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## JOURNAL ARTICLE

# Identification and regulation of receptor tyrosine kinases Rse and Mer and their ligand Gas6 in testicular somatic cells

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Receptor tyrosine kinases act to convey extracellular signals to intracellular signaling pathways and ultimately control cell proliferation and differentiation. Rse, Axl, and Mer belong to a newly identified family of cell adhesion molecule-related receptor tyrosine kinase. They bind the vitamin K-dependent protein growth arrest-specific gene 6 (Gas6), which is also structurally related to the anticoagulation factor Protein S. The aim of this study is to investigate the possible role of Rse/Axl/Mer tyrosine kinase receptors and their ligand in regulating testicular functions. Gene expression of Rse, Axl, Mer, and Gas6 in the testis was studied by reverse transcriptase-polymerase chain reaction (RT-PCR) and Northern blot analysis. The results indicated that receptors Rse and Mer and the ligand Gas6 were expressed in the rat endothelial cell line (TR1), mouse Leydig cell line (TM3), rat peritubular myoid cell line (TRM), mouse Sertoli cell line (TM4), and primary rat Sertoli cells. Axl was not expressed in the testicular somatic cells by RT-PCR or Northern blot analysis. The highest level of expression of Gas6 messenger RNA (mRNA) was observed in the Sertoli cells, and its expression was responsive to the addition of forskolin in vitro. The effects of serum, insulin, and transferrin on Gas6 expression by TM4 cells were examined. It was shown that they all exhibited an up-regulating effect on Gas6 expression. The forskolin-stimulated Gas6 expression was accompanied by an increase in tyrosine phosphorylation of the Rse receptor in vitro, suggesting that Gas6 may exhibit an autocrine effect in the Sertoli cells through multiple tyrosine kinase receptors. Our studies so far have demonstrated that tyrosine kinase receptors Rse and Mer and their ligand Gas6 are widely expressed in the testicular somatic cell lines and may play a marked role in promoting testicular cell survival.

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