to analyze quantitatively, nevertheless, over decades scientists developed increasingly accurate methods to measure cholesterol in the blood compartment. With these technologies in place, clinical researchers adopted the routine measurement of cholesterol in blood to correlate these measures with the relative probabilities of developing atherosclerosis. History now attests to the success of these investigations, although it must be recognized that the scientific investment was massive and almost four dozen Nobel laureates received their prize for working on cholesterol. Because of their success, individuals are routinely monitored for their blood cholesterol in highly quantitative terms. Personal data on cholesterol concentrations are available to both clinicians and individuals. With this critical metabolic information available, various aspects of science and industry worked to understand how individuals could change their cholesterol concentrations through diet, drugs and excercise. This knowledge enables each individual to evaluate personal cholesterol information both as risk and, more importantly, how through drugs, diet and lifestyle they can change their metabolism to reduce their personal risk. The U.S. implemented this strategy as public policy by establishing a very ambitious countrywide project, the National Cholesterol Education Program. Reducing cholesterol became a public goal. When otherwise healthy individuals knew that they were at risk for heart disease because of their cholesterol levels the value of pharmaceuticals that would act to lower cholesterol became clear. This single prognostic marker is now the basis for a multibillion dollar pharmaceutical market bringing significant benefit to millions of people by lowering disease risk. Now it is possible to merge the successful principles developed through cholesterol and atherosclerosis research with the new technologies of genomics and nutrition to move forward with a larger and more comprehensive strategy on metabolic health. Key elements of these new strategies are to distinguish biomarkers from quantitative metabolite profiles, to move from population recommendations to individual guidance, to combine isolated biochemical targets into integrated metabolism and to augment knowledge of essential nutrients to address overall diets. Nutrition is moving forward in this strategy, thus broadening its influence dramatically and providing an opportunity to improve public health through prevention of disease. In this new health paradigm, the toxicity and efficacy of foods and food components are also being reexamined.

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