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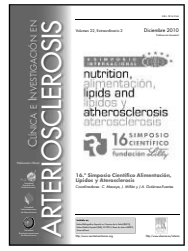

16.º SIMPOSIO CIENTÍFICO ALIMENTACIÓN, LÍPIDOS Y ATEROSCLEROSIS

Globalization of lifestyles: too fast for our genome?

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Genome plasticity: adapting to the environment

Modern human populations have experienced diverse adaptation to environmental changes in climate, geography, culture, food resources, and pathogens. Such adaptation, driven by selection, has been imprinted on the genome as fixation or changes of frequencies of genetic variants[1-3]. These adaptive genetic variants are indeed functional and underlie the phenotypic diversities in modern human populations including, in addition to the visible phenotypes, metabolic rate, body composition, and disease risk. For example, genetic variants at the lactase gene *(LCT)* have been driven to high frequencies in European populations in response to adoption of dairy farming over the past 10,000 years as well as in specific African populations were dairy farming is practiced. Carriers of such adaptive variants in these populations are able to safely consume milk products[4]. A similar notion applies to the copy number of the amylase gene recently reported in populations differing in their consumption of carbohydrates[5]. In order to gain further knowledge about the genetic basis of these environmental adaptations, a number of surveys of the whole genome have been carried out to detect adaptive variants in humans. Moreover, genome wide association (GWA) studies have identified dozens of potential genetic variants/regions influencing the risk disease, including common risk factors associated with cardiovascular diseases, such as the metabolic syndrome (MetS). Merging these data provides an excellent opportunity to identify adaptive genetic variants associated with MetS risk. More importantly, as environmental factors shaped human adaptive genetic variants, these variants are particularly important to the understanding of how such factors (i.e., lifestyle and dietary habits) modulate the effects of genetic variants on the risk of MetS, heart disease and overall, the quality of aging. This has become especially important in view of dramatic life style changes experienced during the last century. Three coincident trends with significant impact on society and health care system have emerged: *a)* food has become abundant, snacking frequency has increased and feeding has shifted towards the end of the day; *b)* the gradual reduction in the sleep time together with increase in sleep-wake interdaily irregularity; and *c)* the increase in the exposure to bright light during the night, inhibiting melatonin secretion[6]. These environmental changes conflict with the positive adaptation changes that have been taking place in the human genome during millennia. Therefore, it will be crucial to understand these regional, ethnic adaptations in the context of traditional metabolic pathways but also in the context of chronobiology and biorhythms.

In this regard, we have been taking a number of approaches to test the hypothesis that natural selection modulates the balance in allele frequencies across populations to maximize the harmony between the genome and the environment. Specifically, we propose that recent immigrants may be particularly vulnerable to common disorders because their genomes are at odds with the newly adopted environment. We focused our interest in Puerto Ricans, the second largest Hispanic ethnic group in the US, and a group with high prevalence of chronic disease. We determined allele frequencies and population differentiation for 101 single nucleotide polymorphisms (SNPs) in 30 genes involved in major metabolic and disease-relevant pathways in about 1000 Puerto Ricans living in Boston and compared them to similarly aged non-Hispanic whites (NHW)[7]. Minor allele frequency (MAF) distributions for 45% of the SNPs

