



## Tri-allelic pattern at the TPOX locus: A familial study

Juliane Bentes Picanço<sup>a</sup>, Paulo Eduardo Raimann<sup>a</sup>, Giorgio Adriano Paskulin<sup>b</sup>, Luís Alvarez<sup>c</sup>, António Amorim<sup>c,d</sup>, Sidney Emanuel Batista dos Santos<sup>e</sup>, Clarice Sampaio Alho<sup>a,\*</sup>

<sup>a</sup> Faculdade de Biociências, Pontifícia Universidade Católica do Rio Grande do Sul, Porto Alegre, RS, Brazil

<sup>b</sup> Universidade Federal de Ciências da Saúde de Porto Alegre – UFCSA e Complexo Hospitalar Santa Casa de Porto Alegre – CHSCPA, Porto Alegre, RS, Brazil

<sup>c</sup> IPATIMUP, Institute of Molecular Pathology and Immunology of the University of Porto, Porto, Portugal

<sup>d</sup> Department of Biology, Faculty of Sciences of the University of Porto, Porto, Portugal

<sup>e</sup> Universidade Federal do Pará, Centro de Ciências Biológicas, Laboratório de Genética Humana e Médica, Belém, Pará, Brazil

### ARTICLE INFO

#### Article history:

Accepted 10 October 2013

Available online 18 October 2013

#### Keywords:

Family pedigree

STR

Tri-allelic pattern

TPOX

### ABSTRACT

Alleles at the TPOX STR locus have 6–14 different numbers of a four-nucleotide (AATG) repeat motif arranged in tandem. Although tri-allelic genotypes are generally rare, the TPOX tri-allelic pattern has a higher frequency, varying widely among populations. Despite this, there are few accurate reports to disclose the nature of the TPOX third allele. In this work we present data obtained from 45 individuals belonging to the same pedigree, in which there are cases of tri-allelic TPOX genotypes. The subjects were apparently healthy with a normal biological development. We noticed six tri-allelic cases in this family, and all of them were women. Karyotype analysis showed no occurrence of partial 2p trisomy. All the tri-allelic cases had the genotype 8–10–11, probably due to three copies of the TPOX STR sequence in all cells (Type 2 tri-allelic pattern). Based on previous data we assumed the allele 10 as the TPOX third allele. The pedigree analyses show evidences that the TPOX extra-allele was the allele10, it is placed far from the main TPOX locus, and that there is a potential linkage of the TPOX extra-allele-10 with Xq. This was the first study that included a large pedigree analysis in order to understand the nature TPOX tri-allelic pattern.

© 2013 Elsevier B.V. All rights reserved.

### 1. Introduction

A forensic paternity test follows simple Mendelian inheritance where the child inherits one allele from the mother and another from the father at each locus. Rare events, such as point mutations in primer binding regions, slippage mutations, and other events such as gene conversion and copy number variations (CNVs) (Freeman et al., 2006) can occasionally cause an aberrant result, including an abnormal number of alleles, which seemingly break the rules of Mendelian inheritance (Lukka et al., 2006). Clayton et al. (2004) have distinguished two types of tri-allelic pattern. Type 1: when after PCR amplification two alleles have different intensity of the third allele and Type 2: when the three peaks have similar intensity. Type 1 is believed to be the result of a mutation in an early somatic cell while Type 2 is thought to represent a constitutional chromosomal rearrangement. Although tri-allelic genotypes are generally rare, data presented on the STRBase website ([http://](http://www.cstl.nist.gov/biotech/strbase)

