Metabolic Syndrome
Underlying Mechanisms and Drug Therapies

Edited by

Minghan Wang
Amgen, Inc., Thousand Oaks, California, USA

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Introduction

It has been more than 20 years since Reaven first introduced the concept of syndrome X or insulin resistance syndrome to describe the clustering of several cardiovascular risk factors. The concept has evolved over the years and is now commonly referred to as metabolic syndrome, which covers the individual metabolic abnormalities of obesity, insulin resistance, hyperglycemia, dyslipidemia (high triglycerides and low HDL), and hypertension. Patients with metabolic syndrome have increased risk of developing cardiovascular disease (CVD) and type 2 diabetes mellitus (T2DM). Despite the debates surrounding the existence and definition of metabolic syndrome, the concept has been useful in understanding the interconnections of the various risk factors that are common in a large population of patients and thereby managing the overall disease risk. From the drug discovery standpoint, all the components of metabolic syndrome are therapeutic targets for the treatment of CVD and T2DM to reduce comorbidities and overall mortality.

While there is a wealth of information concerning the clinical features and mechanisms of metabolic syndrome, putting them in the physiological context relevant to the development of therapeutics is essential for drug discovery. The goal of this book is to provide comprehensive understanding of the molecular and physiological abnormalities associated with metabolic syndrome and the therapeutic strategies for drug development. Part One is devoted to gaining an integrated understanding of the metabolic abnormalities at the tissue and pathway levels that are associated with disease states. In Part Two, metabolic syndrome is discussed at the physiological level and current therapies are summarized. These sections help lay the foundation to identify pathways and molecular targets for the development of antidiabetic therapies in Part Three. Since more than 80% type 2 diabetic patients have metabolic syndrome, a large portion of this book is devoted to antidiabetic therapies. Finally, the successes and failures in developing antidiabetic and cardiovascular drugs and lessons learned are discussed in Part Four. Although the chapters are contributed by different authors, the organization and the content of the book have been carefully designed so that the information is presented systematically. In the meantime, each chapter independently covers a subarea of metabolic or drug discovery topics, the reader has the flexibility to gain information on a specific tissue, pathway, or target in a time-efficient manner. Despite the exciting advances that have been made in developing antidiabetic and CVD therapies in the past several

decades, drug discovery in these areas continues to be a challenge. I hope this book will help the reader better understand the exciting science behind metabolic drug discovery and development and develop a greater appreciation of the complexity of metabolic syndrome as well as the treatment strategies.

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