

An expanded histatin gene polymorphism and test of a possible disease resistant phenotype

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[Motohide Araki](#)

[Nicholas M. Anstey](#)

[Esther D Mwaikambo](#), [Hubert Kairuki Memorial University \(HKMU\)](#)

[Arnavaz Dua](#)

[Ed Amberger](#)

[Edwin Azen](#), [University of Wisconsin–Madison](#)

Abstract

Histatins are small molecular weight salivary proteins that are important in the non-immune host defense system. Two frequent cis-linked coding-change mutations were previously described in exon 5 of the HIS2 gene of Blacks. The polymorphic mutant allele was termed HIS22 and the wild-type allele HIS21. We here describe two new non-coding change polymorphisms of the HIS2 gene: a deletion in intron 5 (7183-7198 del) and a C⇒T mutation in exon 5 [C⇒T (7104)] that characterize two new HIS2 alleles, HIS23 and HIS24 respectively. Both mutations occur on a HIS21 background. The HIS23 allele occurred only in Afro-Americans, but not in 67 Japanese, 51 Chinese and 50 Whites. Among 66 random DNA samples from Afro-Americans, frequencies of HIS21, HIS22, HIS23 and HIS24 were 0.67, 0.22, 0.05 and 0.07 respectively, with a heterozygosity of 0.45. The frequencies of the HIS24 allele in 50 Whites and 50 Chinese were 0.06, and 0.1 respectively. In a comparison of 60 matched saliva and DNA samples from the Afro-American population, the DNA-based mutation analysis reliably identified salivary histatin phenotypes. The salivary histatin polymorphism (inferred from PCR analysis) was used to test a biologically plausible hypothesis, that the mutant histatin phenotype (coded by the HIS22 allele) confers relative resistance to severe and fatal malaria. In a study of 185 Black Tanzanian subjects, there were no significant differences in HIS22 allelic frequencies between the various test groups: for 86 cerebral malaria subjects, 54 uncomplicated malaria subjects, and 45 combined asymptomatic parasitemia and health controls, HIS22 frequencies were 0.16, 0.17 and 0.17 respectively. Thus, there was no support for the hypothesis in this population.