

EPIDEMIOLOGY 6: Genetic Susceptibility II

#2668 Dinucleotide Repeat Length Polymorphism on the 3' Untranslated Region Of the SRD5A2 Gene In Breast Cancer. Bhupinder Bharaj, Andreas Scorilas, Maurizia Giai, and Eleftherios Diamandis. *Mount Sinai Hospital, Toronto, ON, Canada, and University of Turin, Turin, Italy.*

Although the female breast is not generally thought to be an androgen-regulated organ, there is increasing evidence that androgens play a significant role in the progression of breast cancer. 5-alpha-reductase (SRD5A2) is an enzyme expressed in androgen-dependent tissues. It catalysis the reduction of testosterone to its bioactive form dihydrotestosterone, which transactivates a number of other genes. One such gene encodes the prostate-specific antigen (PSA), a favourable prognostic factor in breast cancer. The 3' untranslated region (3' UTR) of SDR5A2 gene contains either no TA dinucleotide repeats (TA)0, (TA)9 or (TA)18 repeats. Variations in the lengths of these repeats have been reported to influence the enzymatic activity of SRD5A2. In the present study, we determined the TA repeats in DNA from 141 well-characterized breast tumors and whole blood of 70 women without cancer. TA repeats were determined using an Automated Sequencer and the total PSA concentration was measured with an ultra sensitive time-resolved immunofluorometric assyay. The TA repeat lengths were then associated with clinicopathological variables, including disease-free survival and overall survival. Three genotypes (TA)0, homozygote (TA)0 / (TA)9 heterozygote and (TA)9 homozygote were identified. No (TA)18 alleles were detected in the two patient groups. A statistically significant relationship between high PSA and (TA)0 / (TA)9 genotypes was observed ($P=0.004$). (TA)0 / (TA)9 and (TA)9 genotypes were found less frequently in patients with stage III or IV disease. TA genotypes were not related with any clinicopathological variables by contingency table analysis. Patients with (TA)0 / (TA)9 or (TA)9 repeats, when compared to those with homozygote (TA)0 allele, showed a significant reduction in risk-free relapse ($P=0.04$). This data supports the idea that longer TA repeats in the 3' UTR of the SRD5A2 gene are associated with more favourable outcome of breast cancer patients.