Ontogeny of FSH receptor messenger ribonucleic acid transcripts in relation to FSH secretion and testicular function in sheep

T A Yarney, M H Fahmy[1], M R Sairam, H Khan and **E A Macdonald**

Reproduction Research Laboratory, Clinical Research Institute of Montreal, Montreal, Québec, Canada H2W 1R7

[1]Research Branch, Agriculture and Agri-Food Canada, Dairy and Swine Research and Development Centre, Lennoxville, Québec, Canada J1M 1Z3

(Requests for offprints should be addressed to T A Yarney, Reproduction Research Laboratory, Clinical Research Institute of Montreal, 110 Pine Ave West, Montreal, Québec, Canada H2W 1R7)

ABSTRACT

The role of alternative splicing of the FSH receptor gene in the generation of FSH receptor proteins and testicular function remains an enigma. To address this issue, this investigation was conducted to determine variations in the expression of alternate FSH receptor mRNA transcripts in relation to changes in FSH release, hormone binding activity and testicular function during pubertal development of ram lambs from two genotypes of sheep (Romanov and a cross between Booroola × DLS) with different sexual precocity. Serum 17β-estradiol and testosterone concentrations were used as indices of Sertoli cell and testicular function. The results indicated that increases in Sertoli cell and testicular function normally seen during pubertal development are accompanied by age-dependent reductions in concentration of functional FSH receptors, as determined by binding of iodinated FSH to testicular membrane preparations. During the course of these changes, FSH release was either maintained at a steady level in Romanov lambs or it was gradually reduced in the Booroola × DLS cross, thus indicating that the testis had become more responsive to hormonal signal. This acquisition of heightened sensitivity was also associated with contrasting changes in the level of expression of FSH receptor mRNA transcripts. For both genotypes of sheep, 5 distinct species of mRNA transcripts of approximately 1·1, 1·5, 2·0, 2·5 and 6·5 kb were highly expressed from 11 to 22 weeks of age. Amongst these transcripts, the 1·1 kb molecular species was the most abundant. Specific probing for a previously cloned transcript called 151A1 representing the first 4 exons of the FSH receptor gene revealed a paradoxical increase in the level of expression from 11 weeks up to a maximum at 18-22 weeks of age for both genotypes. Collectively, the results indicated that contrasting changes in the production of specific alternatively spliced mRNA transcripts may mediate changes in FSH receptor expression which apparently accounts for the augmentation in sensitivity and function of the testis during pubertal development. Furthermore, the data provide the first important indication that the novel truncated transcript (151A1), which predictably encodes a soluble protein of either intra- or extracellular fate, could be physiologically relevant.

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INTRODUCTION

Over the years, a number of experimental approaches have been used to establish the importance of the pituitary glycoprotein hormone, follicle-stimulating hormone (FSH), as an essential hormone for normal development and mature function of the gonads in both sexes. In the male, it stimulates steroidogenesis in Sertoli cells (Dorrington *et al.* 1978) and the production of a variety of testicular proteins which facilitate Sertoli cell differentiation and spermatogenesis during pubertal development (Bardin *et al.* 1988). FSH may also be required for quantitative production of spermatozoa in adulthood but this appears to be species-dependent (Sharpe 1989, McLachlan *et al.* 1995). Although there are unsubstantiated reports implicating action of FSH on spermatogonia lining the periphery of

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