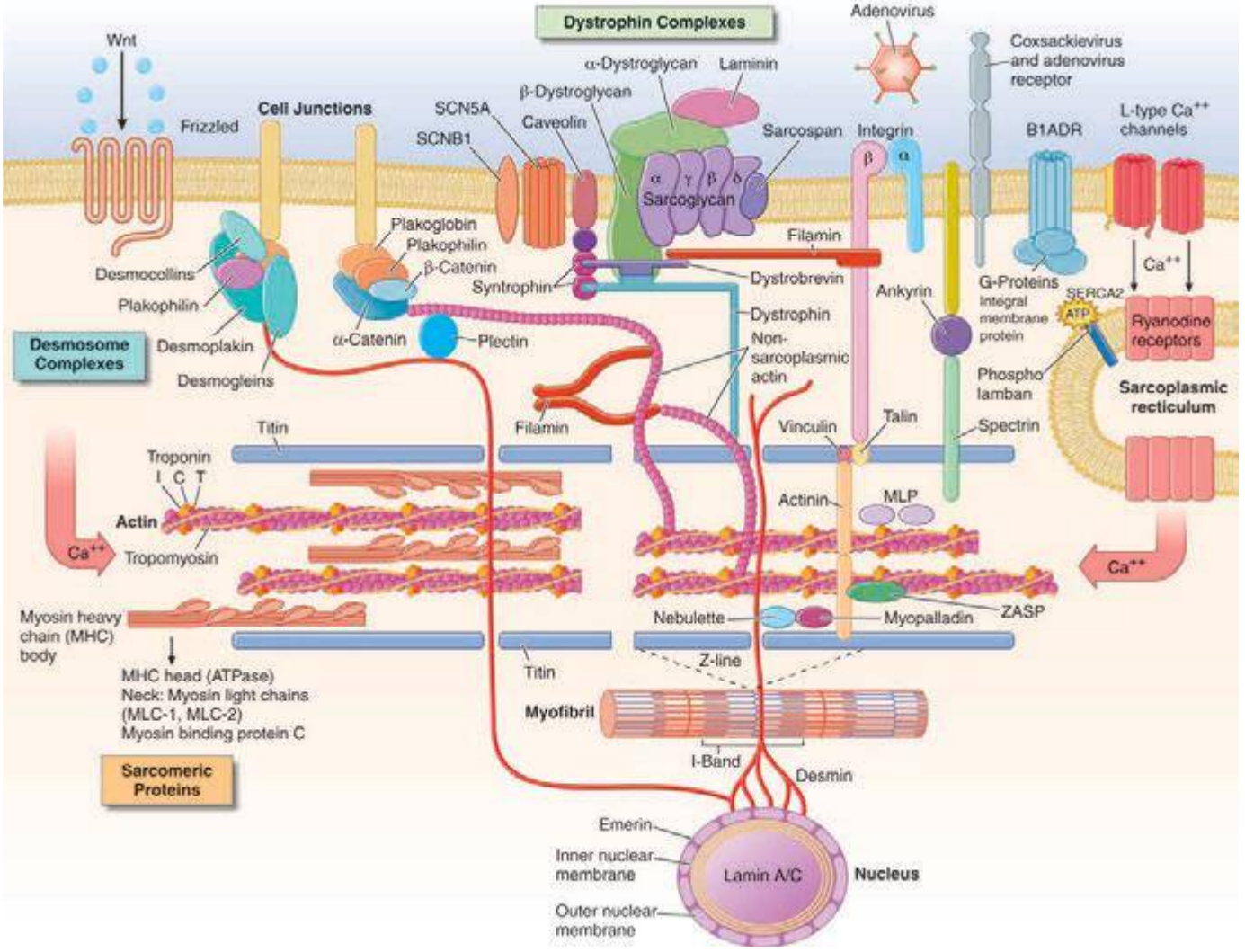

FIGURE 287-1 Drawing of myocyte indicating multiple sites of abnormal gene products associated with cardiomyopathy. Major functional groups include the sarcomeric proteins (actin, myosin, tropomyosin, and the associated regulatory proteins), the dystrophin complex stabilizing and connecting the cell membrane to intracellular structures, the desmosome complexes associated with cell-cell connections and stability, and multiple cytoskeletal proteins that integrate and stabilize the myocyte. ATP, adenosine triphosphate. *(Figure adapted from Jeffrey A. Towbin, MD, University of Cincinnati, with permission.)*

distribution of the maternal mitochondria during embryonic development. Heritable systemic diseases, such as familial amyloidosis and hemochromatosis, can affect the heart without mutation of genes expressed in the heart.

For any patient with suspected or proven genetic disease, family members should be considered and evaluated in a longitudinal fashion. Screening includes an echocardiogram and electrocardiogram (ECG). The indications and implications for confirmatory specific genetic testing vary depending on the specific mutation. The profound questions raised by families about diseases shared and passed down merit serious and sensitive discussion, ideally provided by a trained genetic counselor.

DILATED CARDIOMYOPATHY

An enlarged left ventricle with decreased systolic function as measured by left ventricular ejection fraction characterizes dilated cardiomyopathy (Figs. 287-2, 287-3, and 287-4). *Systolic failure* is more marked than diastolic dysfunction. Although the syndrome of dilated cardiomyopathy has multiple etiologies (Table 287-4), there appear to be common pathways of secondary response and disease progression. When myocardial injury is acquired, some myocytes may die initially, whereas others survive only to have later programmed cell death (apoptosis), and remaining myocytes hypertrophy in response to increased wall stress. Local and circulating factors stimulate deleterious secondary responses that contribute to progression of disease. Dynamic remodeling of the interstitial scaffolding affects diastolic function and the amount of ventricular dilation. Mitral regurgitation commonly develops as the valvular apparatus is distorted and is usually substantial by the time heart failure is severe. Many cases that present "acutely" have progressed silently through these stages over months to years. Dilation and decreased function of the right ventricle may result from the initial injury and occasionally dominate, but more commonly appear later in relation to mechanical interactions with the failing left ventricle and the elevated afterload presented by secondary pulmonary hypertension.

Regardless of the nature and degree of direct cell injury, the resulting functional impairment often includes some contribution from secondary responses that may be modifiable or reversible. Almost half of all patients with new-onset cardiomyopathy demonstrate substantial spontaneous recovery. Even with long-standing disease, some patients have dramatic improvement to near-normal ejection fractions during pharmacologic therapy, particularly notable with the β-adrenergic antagonists coupled with renin-angiotensin system inhibition. For patients in whom left bundle branch block precedes clinical heart failure by many years, cardiac resynchronization pacing may be particularly likely to improve ejection fraction and decrease ventricular size. Interest in the potential for recovery of cardiomyopathy has been