

## P 53 Codon 72 and Past Malaria Morbidity in Sardinia

Gloria-Bottini F<sup>1</sup>, Meloni GF<sup>2</sup>, Saccucci P<sup>1</sup> and Bottini E<sup>1\*</sup>

<sup>1</sup>Department of Biomedicine and Prevention, School of Medicine, University of Tor Vergata, Rome, Italy

<sup>2</sup>Department of Pediatrics, University of Sassari, Sassari, Italy

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.

### References

- van de Sand C, Horstmann S, Schmidt A, Sturm A, Bolte S, et al. (2005) The Liver Stage of Plasmodium berghei Inhibits Host Cell Apoptosis. *Mol Microbiol* 58: 731-742.
- Leiriao P, Albuquerque SS, Corso S, van Gemert GJ, Sauerwein RW, et al. (2005) HGF/MET Signalling Protects Plasmodium-Infected Host Cells from Apoptosis. *Cell Microbiol* 7: 603-609
- Leiriao P, Mota MM, Rodriguez A (2005) Apoptotic Plasmodium-Infected Hepatocytes Provide Antigens to Liver Dendritic Cells. *J Infect Dis* 191: 1576-1581.
- Kaushansky A, Ye AS, Austin LS, Mikolajczak SA, Vaughan AM, et al. (2013) Suppression of Host p53 is Critical for Plasmodium Liver-Stage Infection. *Cell Rep* 28: 630-637.
- Ara S, Lee PS, Hansen MF, Saya H (1990) Codon 72 Polymorphism of the TP53 Gene. *Nucleic Acids Res* 18: 4961.
- Jeong BS, Hu W, Belyi V, Rabadan R, Levine AJ (2010) Differential Levels of Transcription of p53-Regulated Genes by the Arginine/Proline Polymorphism p53 with Arginine at Codon 72 Favors Apoptosis. *FASEB J* 24: 1347-1353
- Manca-Bitti L, Saccucci P, Capasso F, Piccinini S, Angelini F, et al. (2011) Genotypes of p53 Codon 72 Correlate with Age at Onset of Type 1 Diabetes in a Sex-Specific Manner. *J Pediatr Endocrinol Metab* 24: 437-439.

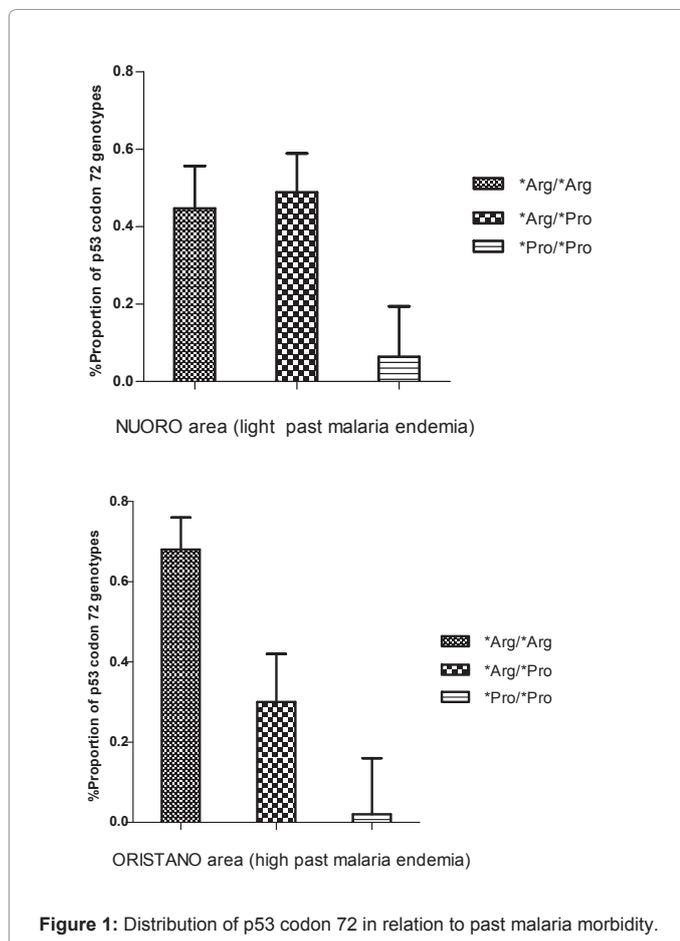


Figure 1: Distribution of p53 codon 72 in relation to past malaria morbidity.

\*Corresponding author: Bottini E, Department of Biomedicine and Prevention, University of Tor Vergata, School of Medicine, Rome, Italy, E-mail: [bottini@med.uniroma2.it](mailto:bottini@med.uniroma2.it)

Received August 16, 2013; Accepted September 06, 2013; Published September 12, 2013

Citation: Gloria-Bottini F, Meloni GF, Saccucci P, Bottini E (2013) P 53 Codon 72 and Past Malaria Morbidity in Sardinia. *Malar Chemoth Cont Elimination* 2: 107. doi: 10.4172/2090-2778.1000107

Copyright: © 2013 Gloria-Bottini F, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.