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Kisspeptin Signaling in Reproductive Biology

 Springer

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Preface

We were lucky to get into the kisspeptin “field” during its early days, though we had different avenues of entry. In early 2004, Sasha was a postdoctoral fellow in Dr. Emilie Rissman’s lab in Virginia, where he was studying the effects of various reproductive neuropeptides, such as GALP and GnRH variants, on sex behavior. Dr. Rissman asked whether Sasha would be interested in studying sexual behavior and sexual differentiation in a newly created transgenic mouse that was lacking an orphan receptor called GPR54. This was just months after several high-profile (and soon-to-be seminal) papers had been published linking this receptor—and its ligand kisspeptin—to reproductive status in humans and mice. The prospect of studying this new, highly uncharacterized reproductive factor was too enticing to pass up.

Meanwhile, across the country in Seattle, Washington, Jeremy was also conducting postdoctoral research in the lab of Dr. Robert Steiner, who had also recently stumbled upon the exciting new kisspeptin system and was currently testing its gonadotropin-releasing ability and sex steroid regulation in mice. Such was our initial foray into kisspeptin reproductive biology, and our paths soon crossed when Sasha headed west in 2005 to work in the Steiner lab. Since then, much has been learned—by us and many others—about kisspeptin and GPR54. Satisfyingly, much of what the field has learned in the past decade has come from a growing community of international scientists and labs situated all around the globe, not to mention from a large variety of species and animal models. Indeed, kisspeptin has now been shown, by numerous investigators, to be important for puberty and reproduction in not only humans and mice, as originally demonstrated in 2003, but in a great assemblage of vertebrate species, ranging from mammals of all shapes and sizes down to frogs and fish.

As we rapidly approach the 10-year anniversary of the “discovery” of kisspeptin’s role in reproductive biology, we believe this textbook is particularly timely. The goal was to critically highlight—in a single cohesive volume—the functions and regulation of kisspeptin as it relates to reproductive biology. To this end, we present in-depth reviews of a wide range of kisspeptin topics, including (but not limited to) hormone-releasing effects of kisspeptin in a variety of species (including humans); consequences and underlying mechanisms of impaired kisspeptin systems;

utility and benefits of specific kisspeptin experimental “tools” (including a variety of new mouse models and novel chemical analogues); development of the kisspeptin system; the role of kisspeptin in puberty; the regulation of kisspeptin circuits by hormones, photoperiod, circadian signals, metabolic conditions, and stress, as well as by other reproductive neuropeptides; alterations in kisspeptin induced by endocrine-disrupting chemicals; and the newest kid on the block: electrophysiological properties of kisspeptin neurons. In addition, this book emphasizes several larger themes, including the importance and benefits of comparative biology (despite—or perhaps because of—the occasional “species differences”), as well as the value of using both molecular and physiological analyses to advance the field, not to mention the growing importance of bedside-to-benchside (and back) research. Another prominent message throughout the book is that there is still much to learn. While a good deal of the “low-hanging fruit” on the kisspeptin experimental tree has now been plucked, there are still many intriguing questions to be answered and many fundamental gaps in our knowledge that demand filling. These numerous key areas of future direction underscore the notion that, while we have come incredibly far in the past decade, we still have a long way to go to solve some of reproductive biology’s greatest puzzles. Thus, our aim for this book is to summarize and celebrate the key findings from the past decade of kisspeptin research, as well as stimulate both future experimentation and further refinement of clinical use of kisspeptin for medical and therapeutic endeavors.

In sum, we hope this cohesive and timely volume of kisspeptin reviews will be a valuable educational and reference tool, useful for both the seasoned kisspeptin researcher and clinician, as well as for new students and doctors wishing to dive into the kisspeptin pool. We believe the comprehensive discussion herein of the numerous kisspeptin topics will provide a fair, yet critical, assessment of the current state of the kisspeptin field, as well as identify key areas of targeted future research and clinical applicability. Indeed, as we pass the first 10-year marker on our kisspeptin journey, it is likely that many of the open questions identified throughout this book will guide the next series of exciting experimental and therapeutic kisspeptin ventures well into the next decade.

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Alexander S. Kauffman
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