
Preface

Twenty years after its discovery, a recombinant form of human leptin has been approved by the US Food and Drug Administration for the treatment of patients with congenital or acquired lipodystrophy. However, the promise of leptin as a general treatment for human obesity and related disorders has remained largely elusive. Nonetheless, a tremendous amount of knowledge has emerged on the biology of leptin, and additional potential areas of therapeutic application in humans are gradually coming into focus. In rodents leptin inhibits food intake, stimulates energy expenditure, reverses obesity, ameliorates insulin resistance, and accelerates sexual maturation. These potent and diverse effects have stimulated interest in exploring a role for leptin in the treatment of human metabolic disorders. This book presents current understanding of the biology and regulation of leptin, and discusses established and emerging areas of therapeutic application of leptin in humans.

Beginning with a succinct synthesis of the vast amount of work—in experimental models, in vitro systems, and other avenues—that has enriched our understanding of leptin's biology, the focus of this book shifts to a fuller consideration of the regulation and role of leptin in humans. The emphasis on human-level data is a unique feature of this book. The results of numerous studies indicate that leptin is indeed a regulated human hormone that interacts with a vast array of physiological, hormonal, immunological, and inflammatory mediators and targets. The detailed consideration of these interactions expands our understanding of the role of leptin in human metabolic pathophysiology.

Next follows a comprehensive presentation of the therapeutic trials of recombinant leptin replacement in human subjects with congenital leptin deficiency, diagnosed either in childhood or during adulthood; leptin supplementation in lean and obese leptin-replete subjects; leptin therapy in patients with lipodystrophy; and other emerging therapeutic areas, including treatment of hypothalamic amenorrhea and emerging novel combination regimens of leptin and other biogenic peptides. Unanswered questions and future directions in leptin research are highlighted in the Foreword by Dr. Jeffrey Friedman and throughout the volume. A fuller understanding of the regulation of leptin, under physiological and pathological conditions, is a critical prerequisite to its rational deployment in the treatment of diverse human disorders.

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Memphis, TN, USA

Sam Dagogo-Jack

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