In this book, *The Life Cycle of the Corpus Luteum*, we try to provide state-of-the-art knowledge of the corpus luteum, throughout its lifespan, in different species.

The corpus luteum is a fascinating endocrine organ that is essential for fertility in mammals. Recent developments in understanding the lifespan of the corpus luteum provide new insights for reproductive biologists and also provide insights into tissue dynamics that translate to other research disciplines (e.g., developmental biology, vascular development, metabolic disorders, cancer). More research on the corpus luteum is needed to provide clinicians, veterinarians, researchers, and livestock producers with the information they require to successfully intervene in human, and other mammalian, fertility outcomes.

The ovarian corpora lutea (yellow bodies) were first named by Marcello Malpighi and then described by Regnier de Graaf in the late 1600s. Two centuries later, Prenant suggested that the corpus luteum may serve as a gland that produces substances which regulate pregnancy. This observation was confirmed rapidly by several groups in the early 1900s, and the biologically active substance progesterone was crystallized and characterized nearly simultaneously in 1934 by four independent groups. The corpus luteum is a temporary endocrine structure that forms within the ovary after ovulation and is essential to the establishment and early maintenance of pregnancy in most mammals, including humans, primates, livestock, rodents, canines, and felines. The ephemeral corpus luteum is generally considered to have three phases during its life cycle: formation, maintenance, regression, and a fourth potential phase: rescue and sustained function during pregnancy. Each stage of the corpus luteum life cycle has unique regulatory and signaling events that differentiate each stage from another. The chapters in this book review current research advances into each phase of the life cycle of the corpus luteum.

Enormous structural reorganization occurs as the postovulatory follicle transitions to a highly vascularized corpus luteum. Based on its size when fully functional, the blood supply to the corpus luteum exceeds that of most other organs. Much interest has been focused on factors and the cellular mechanisms that contribute to the development of new blood vessels in the corpus luteum and their importance to the function of the gland. Immune cells and factors released from these cells
contribute to tissue remodeling and new blood vessel development. As the process of angiogenesis is important in cardiovascular disease, inflammatory responses, and cancer biology, understanding how the vascular supply to the corpus luteum is regulated may provide unique insights that translate to other research disciplines. The chapters provided by Robert S. Robinson (Chap. 1), Kiyoshi Okuda, and Akio Miyamoto (Chaps. 2 and 6, respectively) provide new insight into the process and regulation of angiogenesis and immune cell infiltration in the corpus luteum.

Luteinizing hormone (LH) surge is responsible for initiating the differentiation of the somatic cells of the ovarian follicle (theca and granulosa cells) into the small and large steroidogenic cells of the corpus luteum. The newly formed corpus luteum is an extremely active gland that produces enormous amounts of the hormone progesterone, which provides an intrauterine environment that supports implantation, placentation, and fetal–placental growth and development. Insufficient progesterone secretion early in the first trimester is associated with pregnancy loss and is attributed to premature loss of luteal function. To further highlight the significance of progesterone to fertility research, studies indicate that progesterone acting locally via its nuclear receptor acts to promote ovulation and serves as a luteal cell survival factor. Therefore, understanding the control of progesterone synthesis is crucial for control of fertility in mammals. The chapters by Holly A. LaVoie (Chap. 3) and John S. Davis (Chap. 4) focus on understanding the control of steroidogenic processes and ovarian metabolic events and their potential for controlling progesterone synthesis. The chapter by Jan Kotwica et al. (Chap. 5) discusses the impact of steroid receptors and orphan nuclear hormone receptors on luteal function. Reproductive strategies vary considerably among species; these are especially evident with regard to the ovarian cycle and luteal function and lifespan. The chapter by Marta Tesone et al. (Chap. 7) reviews the rodent corpus luteum, and the chapter by Mariusz Pawel Kowalewski (Chap. 8) reviews the canine and feline corpus luteum, describing unique features of corpus luteum development and regression.

In the absence of pregnancy, the corpus luteum will regress so the next reproductive cycle can begin. The process of luteolysis is associated with a marked reduction in progesterone production and intense tissue remodeling, resulting in the loss of steroidogenic cells and the blood supply; and an increase in the deposition of fibrotic connective tissue, forming the so-called corpus albicans (white body). Luteolysis is accompanied by the influx of immune cells and the activation of inflammatory signaling pathways that act in concert with luteolytic factors to inhibit progesterone and remodel the corpus luteum. Luteal regression in ruminants is covered in the chapter by Rina Meidan et al. (Chap. 9), and luteal regression in pigs is discussed in the chapter provided by Adam J. Ziecik (Chap. 12). Understanding how pregnancy hormones act to block corpus luteum regression gives us insights into the prevention of fibrotic processes observed in other tissues during inflammation and disease states and may provide insight into mechanisms responsible for tissue repair and regeneration. The impact of the corpus luteum in women’s health is explored in the chapter by W. Colin Duncan (Chap. 13). If pregnancy occurs, a hormone released from the developing conceptus (embryo and its associated membranes) blocks or rescues corpus luteum structure, function, and blood supply. The interruption of
luteolysis allows the corpus luteum to support the pregnancy: in women, this hormone is hCG. The chapter by Richard Stouffer and Jon D. Hennebold (Chap. 10) reviews corpus luteum rescue from luteolysis in primates. In cows and sheep this factor is interferon tau, which acts to prevent uterine production of PGF2α and possibly acts by direct actions on the corpus luteum. In Chap. 11, Thomas R. Hansen discusses corpus luteum maintenance during early pregnancy of ruminants, and Adam J. Ziecik (Chap. 12) presents a chapter devoted to maintenance of the corpus luteum in early pregnancy in pigs.

I thank the authors for contributing their time, effort, and expertise to this book and hope the information presented will be a valuable source of the current state of knowledge for experts as well as beginners who wish to pursue future research in this exciting area. I thank John Davis and Heather Talbott (University of Nebraska Medical Center) for their help in composing these introductory notes.

Rina Meidan
Rehovot, Jerusalem, Israel
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