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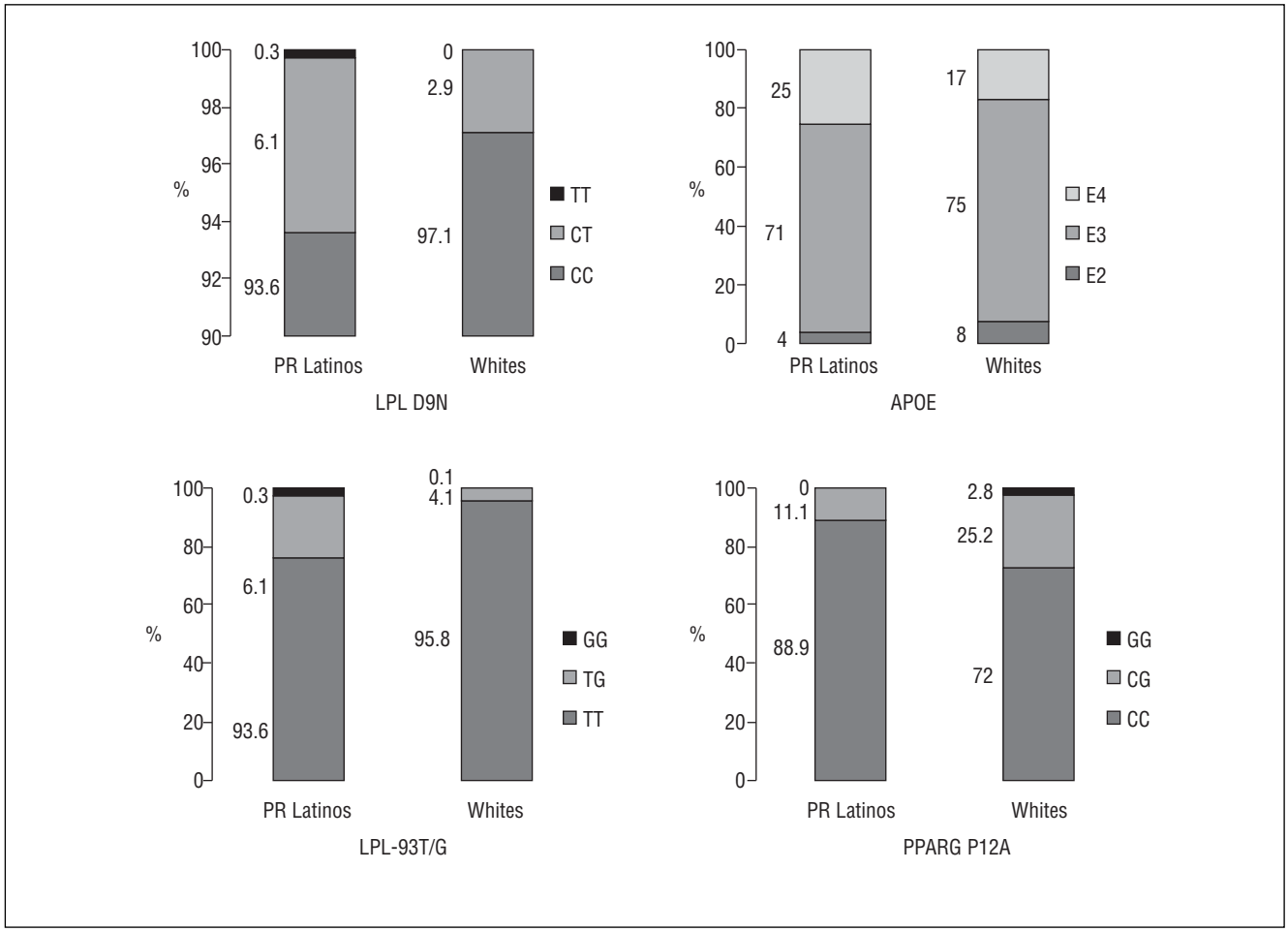

Figure 1 Comparison of genotype (LPL D9N; LPL -93T/G; PPARG P12A) and allele (APOE) frequencies in Puerto Ricans and Whites. Risk alleles (T for the LPL D9N; E4 for the APOE; G for the LPL -93T/G and C for the PPARG P12A) are higher in Puerto Ricans than in Whites.

assessed in Puerto Ricans were significantly different from those of NHW. Interestingly, Puerto Ricans carried those alleles conferring disease risk in higher frequency than NHW. Some representative differences are presented in figure 1. Conversely, those alleles conferring disease protection were under represented in Puerto Ricans. These observations may serve to explain the elevated risk of chronic diseases affecting Puerto Ricans living in the US and can be extrapolated to other migrations such as those of Asian Indians to Europe and the USA or those from Central and South America to Spain. Moreover, this knowledge underscores the relevance of genome-based prevention strategies to decrease the prevalence of chronic diseases, more specifically, the personalization of dietary recommendations.

