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Basic genetics for cardiologists: molecular approach

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Genomics serves several roles in cardiovascular health and disease, the field of cardiovascular genomics has two distinct goals: understanding biologic mechanisms and applying that knowledge to personalized medicine. Advances in molecular diagnostics, have the potential to improve identification of cardiac diseases and further understanding of mechanisms responsible for their pathogenesis and phenotypic expression.

For the most part, clinical molecular diagnostic technologies remain focused on identifying patients underlying pathogenic mechanisms. With direct genetic testing, the laboratory looks for the particular genetic variant (or variants) that contribute to a condition, whereas indirect genetic testing relies on the comparison of DNA markers that are linked to a trait of interest but that do not cause the genetic condition.

The common disease–common variant hypothesis proposes that common variants, which are defined as variants with a prevalence of at least 5% in the population, have a role in the cause and pathophysiology of common diseases. It is on this premise that the genome wide association study is based, since it comprises tests of association between disease and common variants spread throughout the genome. On the basis of this approach, researchers have assembled catalogues of cardiovascular variants, using genotyping arrays, haplotype maps, and statistical methods. The astonishingly large number of new loci associated with cardiovascular risk factors, subclinical indexes, and disease end points have provided insights into the biologic pathways that underlie disease. The continued erosion of sequencing costs, driven in part by increased capacity of existing technologies and improvements in chemistry, as well as the emergence of single-molecule third- and fourth-generation sequencing, suggests that in the fullness of time, most patients entering the health-care system will have had their genome sequenced before clinical evaluation. These tests may also predict the need for specific treatment, or help avoid unnecessary therapies and invasive diagnostic procedures.