EDITORIAL COMMENT

Genetics in coronary artery disease

A genética na doença coronária

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Worldwide, coronary artery disease (CAD) is predicted to remain the leading cause of death, posing a significant socioeconomic burden.[1] Preventing and managing this disease is a major challenge due to its multifactorial nature. CAD appears to be caused by the interaction of environmental risk factors and multiple predisposing genes. However, the complex etiology of CAD has not been fully clarified to date. Several conventional risk factors, such as hypertension, hyperlipidemia, diabetes, family history and smoking are linked to CAD.[2] Other factors, such as lipoprotein (a), homocysteine, higher oxidative stress, low levels of antioxidants, being sedentary and leading a stressful lifestyle are also thought to play a key role in the development of the disease.[2] Identifying the causative factors for CAD development and/or progression is challenging due to its etiologic heterogeneity.

The standard treatment for CAD can be medical, surgical or a combination of both according to the extent, severity, and clinical presentation of the disease.[3] Nowadays, technological and scientific progress has led to the development of novel therapeutic approaches, such as stem cells, nanotechnology, robotic surgery, three-dimensional printing and drugs.[3] Some of these strategies already have evidence supporting their clinical use, while others are still in an experimental stage.[3]

Since we live in the era of Big Data, MultiOmics technologies and artificial intelligence, the future for characterizing the genetic architecture of CAD and developing novel therapeutic options looks promising. The development of massive parallel sequencing technology, also known as next-generation-sequencing technology has ushered in a new era in genetic information, opening unexplored avenues in genomic medicine and ultimately advancing precision medicine with a huge growth in available genetic tests. The explosion of knowledge of how genomic variations in an individual's DNA can affect disease and health because of the Human Genome Project has meant we are now witnessing new discoveries in genetic cardiovascular disease; patient management has changed substantially over the last decade.

Several studies using high-throughput sequencing methods have addressed single nucleotide polymorphisms (SNPs) with cardiovascular disease.[4] Genome-wide association studies (GWAS) have identified about 208 susceptibility loci for CAD.[5,6] Several studies have focused on the association of variants at the GWAS loci with CAD in specific populations.

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Despite the lack of consistency in the association patterns of these genes/loci across the populations, 11q23.3 and 9p21.3 chromosomal regions are the most frequently CAD-associated loci reported. Tcheandjieu et al.[7] reported a GWAS of CAD with cohorts of Caucasian, Black, and Hispanic individuals from the Million Veteran Program, identifying 95 novel loci, including the first nine to be identified on the X-chromosome, and reporting near equivalent heritability of CAD across multiple ancestral groups.

In the current issue of the Journal, Kordkheyli et al.[8] investigated the potential correlation between *KLF5* (rs3812852) and *KLF7* (rs2302870) SNPs with the risk of CAD in the Iranian population. It is known that Krüppel-like factors are DNA-binding proteins belonging to the family of zinc-finger transcription factors that can regulate gene expression linked to numerous biological processes, such as cell growth, differentiation, and death, as well as the development and maintenance of specialized tissues, under both physiological and pathological conditions.[9] KLFs are also known to be involved in regulating several key processes of cardiovascular diseases, including inflammation, oxidative stress, and cell proliferation.

Kordkheyli et al.'s study has shed new light on the molecular pathogenesis of CAD by identifying the *KLF7* gene as a candidate for CAD susceptibility, while also suggesting that the *KLF5* SNP is unlikely to influence CAD risk.

The authors acknowledge that more functional studies are needed to fully understand the molecular mechanisms underlying the pathogenesis of CAD and to clarify the precise correlation of other polymorphisms in *KLF5* and *KLF7* with the CAD risk across different populations.

Currently, there is still much to learn about the role of KLFs in the risk of cardiac diseases, as well as the potential contribution of these proteins as therapeutic targets.

As a final remark, CAD, a disorder with complex inheritance pattern, should be analyzed at different biological levels. Therefore, it is also important to understand the epigenetic mechanisms that regulate the expression of these genes. The advancement in molecular technology allows for a thorough characterization of cardiac diseases at different omic levels (e.g. genomics, transcriptomics, proteomics, epigenomics, metabolomics, etc.), empowers physicians to treat these diseases based on each patient's unique profile by understanding the individual differences and characteristics, including specific genotypes, of patients with similar clinical presentations, thereby enhancing risk stratification, diagnosis, and therapeutic decision-making.[10]

Conflicts of interest

The author has no conflicts of interest to declare.

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