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CLONING OF A HUMAN GENE, ENCODING A MEMBER OF THE SER/ARG-RICH FAMILY OF PROTEINS THAT INTERACT WITH RNA POL-II

Scorilas, A., Kyriakopoulou, L., and Diamandis, E.P. Department of Pathology and Laboratory Medicine, Mount Sinai Hospital, and Department of Laboratory Medicine and Pathobiology, University of Toronto, Toronto, Ontario, Canada

Objectives: Identification and characterisation of the human homologue of the rat A1 gene which may be involved in the pathogenesis of various human cancers.
Methods: Positional cloning gene analysis was employed to characterize in detail a large region of chromososme 19q13.3 that has been shown to contain known oncogenes. Screening of expressed sequence tags (ESTs) was used to delineate the genomic organization of a novel gene and determine its splicing sites.
Results: The novel gene spans 16.7 Kb of genomic sequence it is formed of 11 coding exons and 10 intervening introns and it is transcribed from telomere to centromere. The predicted amino acid sequence showed an extensive identity (78%) to the rat A1 protein which is a member of the Ser/Arg-rich protein family. Members of this family in rat, have been shown to interact with the C-terminal domain of the large subunit of the RNA polymerase II. Thus we speculate that the newly cloned gene is the human homologue of the rat A1 gene. RT-PCR analysis has shown that hA1 gene transcripts are expressed in prostate, thymus, lung, testis, uterus, colon and thyroid but not ovaries. Preliminary data suggest that this gene is overexpressed in a subset of ovarian tumors. Furthermore, studies with the steroid hormone receptor-positive breast carcinoma cell line BT-474 show that this gene is upregulated by estrogens and progestins and to a lesser extend by androgens.
Conclusions: The new gene is the human homolog of the rat A1 gene. It is up-regulated in ovarian cancer and it is also regulated by steroid hormones.