Nutrigenomics: towards personalization of dietary recommendations

Changes in diet are likely to reduce cardiovascular disease, but after decades of research the definition of the optimal diet remains elusive. A well-known phenomenon in nutrition research and practice is the dramatic variability in interindividual responses to any type of dietary intervention. There are many other factors influencing response, and they include, among many others, age, sex, physical activity, alcohol, and smoking as well as genetic factors that, as highlighted above, should allow the identification of vulnerable populations/individuals that will be benefit from a variety of more personalized and mechanistic based dietary recommendations. This potential could and needs to be developed within the context of nutritional genomics that in conjunction with systems biology may provide the tools to achieve the holy grail of dietary prevention and therapy of cardiovascular diseases (Fig. 2). This approach will break with the traditional public health approach of "one size fits all." The current evidence based on nutrigenetics has begun to identify subgroups of individuals who benefit more from a low fat diet, whereas others appear to benefit more from a high monounsaturated or polyunsaturated fat (PUFA) diets[8]. Another interesting series of findings relate to the relation between diet, obesity and metabolic syndrome where the perilipin (PLIN) gene appears

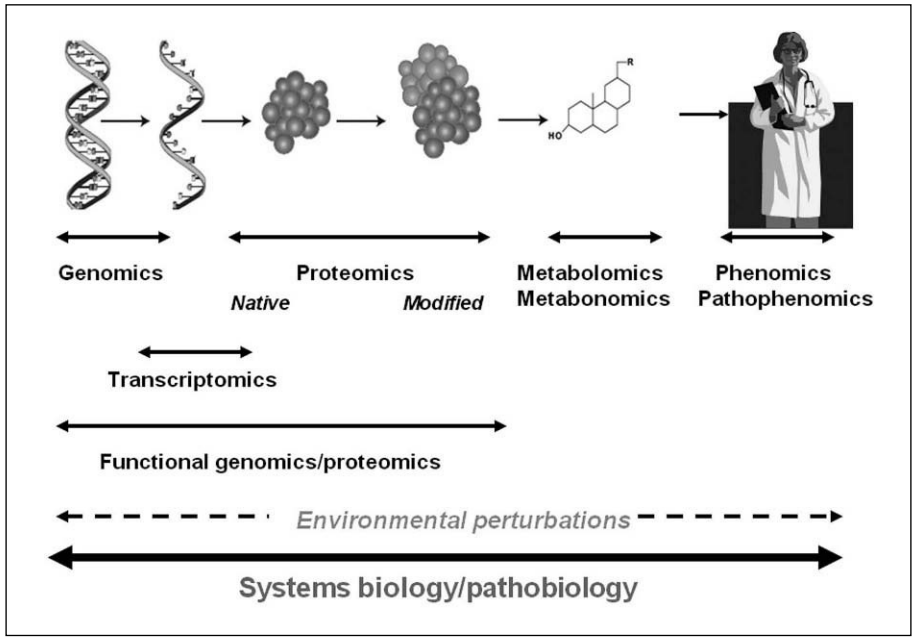

Figure 2 Systems biology unifies the information from a number of "omics" and environmental factors to gain better understanding about the molecular basis defining individual phenotypes and pathophenotypes. This knowledge should provide both, better prevention and therapies through more personalized approaches.

to be playing a significant role[9]. The current evidence suggests that the PLIN gene may help to identify in addition to those predispose to obesity, those who will be benefit from low caloric diets or alternatively from high complex carbohydrate diets. The continuous progress in Nutrigenomics will allow us to identify those persons for whom diet plays no major role in their risk CVD risk factors as well as those persons who may benefit from specific gene-based dietary advice. However, in order to gain knowledge in this area, the overwhelming amount of genetic data being generated needs to be balanced with reliable and comprehensive phenotypic information gathered over time in very large numbers of subjects. Unfortunately, the existing longitudinal studies lack, individually, the size needed to deal with the complexity of the gene-environment interactions modulating human health and disease, nor are the statistical tools ready to deal with these complex interactions. Moreover, the evidence needs to be supported by properly designed intervention studies. Nevertheless, despite the current shortcomings, the current evidence suggests that personalized nutrition is a valid concept with potentially great benefits for disease prevention and optimal health.

Conflict of interest

The author declares he has not any conflict of interest.

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