

**Abstract:**

Thymidylate synthase (TS) regulates the production of DNA synthesis precursors and is an important target of cancer chemotherapy. A polymorphic tandem repeat sequence in the enhancer region of the TS promoter was previously described, where the triple repeat gives higher in vitro gene expression than a double repeat. We recently identified ethnic differences in allele frequencies between Caucasian and Asian populations. We now describe assessment of genotype and allele frequencies of the TS polymorphism in 640 African (African American, Ghanaian and Kenyan) and Caucasian (UK, USA) subjects. The double and triple repeat were the predominant alleles in all populations studied. The frequency of the triple repeat allele was similar between Kenyan (49%), Ghanaian (56%), African American (52%), American Caucasian (54%) and British Caucasian (54%) subjects. However, two novel alleles contained 4 and 9 copies of the tandem repeat. These novel alleles were found at a higher allele frequency in African populations (Kenyan 7%, Ghanaian 3%, African American 2%) than Caucasians (UK 1%, USA 0%). The novel alleles identified in this study decrease in frequency with Western migration, while the common alleles are relatively stable. This is a unique example suggesting the influence of multiple selection pressures within individual populations.