Preface

The question as to why individuals of the same species can develop in two quite different forms, males and females, already intrigued classical Greek philosophers, but it was not until the mid-20th century when science significantly advanced our understanding of mammalian sex differentiation. Two outstanding discoveries opened the doors for subsequent research: first, the demonstration by Jost that testes are essential for male development, and when absent, the result is a female, thus showing that the phenotypic sex of mammals depends on gonadal sex; secondly, the new air-drying cytogenetic techniques unravelled the karyotypes of diverse human sex chromosome aneuploidies, showing that testis development depends, in turn, on the presence of a Y-linked gene encoding a testis-determining factor, the elusive *TDF*. In this way, the crucial importance of investigating the genetic control of gonad development was clearly established.

Afterwards, a long race began for the isolation of the human *TDF* (*Tdy* for the mouse), in which several candidates, including the HY antigen, the Y-linked Bkm DNA sequences and the *ZFY* gene, were consecutively proposed and ruled out. The use of positional cloning techniques with human patients showing different cases of both XY and XX sex reversal led ultimately to the identification of the *SRY* gene in 1990, which can indeed be equated to *TDF*. However, unlike the cases of *Drosophila* or *Ceanorhabditis*, this fact did not start a period of rapid elucidation of the rest of the process of sex determination in mammals. Rather, advances in this field proceeded more slowly than expected.

Twenty-two years later, this themed issue of *Sexual Development* presents a series of articles describing the state

of the art of the genetic control of gonad development in mammals and other vertebrates. Ungewitter and Yao open this compendium by reviewing the cellular mechanisms governing the formation of the testes and ovaries and focussing on the compartmentalization processes that give rise to the formation of the testicular cords and ovarian follicles. Next, two articles review the genetic mechanisms controlling gonad development in mammals. Sekido and Lovell-Badge summarize our current understanding of genetic pathways of mammalian testis determination with special attention to Sertoli cell differentiation. Similarly, Tevosian reviewed the genetic clues of ovarian development, a process that has received less attention than testis development. Moreover, some particular aspects of mammalian gonad development, including the role of the germ-cell lineage or that of steroid hormones have also been reviewed in two separate articles. Bowles and Koopman summarize the mechanisms regulating sex-specific germ-cell differentiation in mice, with a special focus on the control of meiosis induction and prevention in developing ovaries and testes, respectively. Morohashi et al. have reviewed the origin and function of most steroid hormones, the differentiation of steroidogenic cell lines in both testes and ovaries and their role in the development of reproductive organs.

The issue continues with a group of articles dealing with the regulation of sex differentiation and gonad development in other vertebrates. Ayers et al. discuss sexual differentiation in chick embryos, highlighting those genes that may play a conserved role in this process. Merchant-Larios and Díaz-Fernández analyse the wide variety of temperature sex determination mechanisms currently known to operate in reptiles. Nakamura questions

whether a sex-determining gene(s) is necessary for sex determination in amphibians and suggests that steroid hormones may be the key factor for sex differentiation in these animals. Kobayashi et al. review the mechanism of sex determination and differentiation in fish, which is characterized by high diversity and plasticity, including various types of sex change occurring in hermaphrodite fishes.

The last block of articles in this volume deal with some other noteworthy aspects of the control of gonad development. Two of these refer to situations and cases in which normal gonad differentiation is not reached. Bashamboo and McElreavey discuss recent progress on the genetic anomalies that interfere with the differentiation of the somatic cells in the human gonad, giving rise to a variety of disorders of sex development (DSD), and Jiménez et al. analyse the most significant cases of natural exceptions to normal gonad development in other mammalian spe-

cies, including both classical and more recent reports. Finally, the Evo-Devo touch to this themed issue is given by Pires-da Silva and Parihar, who reviewed how the germline and somatic gonad have evolved in nematodes.

This themed issue of *Sexual Development* was conceived in the hope that readers of this booming journal who are interested in the control of gonad development will find here a useful source of updated information on this fascinating area of knowledge. I feel indebted to all the authors of this issue for their effort to provide high-quality manuscripts and to the reviewers who contributed to improve them, for their time and expert advice. Finally, I would like to give special thanks to Dr. Michael Schmid, the Editor-in-Chief of the journal, for his offer to lead this project and for his continuous help and advice, and mainly for becoming a friend.

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