

P 53 Codon 72 and Past Malaria Morbidity in Sardinia

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Infection of liver cells is the first stage of malaria: parasites replicate inside the cells and then invade erythrocytes. Apoptosis mechanism in liver cells is triggered by the growth of parasites: this provides a release of parasite antigen that initiates a protective immune response. On the other hand, the parasite interferes with cell apoptosis mechanism resulting in resistance to apoptosis and successful infection [1-3]. Recently it has been observed that p53 pathway is involved in parasite survival, increased level of p53 reduces the liver parasite load whereas p53 knockout mice suffers increased liver load [4].

The p53 codon 72 is characterized by a polymorphism in exon 4 with CGC to CCC transition (rs1042522) that confers a change of arginine to proline in amino acid sequence of protein [5]. Amino acid change affects biochemical and functional properties of p53 protein. The arginine variant is a stronger apoptosis inducer while the proline variant is a stronger transcriptional activator [6].

Since apoptosis of liver cells seems to have a protective effect against malaria one would expect a positive selection of *Arg allele in areas of heavy malaria endemicia.

We have studied 46 consecutive newborn infants from Oristano

area of Sardinia and 47 consecutive newborn infants from area of Nuoro. Oristano was in the past a heavy malaria endemic area whereas the endemicia was very light in Nuoro area. Blood was collected from the placental side of umbilical vein after cord section. Written informed consent was obtained by parents to participate to the study that was approved by I.R.B. p53 codon 72 genotypes were determined by DNA analysis as previously described [7].

Figure 1 shows the proportion of p53 codon 72 genotypes in Nuoro and Oristano areas: *Arg/*Arg genotype is much more frequent in Oristano than in Nuoro ($p=0.024$). The frequency of *Arg allele is 82.6% in Oristano and 69.1% in Nuoro ($p=0.04$).

In accordance with experimental studies suggesting apoptosis of the liver cells as a defense mechanism against parasite invasion, *Arg allele favoring apoptosis seems to have been selected positively in area of Sardinia exposed in the past to heavy malaria endemicia.

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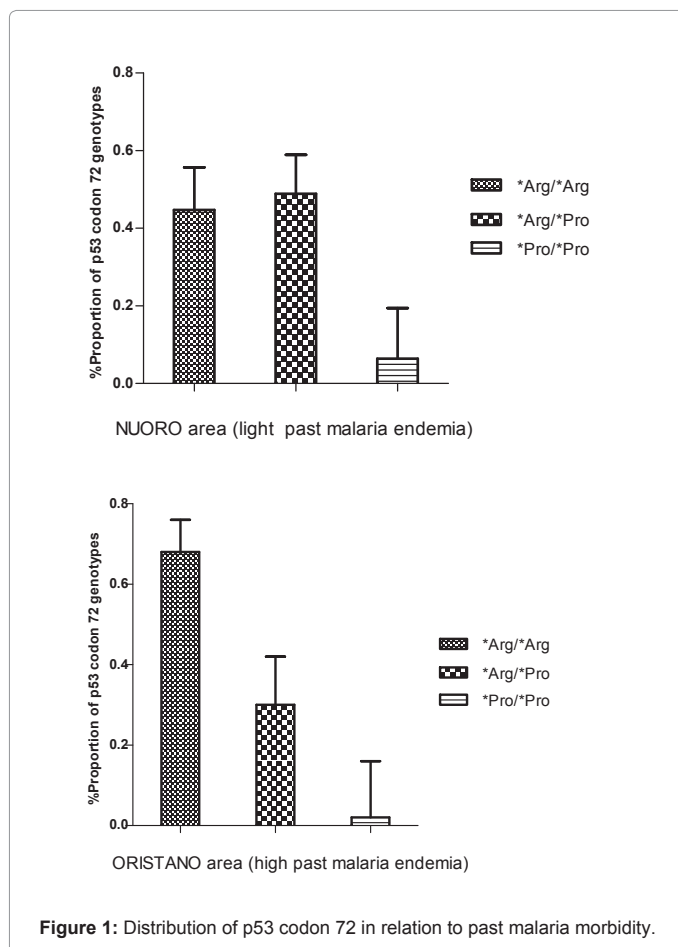


Figure 1: Distribution of p53 codon 72 in relation to past malaria morbidity.

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