Androgen receptor CAG polymorphism and breast cancer

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INTRODUCTION

Androgens have been hypothesized to influence risk of breast cancer through several mechanisms, including their conversion to estradiol or their binding to the estrogen receptor and/or androgen receptor (AR) in the breast. Androgenic stimulation may oppose breast cell proliferation, that it is mediated by AR. The first exon of AR gene contains a translated polymorphic CAG (poly-glutamine) repeat (from 8 to 35 in normal population), and its' length is inversely correlated to the transactivation power of the receptor. Longer CAG repeats have been associated with increased risk of breast cancer.

AIM OF THE STUDY

The aim of this study was to examine whether AR-CAG repeat lengths are related to breast cancer susceptibility in Macedonian patients with breast cancer.

MATERIALS AND METHODS

We studied 71 patients with breast cancer and 76 controls. The CAG repeat number was determined by fluorescent polymerase chain reaction (PCR) amplification of exon 1 of the AR gene and capillary electrophoresis on ABI3130 Genetic Analyzer. The number of CAG repeats predicted by the Genescan software were compared with the actual CAG repeats determined by direct dideoxy terminator cycle sequencing using Big Dye Terminator Sequencing Kit v1.0 (Applied Biosystems). A representative electrophoreograms from DNA samples with 17/26, 18/29, 19/24, 20/22 and 27/28 CAG repeats.samples are given in Figure 1.

RESULTS

Comparisons were made for mean allele length, and separately for the shorter and the longer alleles. Dichotomous categories for CAG repeats were generated at all possible cut-points. The AR CAG repeat ranged from 10 to 34 in all tested women. The distribution of shorter and longer CAG repeats among breast cancer patients and controls are given in Figure 2a and 2b respectively. The mean number of the repeats was not statistically different between patients (22.32+1.96) and controls (21.81+1.97). We found a significantly higher percentage of longer alleles ≥25 repeats in breast cancer patients than in controls (p=0.0002, O.R. (1.87-8.32).

CONCLUSION

This finding suggests that women with longer allele ≥ 25 CAG repeats may be at increased risk of breast cancer.

ACKNOWLEDGMENTS

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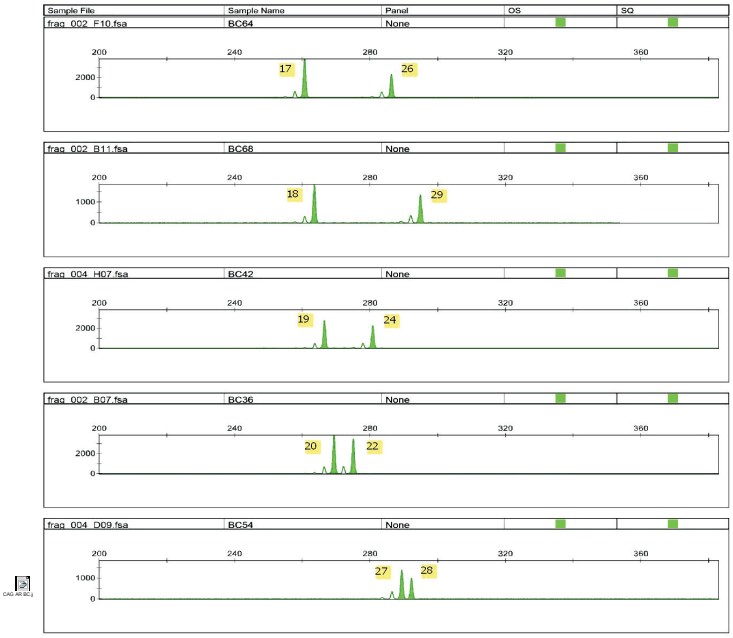


Figure 1. Genescan profiles of DNA samples with 17/26, 18/29,19/24, 20/22 and 27/28 CAG repeats in the exon 1 of the AR gene.

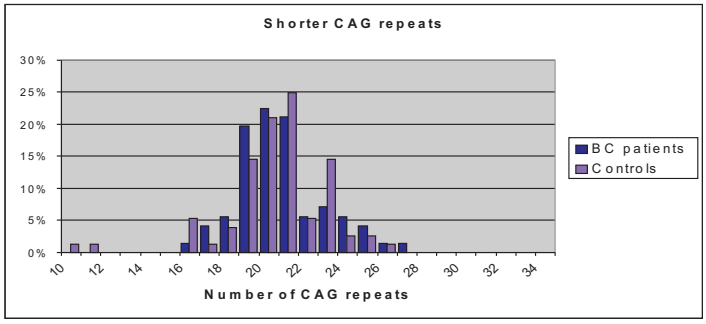
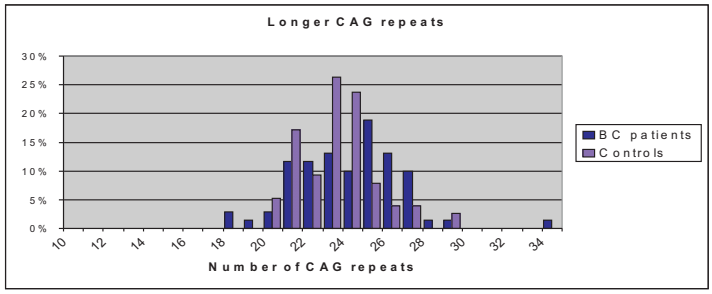


Figure 2. a. Distribution of shorter CAG repeats in exon 1 of AR gene among breast cancer patients and controls.



b. Distribution of longer CAG repeats in exon 1 of AR gene among breast cancer patients and controls.