(TTTA)n polymorphism of CYP19 (aromatase gene) in Euro- and Afro-Brazilians

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Abstract

We investigated the polymorphic tetranucleotide repeat (TTTA)n located in the fourth intron of the CYP19 gene in two Brazilian populations. The frequencies of the five common alleles (A) in Euro- and Afro-Brazilians were, respectively: seven repeats (A5), 0.586 and 0.80; eight repeats (A4), 0.092 and 0.06; nine repeats (A3), 0.014 and 0.01; eleven repeats (A2), 0.284 and 0.09; twelve repeats (A1), 0.021 and 0.04. In addition, one Euro-Brazilian individual had a rare allele with 13 repeats. The allelic frequencies in Euro- and Afro-Brazilians differed statistically (p < 10^-3). The two samples were found to be in Hardy-Weinberg equilibrium (p = 0.828 and p = 0.995).

Key words: CYP19, gene polymorphism.

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The CYP19 gene encodes an aromatase protein, which has a role in the conversion of C19 androgenic steroids into estrogens. A polymorphic tetranucleotide repeat (TTTA)n is located in the fourth intron of CYP19, some alleles apparently determining a higher susceptibility to breast cancer (Kristensen et al., 1998, 2000). A few studies have demonstrated ethnic differences related to this polymorphism (Probst-Hensch et al., 1999; Gu et al., 2001).

The aim of the present study was to investigate if this polymorphism differed between Euro-derived and Afro-derived Brazilian populations.

The European-derived sample consisted of 146 unrelated healthy individuals referred for paternity testing. The 124 Afro-Brazilians were ascertained at the central laboratory of a general public hospital to which they went for routine blood examination. The University Ethical Committee approved the investigation.

Genomic DNA was extracted from total blood by a salting out method (Miller et al., 1988). The region encompassing the fourth intron of CYP19 was amplified by the polymerase chain reaction (PCR), primers and the temperature profile of each cycle being as previously described (Kristensen et al., 1998). Genotype patterns were determined after 10.5% polyacrilamide gel electrophoresis and ethidium bromide staining. Allelic frequencies were estimated by gene counting. Agreement of genotypic frequencies with Hardy-Weinberg expectations was evaluated by the χ² test (Roff and Bentzen, 1989) and Fisher’s exact test. Comparisons of allelic frequencies were performed using the PEPI software program.

Allele and genotype frequencies are shown in Tables 1 and 2. The two samples were in Hardy-Weinberg equilibrium (p = 0.828, Euro-Brazilians; p = 0.995, Afro-Brazilians). The Euro-Brazilian allele prevalence was quite similar to those previously detected in a healthy Norwegian population (Kristensen et al., 1998), in a study of Belgians (Pottelberg et al., 2003), and in a British population (Baxter et al., 2001). However, it differed from those found in an Euro-American sample (p < 10^-3) (Siegelman-Danieli and Buetow, 1999), in Japanese women (p < 10^-3) (Miyoshi et al., 2000), in Russians (p < 10^-4) (Suspitsen et al., 2002), in a British population (p = 0.006) (Healey et al., 2000) and in a Latin-American sample (p = 0.0029) (Probst-Hensch et al., 1999). In addition to the five common alleles with seven (A5), eight (A4), nine (A3), eleven (A2) and twelve (A1) TTTA-repeats, we observed in one European-derived individual a rare allele with 13 repeats classified as A1V.

The allele frequencies of the TTTA repeat differed statistically between Euro- and Afro-Brazilians, due to A2 and A5 allele distributions in these populations (p < 10^-3 for both alleles). Two previously studied Afro-derived populations also showed allelic differences when compared to Euro-derived populations (Probst-Hensch et al., 1999; Gu et al., 2001). The allelic frequencies reported by Probst-Hensch et al. (1999) in an Afro-American sample from California (USA) were similar to the frequencies detected in the present study.
Previous studies had shown that CYP19 might be involved in breast cancer susceptibility (Kristensen et al., 1998; 2000; Siegelmann-Danieli and Buetow, 1999; Miyoshi et al., 2000), probably due to its role in the conversion of C19 steroids into estrogens. Population differences in the frequency of the CYP19 polymorphism as we disclosed here between Afro- and Euro-derived Brazilian populations are crucial in the interpretation of these association studies.

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