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Title:	Understanding the molecular and genetic basis of pericardin expression in adult Drosophila melanogaster
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Abstract:	Understanding the molecular and genetic basis of pericardin expression in adult Drosophila melanogaster Jayati Gera (PH13039) Abstract: The extracellular matrix (ECM) is an intricate three-dimensional network of macromolecules responsible for providing physical scaffolding and biochemical cues essential for tissue morphogenesis, differentiation and homeostasis. Like all other organs, the cardiac tissue is surrounded by the ECM composed mainly of collagens, laminin, fibronectin, proteoglycans, glycosaminoglycans, and elastin. The cardiac ECM is a dynamic structure as it undergoes remodeling under stress, injury and disease to potentiate inflammatory processes, myocardial protein turnover, tissue repair, and regeneration. However, sustained ECM remodeling can compromise proper diastolic and contractile functions as seen with fibrosis. In the recent past the Drosophila heart has emerged as an excellent in vivo model to provide several important insights into how the cardiac ECM undergoes developmental remodelling to ensure tissue integrity and functionality. Pericardin (Prc), which displays certain homologies to mammalian collagen IV, is a unique component of the cardiac ECM in flies. Genetic evidence suggests that Prc is not only essential for proper cardiogenesis, but also plays a crucial role for organ integrity. However, our knowledge about any regulatory mechanism for Prc production essential for cardiac homeostasis is still unmet. Our quest for the mechanism that governs Pericardin expression in adult flies has unraveled a fascinating inter-organ communication circuitry that connects the metabolic state of the renal nephrocytes (pericardial cells) in regulating cardiac function. The high levels of physiological ROS in the pericardial cells control the expression of the cytokine Upd3. In turn, Upd3 released by the pericardial cells modulates cardiac function by regulating the expression of the cardiac ECM protein, Pericardin, in the fat cells. From a broader perspective, regulation of cardiac function by pericardial cells sheds light on a robust physiological process critical for systemic homeostasis as it coordinates the rate of movement of hemolymph within the body with the filtration capacity of the pericardial cells. In a sense, this appears to be a rudimentary and evolutionarily primitive version of the heart-kidney link observed in higher vertebrates. Our further research work focuses on understanding the contribution of the peripheral organs in maintaining the high ROS levels in the pericardial cells, thereby regulating cardiac function. Moreover, our work also displays the mechanism underlying the impact of high dietary sugar in upregulating the expression of cytokine Upd3 responsible for the excessive synthesis of Pericardin from the fat cells leading to progressive cardiac fibrosis. Thus, besides unraveling an unknown paradigm of interorgan crosstalk that controls Pericardin (collagen) expression under normal physiological conditions, the outcome of my study identifies a unique metabolic control over cardiac ECM remodeling under high sugar diet conditions with far-reaching implications in disease biology.
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