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Mitochondrial DNA lineages of elite Ethiopian athletes

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Abstract

Previous studies have hypothesised that mitochondrial DNA (mtDNA) polymorphisms may influence aerobic performance. The matrilineal inheritance and accumulation of polymorphisms in mtDNA means that mtDNA haplogroups, characterised by key polymorphisms, are often represented at different frequencies in different populations. The present study aimed to compare the mtDNA haplogroup distribution of elite Ethiopian athletes relative to the general Ethiopian population. The haplogroup distribution of 76 endurance athletes (E), members of the Ethiopian national athletics team, was compared to 108 members of the general Ethiopian population (C). DNA was extracted from buccal swabs and haplogroups assigned by sequencing part of the hypervariable sequence (HVS-I), followed by analysis of key coding-region polymorphisms. A high proportion of African 'L' haplogroups was found in athletes and controls (C=53%; E=55%). Haplogroup distribution of endurance runners did not differ from that of C (P=0.63). Elite Ethiopian athletes are not a mitochondrially distinct group relative to the Ethiopian population. It appears that environment and, perhaps, polymorphisms in the nuclear genome are more important determinants of Ethiopian running success than mtDNA polymorphisms.

Keywords: Ethiopia; Mitochondrial DNA; Athletics; Genetics; East Africa; Endurance; HVS-I; Polymorphisms

1. Introduction

In recent times, East African athletes have been continually successful in international distance running, and currently hold the majority of distance running world records. Many explanations have been proposed to account for their continuing success. A recent study has highlighted the importance of environmental factors in the selection of elite Ethiopian athletes from the general population (Scott et al., 2003), and although no genetic link has yet been shown to explain the success of East African athletes, factors such as favourable physiological characteristics (Saltin et al., 1995a,b) and favourable genetic endowment (Saltin, 1996; Larsen, 2003) have previously been proposed to account for their success. Although athletes of West African origin tend to dominate in sprint events, and East African athletes in distance running events, the success of African runners on the whole has led to the idea that 'black' athletes are in some way superior. This belief has led some studies to compare physiological characteristics such as maximal oxygen uptake ($\dot{V}_{O_2}$max) and lactate accumulation between groups of 'black' (often South African) and 'white' athletes (Bosch et al., 1990; Coetzer et al., 1993), in an attempt to explain the dominance of East African athletes in distance running. However, the approach of comparing 'black' and 'white' athletes does not account for the fact that there are more genetic differences within populations than between (Yu et al., 2002).

Although no direct genetic effect has been found to account for the success of East African athletes, it is recognised that environmental factors alone may not

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influence athletic success. There is an increasing volume of support for the role of favourable genetics in the determination of athletic success (Rankinen et al., 2001, 2002; Perusse et al., 2003). A number of nuclear genes have been proposed as being influential in the determination of athletic success. Polymorphisms of genes such as the angiotensin-converting enzyme (*ACE*) gene (Gayagay et al., 1998) and the alpha actinin 3 gene (*ACTN3*) (Yang et al., 2003) have been shown, in some cases, to be over-represented in groups of elite athletes compared to non-athlete control populations. However, support for the role of such 'performance genes' in the determination of athletic performance is not universal and some studies do not find a role for the *ACE* gene in elite endurance athlete status (Rankinen et al., 2000). Findings of a maternal effect in the inheritance of $\dot{V}_{O_2}$max (Lesage et al., 1985) hinted to a possible influence of mitochondrial DNA (mtDNA) in the determination of aerobic capacity. In addition to polymorphisms in the nuclear genome, some studies have suggested that polymorphisms in mtDNA may account for some of the inter-individual differences in endurance performance and response to endurance training (Dionne et al., 1993; Murakami et al., 2002; for review, see Rupert, 2003). Although the findings concerning the influence of mtDNA polymorphisms are equivocal, many studies have shown that mtDNA mutations are linked to various exercise intolerance pathologies (Perusse et al., 2003), and evidence is growing of adaptive selection of particular mtDNA types in different geographic regions due to climate variation (Ruiz-Pesini et al., 2004).

