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LXRs: The Key Regulators of Intermediary Metabolism in Metabolic Syndrome

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ABSTRACT

Metabolic syndrome and its various manifestations are considered to be a significant health epidemic in the developed and developing countries across the world. Metabolic syndrome is characterized by a series of metabolic abnormalities, such as central adiposity, insulin resistance, hypertension, glucose intolerance, and dyslipidemia. Patients with metabolic syndrome are at a higher risk of major complications, including fatty liver, type II diabetes mellitus, and cardiovascular diseases. Nuclear receptors are the key regulators of gene transcription, as well as several metabolic pathways. Among these receptors, LXRα and β play a major role in the regulation of lipogenesis, cholesterol/glucose homoeostasis, and inflammatory pathways through the induction or repression of target genes. In addition to metabolic homeostasis and diseases, lipogenesis and hypertriglyceridemia are regarded as the most significant adverse effects of liver X receptor (LXR) activation. Given the importance of lipid and carbohydrate metabolism and inflammation in the development of metabolic disorders, the present study aimed to review the impact of LXR signaling on the risk of metabolic syndrome and its phenotypes, with an emphasis on their potential therapeutic applications in the treatment of metabolic syndrome. In general, growing evidence supports the notion that LXRs may represent the potential drug targets for the treatment of metabolic syndrome.

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Introduction

Metabolic syndrome, also known as syndrome X or insulin resistance, refers to a series of metabolic abnormalities, such as central obesity, dyslipidemia, insulin resistance, hyperglycemia, and hypertension (1). Patients with metabolic syndrome are at a higher risk of diabetes and cardiovascular diseases compared to normal individuals (2). Statistics suggest that the prevalence of the metabolic syndrome is on the rise across the world, while the patterns vary depending on the geographical region and ethnicity. The prevalence of the metabolic syndrome has been reported to increase at an alarming rate in Asia (3).

Developing proper strategies to reduce the incidence of the metabolic syndrome requires a thorough examination of the genetic and environmental contributing factors, as well as a comprehensive knowledge of the development and pathophysiology of this syndrome. Etiology of metabolic syndrome remains unknown. Similar to many other multifactorial diseases, the full expression of the syndrome depends on a complex interaction between genetic susceptibility and environmental factors (e.g., sedentary lifestyle and

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