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Expression, action, and regulation of transforming growth factor alpha and epidermal growth factor receptor during embryonic and perinatal rat testis development

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The objective of the current study was to extend previous observations and examine the expression pattern and effects of transforming growth factor alpha (TGFalpha) and epidermal growth factor receptor (EGFR) on embryonic testis morphogenesis and growth. The expression of TGFalpha was determined after morphological sex determination (seminiferous cord formation at embryonic day 13 [ED13]) through perinatal testis development (postnatal day 5 [PD5]) with a quantitative reverse transcription-polymerase chain reaction procedure. Expression of messenger RNA (mRNA) for TGFalpha appeared to be more dynamic during testis development when compared with the expression of mRNA for EGFR. Message for TGFalpha was reduced at ED16 and PD4, and was elevated at PD0 during testis development. In contrast, EGFR mRNA levels were negligible at ED15 and were elevated constitutively from ED16 through PD5. Immunohistochemistry was conducted at ED14, ED16, ED19, PD0, PD3, and PD5 to localize cellular expression of both TGFalpha and EGFR. At ED16, positive staining for EGFR was localized to the cords, and by ED19, was mainly in the cords with slight expression in the interstitium. From PD0 to PD5, positive staining for EGFR was detected in the germ, Sertoli, and interstitial cells. Immunohistochemistry for TGFalpha detected localization at ED14 and ED16 to the Sertoli cells and to specific cells in the interstitium. From ED19 through PD5, TGFalpha was detected in the Sertoli, germ, and interstitial cells, and in endothelial cells within the interstitium. To determine the effects of TGFalpha on embryonic testis growth and seminiferous cord formation, ED13 testis organ cultures were treated with sense and antisense TGFalpha oligonucleotides. Antisense TGFalpha inhibited testis growth by 25%-30% in ED13 testis organ cultures when compared with sense oligonucleotide control pairs. To examine the effects of TGFalpha on perinatal testis growth, PD0 testis cultures were treated with different doses of TGFalpha. TGFalpha increased thymidine incorporation into DNA in PD0 testis cultures. Therefore, TGFalpha appears to have actions on both embryonic and perinatal testis growth. The regulation of TGFalpha and EGFR mRNA levels were examined using PD0 testis cultures treated with hormones that stimulate testis growth. Follicle-stimulating hormone (FSH) stimulated ($P < .05$) and testosterone tended to stimulate ($P < .07$) mRNA expression of EGFR. Epidermal growth factor stimulation of PD0 testis cultures did not affect levels of mRNA expression for EGFR, but did suppress expression of

mRNA for TGFalpha. These results taken together demonstrate that TGFalpha can act to regulate early embryonic and perinatal testis growth. Furthermore, TGFalpha and EGFR expression can be regulated through growth stimulatory hormones such as FSH and testosterone.

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