mtDNA is a circular, double-stranded DNA molecule of 16,569 bp which encodes 13 subunits of a number of enzyme complexes of oxidative phosphorylation, as well as components of the mitochondrial protein synthesis system (Anderson et al., 1981). In addition, proteins that interact with the non-coding D-loop region of the sequence regulate the replication of mtDNA and its transcription to mRNAs. mtDNA is highly mutable and is inherited in a matrilineal fashion, undergoing no recombination. This results in the accumulation of linked complexes of polymorphisms down different lines of descent from an ancestral mtDNA molecule. The branching pattern of descent can be used to trace the ancestry of individuals or populations (Richards et al., 2000). Each of these branches, as shown in Fig. 1, is referred to in the present study as a haplogroup. All present-day human mtDNA sequences can be traced back to an ancestral mtDNA that existed over 120,000 years ago (Ingman et al., 2000). Since then, mtDNA sequences have accumulated between 40 and 70 mutations from the ancestral human mtDNA sequence (Maca-Meyer et al., 2001), about 1 mutation per 2500 years, or 100 human generations. The non-coding D-loop region of mtDNA is exceptionally mutable, and the hypervariable sequence I (HVS-I) of the D-loop is commonly used to assess mtDNA relatedness (Richards et al., 2003).

There are a wide variety of mtDNA haplogroups in Ethiopia (Salas et al., 2002), some of which are ancient

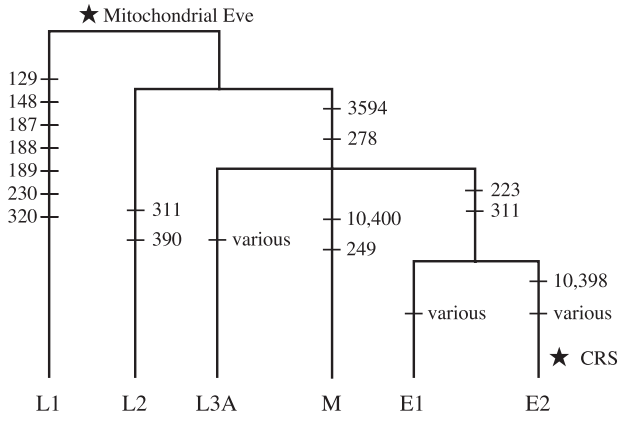

Fig. 1. Human mitochondrial tree. Approximate positions of polymorphisms relative to the Cambridge Reference Sequence (CRS) are shown (HVS-I polymorphisms are shown minus 16,000). Haplogroup topology is modelled upon more detailed human phylogenies (Macaulay et al., 1999; Maca-Meyer et al., 2001). Approximate positions of the ancestral mtDNA sequence 'mitochondrial Eve', and the CRS are also shown. See text for haplogroup classification criteria.

African 'L' haplogroups that have remained in Africa (Chen et al., 1995). There are also a proportion of sequences similar to those commonly found outside Africa (Richards et al., 2003). These sequences are thought to be found in high numbers in Ethiopia either as a result of substantial gene flow into Ethiopia from Eurasia (Chen et al., 2000; Richards et al., 2003), or as a result of having undergone several branching events in demic diffusion, acting as founder lineages for non-African populations. Regardless of the mechanism, the high divergence time of Ethiopian mtDNA means that there has been time for a number of haplogroup specific polymorphisms to occur, all of which have the potential to affect endurance performance through influences on oxidative phosphorylation (Dionne et al., 1993; Murakami et al., 2002). Given the lack of recombination, if mtDNA polymorphisms were important in the success of Ethiopian distance runners, selection for variants beneficial to exercise performance would lead to an increased frequency of the haplotypes on which the polymorphism occurred amongst elite athletes relative to the general population through linkage disequilibrium. In addition, as some of the mtDNA haplogroups are more commonly found in individuals indigenous to Ethiopia, if any of these haplogroups contain beneficial variants, this may partially account for the success of Ethiopian athletes in international distance running.

The present study, therefore, aimed to compare the mtDNA haplogroup distribution amongst elite Ethiopian athletes relative to the general Ethiopian population.

2. Methods

A total of 184 subjects provided written informed consent prior to participation in the study, which was approved