Mechanisms of Insulin Action

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We now know that the pathophysiology of Type 2 diabetes involves defects in three organ systems that conspire together to produce abnormal glucose and lipid metabolism. While there is some uncertainty regarding the primary lesion, or relative importance of different tissues, metabolic defects in liver, peripheral target tissues such as fat and muscle and pancreatic β cells all contribute to the syndrome. Insulin resistance, which is defined as a state of reduced responsiveness to normal circulating concentrations of insulin, is now recognized as a characteristic trait of Type 2 diabetes, and contributes to abnormalities in all of these tissues. Even in the absence of diabetes, insulin resistance is a key feature of other human disease states. These findings suggest that studies on the molecular mechanisms underlying insulin action are crucial to further the understanding of this devastating disease. Thus, we have gathered together several renowned experts in this field to produce this monograph *Mechanisms of Insulin Action*.

These articles provide novel insight into the key issues underlying the molecular biology of insulin action and insulin resistance. De Meyts et al cover the structure and function of insulin and insulin-like growth factor receptors. Watson and colleagues outline the important events at the intersection of signal transduction and vesicle trafficking that are crucial to the stimulation of glucose uptake by insulin. Thurmond reviews the important events that occur when GLUT4 vesicles dock and fuse at the plasma membrane. Christian and Lawrence comment on the mechanisms responsible for the regulation of protein synthesis by insulin, while Clark and Newgard review those mechanisms responsible for changes in hepatic fuel metabolism. Because gene expression is so important in metabolism, Sutherland et al outline the steps that are involved in the regulation of transcription by insulin. As the primary event in metabolic control, Kulkarni describes how the beta cell is regulated by insulin, and in related work, Obici and Rossetti cover the central control of peripheral insulin sensitivity. Much progress on studies in insulin action have been made in animal models, and Oriente and Accili review transgenic and knock out models of insulin action and resistance. Finally, Courtney and Olefsky review the occurrence and treatment of insulin resistance. Together, these authors have provided a comprehensive summary of our understanding of insulin action from cellular physiology to the integration of tissue specific signaling events that are responsible for whole body glucose homeostasis.

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