Complex Roads from Genotype to Phenotype in Dilated Cardiomyopathy.


Abstract
Dilated cardiomyopathy (DCM) frequently affects relatively young, economically and socially active adults, and is an important cause of heart failure and transplantation. DCM is a complex disease and its pathological architecture encounters many genetic determinants interacting with environmental factors. The old perspective that every pathogenic gene mutation would lead to a diseased heart, is now being replaced by the novel observation that the phenotype depends not only on the penetrance -malignancy of the mutated gene- but also on epigenetics, age, toxic factors, pregnancy and a diversity of acquired diseases. This review discusses how gene mutations will result in mutation-specific molecular alterations in the heart including increased mitochondrial oxidation (sarcomeric gene e.g. TTN), decreased calcium sensitivity (sarcomeric genes), fibrosis (e.g. LMNA and TTN) or inflammation. Therefore, getting a complete picture of the DCM patient will include genomic data, molecular assessment by preference from cardiac samples, stratification according to co-morbidities, and phenotypic description. Those data will help to better guide the heart failure and anti-arrhythmic treatment, predict response to therapy, develop novel siRNA-based gene silencing for malignant gene mutations, or intervene with mutation-specific altered gene pathways in the heart.

PMID: 29800419 DOI: 10.1093/cvr/cvy122