Molecular basis of hypertrophic cardiomyopathy

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Hypertrophic cardiomyopathy (HCM) is a disorder which has fascinated clinicians for many years. The remarkable diversity in clinical presentations, ranging from no symptoms to severe heart failure and sudden cardiac death, illustrates the complexity of this disorder. Over the last decade, major advances have been made in our understanding of the molecular basis of several cardiac conditions. HCM was the first cardiac disorder in which a genetic basis was identified and as such, has acted as a paradigm for the study of an inherited cardiac disorder. At least eleven genes have now been identified, defects in which cause HCM. Most of these genes encode proteins which comprise the basic contractile unit of the heart, i.e. the sarcomere. Genetic studies are now beginning to have a major impact on diagnosis in HCM, as well as in guiding treatment and preventative strategies. While much is known about which genes cause disease, relatively little is known about the molecular steps leading from the gene defect to the clinical phenotype, and what factors modify the expression of the mutant genes, including alterations in calcium handling within myocytes. Concurrent studies in cell culture and animal models of HCM are now beginning to shed light on the signaling pathways involved in HCM, and the role of both environmental and genetic modifying factors. Understanding these basic molecular mechanisms will ultimately improve our knowledge of the basic biology of heart muscle function, and will therefore provide new avenues for diagnosis and treatment not only for HCM, but for a range of cardiovascular diseases in man.