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Ovarian Follicular Development a... n

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Ovarian Follicular Development and Function

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Preface

This meeting was possible only because the Center for Population Research of the National Institute for Child Health and Human Development chose to provide from highly limited discretionary funds sufficient support to permit the attendance of many of the participants from the United States and Canada. We hope this book will justify the wisdom of that decision and will encourage them to continue to support similar workshops in the future. Grateful appreciation is also extended to Mr. Antonio Scarpa of Serono Ltd. who made it possible for several European scientists to attend. In addition, the editors wish to acknowledge the special efforts of Dr. Robert B. Jaffe in arranging for the meeting to be held in Santa Cruz and the efforts of other members of the Organizing Committee (Dr. Georgianna Jagiello, Dr. Bruno Lunenfeld, Dr. A.V. Nalbandov, Dr. Griff T. Ross, Dr. Kenneth J. Ryan, and Dr. Robert J. Ryan) whose planning assistance and chairing of sessions contributed to all phases of the workshop. Finally, we wish to give special acknowledgment to Ms. Susan Bareis. To a large extent, her organizational efforts were responsible for making this workshop so successful.

Acknowledgments

Few areas in biology have received greater attention in recent years than that of ovarian follicular development and function. Buried within the complex of interactions that result in the selection for ovulation of but a very few oocytes from the thousands available are the potentialities for fertility regulation at many levels. The problems of hormonally and nonhormonally controlled progressive functional and morphologic differentiation of thecal cells, granulosa cells and oocytes; exogenous and endogenous hormonal regulation of receptors for protein and steroid hormones; eventual death through atresia or rescue by ovulation and luteinization are complex but the solutions will be highly relevant to our understanding not only of reproductive biology but of eucaryotic regulatory biology in general. These problems have relevancy for biologists in many disciplines.

Largely as a consequence of advances in technology, work on these problems has been progressing rapidly in many unrelated disciplines. In an attempt to bring together representatives of these disciplines, to define important problems ripe for experimental investigation, and to achieve collectively a better understanding of the latest developments in the field, a workshop was held at the University of California at Santa Cruz. The workshop consisted of eight formal presentations, each followed by a number of brief contributions and an active discussion. To facilitate discussion written versions of all presentations and contributions were circulated to the participants in advance of the meeting. For this publication the presentors, working with typed transcripts, summarized the discussion following their presentation. Thus this book consists of eight sections, each prepared by a different presentor and each consisting of the presentor's text, contributions largely submitted in advance of the workshop, and a brief summary reflecting the discussions following each presentation. If the readers of this book realize even a small amount of the excitement and understanding achieved by participants at the workshop, this publication will have fulfilled its purpose.

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Some Aspects of Early Follicular Development

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Follicular development represents one of the essential functions of the ovary. It depends on the interplay of several control mechanisms, which lie partly outside the ovary--mainly in the pituitary and the central nervous system--and partly within the ovary and the follicle itself.

Follicular development has many facets, including (1) follicular organization, which establishes the pool of nonproliferating small follicles and (2) follicular growth, which begins with the follicle's emergence from the nongrowing state and at times results in the cyclic event of ovulation, but most often ends in atresia.

FOLLICULAR ORGANIZATION

The Establishment of the Nonproliferating Follicular Pool

The majority of the germ cells are found enclosed in small nongrowing follicles in the ovary and form a most important (and perhaps a most neglected) portion of the total follicle stock. How is the stock of nonproliferating follicles established? In most mammals at birth the oocytes are lying close together in cell nests and are the most conspicuous within the ovary at that time, although they share the space within the organ with a fine and intricate network of cords and tubules, i.e., the intraovarian rete. Byskov and Lintern-Moore (1973) have shown that the oocytes actually lie within this rete system, and that cells from the rete become attached to the surface of the oocyte, thus establishing the first granulosa cells. In the early stage of follicular formation, there are open connections between the forming follicles and the rete tubules, but at a

certain point the basement membrane surrounding the oocyte and the cells that have become attached to it closes, and the follicle becomes an independent unit. These units, consisting of a small oocyte, the cells attached to it, and the basement membrane surrounding them, become the pool of nonproliferating follicles, from which the follicle emerges when it starts to grow.

The rete ovarii within which the oocytes originally lie represents the rest of mesonephric tubules, which in the male develops into the epididymus. The epididymus is known to have the ability to transform steroid precursors such as acetate and cholesterol into testosterone as well as to change testosterone into various metabolites (Fawcett et al., 1969; Rivarola and Podesta, 1972). Therefore, it is understandable that the stroma of the ovary, part of which consists of mesonephric tubule derivatives, i.e., the rete, might later become implicated in androgen metabolism.

Influence of the Small Follicular Pool on Growth Initiation

Very little is known about the nonproliferating small follicles and their influence on ovarian physiology. One of the few known facts is that their total number has an influence on the number of follicles that start to grow. The larger their number, the larger the number of follicles that begin to develop (Krohn, 1967; Krarup et al., 1969). With advancing age, the number of small follicles is reduced (Jones and Krohn, 1961) and so is the number of follicles that start to grow per unit time (Pedersen, 1972). That the pool size, i.e., the number of small, nonproliferating follicles, is apparently the main controlling factor in the immature animal can be shown by artificially reducing their number in infancy. This can be accomplished by giving a single small dose (20 R) of radiation or a single oral dose of 9:10 dimethyl 1:2 benzanthracene (DMBA) to young mice. The immediate reduction of the number of small follicles is followed by a secondary reduction in the number of developing follicles (Peters, 1969a; Krarup et al., 1969). How this control is mediated is at present unknown, and whether the mass of small follicles acts via the feedback mechanism or directly within the ovary cannot be determined at this time.

However, that the (small) follicular pool size is not the only controlling factor is likely if we consider the number of follicles that start to grow in the mouse ovary per 24 hr at different ages (Pedersen,