Preface

In this monograph we focus on the molecular mechanisms through which hormones regulate reproductive activity and function in fish. Over the past decade or so this field has changed dramatically. Although it was known for many years that GnRH promotes reproductive activity by stimulating production and release of the pituitary gonadotropins, recent discoveries of multiple forms of GnRH with wide expression patterns have complicated the picture. Cloning and localization studies of the various isoforms have revealed that two or three forms are expressed in the brain alone, but only one of these is found in the preoptic area and this comprises the major regulator of the gonadotropins. This has led to interesting studies on the differential regulation of expression of these genes (Sherwood and Adams). At the pituitary gonadotrope, the GnRH binds a seven-transmembrane G-protein coupled receptor which was seen in mammals to lack the C-terminal intracellular tail. This was shown to affect its internalization, but not its desensitization. The cloning of the catfish GnRH-R that does contain a C-terminal intracellular tail, as do other non-mammalian receptors, and subsequent structure-function studies have done much to elucidate the receptor-ligand interactions and pharmacology of these receptors (Blomenröhr *et al.*).

We now know that the pituitary produces two gonadotropins, but it was only in the late 1980s and early 1990s that the cDNAs encoding the teleost equivalent of the follicle stimulating hormone (FSH), initially known as GtH I, and luteinizing hormone (LH or GtH II), were first isolated. Further studies in additional species showed that the structures of the two fish gonadotropins largely parallel the mammalian LH and FSH, while their circulating levels and actions indicate they are true homologs. This has established the duality of gonadotropins in teleost fish and opened up new areas of research into the mechanisms through which they are differentially regulated. Molecular analysis of the regulatory regions of these genes has been somewhat elusive, owing to difficulties in isolating these genes, but the field is rapidly advancing. The Chinook salmon LHβ gene promoter has been particularly well studied and shows interesting variations from the conserved mammalian LHβ genes, while similar studies are underway on the FSHβ gene (Chong *et al.*). A part of the differential regulation of the gonadotropins undoubtedly comes from opposing effects of activin which stimulates FSHβ expression and, perhaps uniquely in fish, has an inhibitory effect on the LH. At the level of the gonad, the activin βA is stimulated by the gonadotropins and, in turn, it powerfully stimulates oocyte maturation (Ge).

The gonadotropins stimulate steroidogenesis through an elaborate pathway of steroidogenic enzymes. The starting point of this pathway is the StAR enzyme which mobilizes cholesterol and is expressed in a wide range of tissues. In mammals StAR expression results from activation of cAMP, although this may differ in teleosts. As the fish progress through reproductive development, the steroid production shifts due to alterations in the levels of the relevant steroidogenic enzymes from androgen/estrogen production to producing primarily progestogens (Young *et al.*). The resulting circulating steroids stimulate gametogenesis, gamete release and they affect reproductive behavior. These effects are mediated through specific steroid hormone receptors, of which the estrogen receptor (ER) has been studied in most detail. In fact, two distinct estrogen receptors and several isoforms are present in fish, and many show tissue restricted expression. In this way estrogen can exert specific effects on its target genes, some of which are mediated through synergistic interactions of ER with factors activated by alternatively stimulated pathways (Menuet *et al.*).

In females, a vital role of estrogen is stimulation of the production of vitellogenin which provides nutrition for early development of the larvae. Although this gene is highly sensitive to stimulation by estrogen, the ER binding sites differ considerably from the consensus, yet are clearly involved in transactivation by ER. Subsequent to its production, the vitellogenin must then be transported into the oocytes where the protein is cleaved into yolk proteins for consumption by the young (Ding). In some teleost species, as in mammals, estrogen also stimulates production of prolactin which has diverse roles in reproduction of mammals and fish, the latter of which have only partially been elucidated but may include regulating reproductive behavior and steroidogenesis (Le Rouzic and Prunet).

Although this field is constantly expanding and no work could present a complete picture, this volume presents an up-to-date picture of some of the recent advances in molecular mechanisms involved in regulating fish reproduction and will be of interest those working in or new to the field.