Role of the extracellular matrix in normal and diseased heart

Schematic showing meachisms for heart failure. In this example, ventricular stiffening is a runaway train where external stress throttles multiscale remodeling of myofilaments, the myocyte cytoskeleton and the extracellular matrix (ECM) that collectively impair cardiac function. External stress is sensed by the myocardium which responds by remodeling its cardiomyocytes and ECM, the ECM in turn signals cardiomyocytes to alter their contractile performance and further remodel their cytoskeleton. Yet in patients with heart failure, removing stress seldom reverses pathological remodeling (shown by blue arrows). This is because signaling between pathologically remodeled cardiomyocytes and ECM continue to reinforce each other's disease state. Much remains unknown about the molecular mechanisms of this cross-talk which makes it difficult to target therapeutically.