BASIC SCIENCE: GENE REGULATION AND STRUCTURE

195

page 112
ENDO 2000
THE ENDOCRINE SOCIETY

437 *Gene Expression: Reproductive Biology Poster Session, Wednesday, 6/21, Board 48*

Molecular Characterization of a Human Homolog of the Rat A1 Gene. Andreas Scorilas, Lianna G Kyriakopoulou, George M Yousef, Eleftherios P Diamandis, [1]*Pathology and Laboratory Medicine, Mount Sinai Hospital;* [2]*Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, ON, Canada*

Using positional candidate gene analysis, we were able to identify a novel gene that maps on chromosome 19q13.3-19q13.4. EST analyses, were used to delineate the genomic organization of the gene and predict a putative mRNA coding region. Sequence analysis of the genomic clones containing the gene, revealed an 82% nucleotide identity to the rat A1 gene (rA1). Thus the gene will be referred to as human A1 (hA1). In rat as well as in yeast, the A1 protein has been shown to be a member of the serine/arginine-rich (SR) family of proteins. The SR and the SR-related proteins have been shown to regulate splicing by virtue of their association with the C-terminal domain of the RNA pol II. The hA1, spans a 13.7 Kb of genomic sequence on chromosome 19 and is formed of 11 coding exons and 10 intervening introns. Our data indicate that the hA1 gene is transcribed in a centromeric to telomeric direction. RT-PCR analyses have shown that the hA1 gene is expressed at high levels in pancreatic tissue as well as in testicular, prostatic, mammary and adrenal gland and in the uterus. We have performed precise mapping to localize the hA1 gene on chromosome 19 in relation to known neighboring genes. Our studies localize the hA1 gene in a region where other cancer- and steroid hormone-regulated genes have been identified. Thus we speculate that this gene may also be involved in the pathogenesis and/or progression of prostate and/or breast cancer and possibly other malignancies. In addition, expression of the hA1 gene might be regulated by steroid hormones. Therefore, we are currently investigating the expression of the hA1 gene in the breast and prostate carcinoma cell lines, LNCaP and BT-474 that have been stimulated by estrogens and androgens.