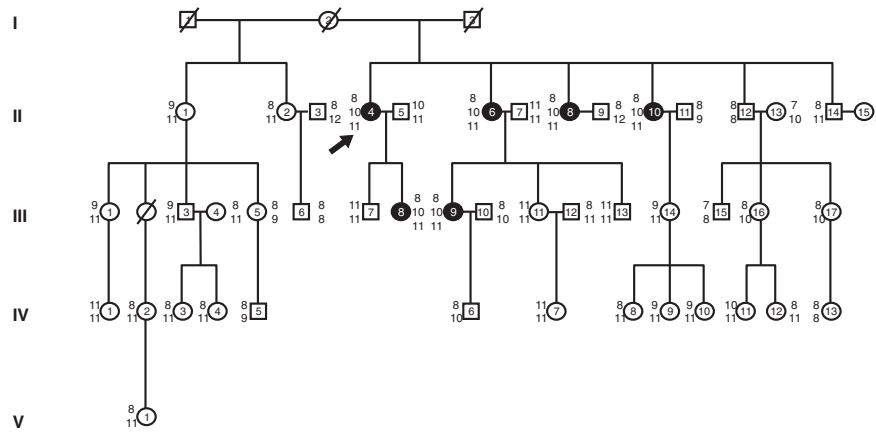
[www.cstl.nist.gov/biotech/strbase](http://www.cstl.nist.gov/biotech/strbase)) indicate that short tandem repeats (STR) tri-allelic genotypes can be unusually frequent in the TPOX human STR locus. Alleles at the TPOX locus have different numbers of a four-nucleotide repeat motif arranged in tandem (Anker et al., 1992). Therefore, TPOX polymorphism is widely used for paternity testing and personal identification, and is one of the FBI's CODIS STR loci (<http://www.cstl.nist.gov/strbase/fbicore.htm>). The TPOX tri-allelic profiles are due to some duplication of the STR segment and flanking regions recognized by the TPOX primers.

For more than a decade, TPOX tri-allelic genotypes have been reported with a widely varied frequency among human populations. Crouse et al., 1999 reported 18 tri-allelic genotypes in a sample of over 10,000 individuals drawn from Alabama, USA, which is equivalent to a frequency of 0.18% (18/10,000). Later, Huel et al. (2007) typed 32,800 individuals from Bosnia, Kosovo, and Serbia, but found only one subject with a TPOX tri-allelic genotype (1/32,800; 0.003%), and Fridman et al. (2008) analyzing 561 unrelated individuals (410 females and 151 males) from Brazil also observed one single occurrence of a tri-allelic pattern at the TPOX locus (1/561; 0.2%). In contrast, more than 2% of indigenous South Africans exhibit tri-allelic TPOX genotypes: 165 tri-allelic genotypes (116 females and 49 males) were found among a total of 6827 black South Africans (3399 females and 3428 males) (Lane, 2008). And in a larger study from Brazil, Poiares et al. (2010) typing 12,886 unrelated individuals were unable to find any TPOX tri-allelic genotype.

**Abbreviations:** CNVs, copy number variations; STR, short tandem repeat; TPOX, thyroid peroxidase; FBI, Federal Bureau Investigation; CODIS, Combined DNA Index System; DNA, deoxyribonucleic acid; GTG, G-banded chromosome; pb, base pair; PCR, polymerase chain reaction; X-STR, short tandem repeat of X-chromosome; IBGE, Instituto Brasileiro de Geografia e Estatística.

\* Corresponding author at: Faculdade de Biociências, Pontifícia Universidade Católica do Rio Grande do Sul. Av. Ipiranga, 6681, 90619-900 Porto Alegre, RS, Brazil. Tel.: +55 51 33203545.

E-mail address: [csalho@puccs.br](mailto:csalho@puccs.br) (C.S. Alho).



**Fig. 1.** Family pedigree with the DNA profiles of the TPOX locus. Roman numerals show the five generations of this family. Females are represented by circles. Males are represented by squares. Shaded circles indicate women with tri-allelic TPOX genotype. Numbers within the symbols (circles and squares) indicate each subject. Numbers outside the symbols indicate the individual's genotype for the TPOX STR locus.

In the African population (Lane, 2008), Dr. Lane was able to suggest that the TPOX extra allele were the allele 10. Indeed, according to STRBase website (with 102 TPOX tri-allelic reported subjects) the allele 10 is present in 90% of individuals reported with TPOX tri-allelic pattern, and all other alleles were present in lower percentage. In this database, comparing TPOX allele frequencies among bi and tri-allelic subjects, the frequency of the allele 10 in tri-allelic subjects is around five times higher than in bi-allelic subjects. Thus, it was possible to strengthen the hypothesis that the third-extra allele would be the allele 10. Only ten tri-allelic subjects from the STRBase without the allele 10 were reported. All of them had the allele 9 or 11 (genotypes were: 8–9–11; 8–11–12; 8–11–14.3; 9–11–12), which could denote slippage mutation from an ancestral third-extra allele 10.

As pointed out by Clayton et al. (2004), a Type 2 tri-allelic pattern may result from a chromosomal duplication and, in this case, it may be associated with severe clinical syndromes (Lukka et al., 2006). However, the partial maternal isodisomy for chromosome 2p (2pter–2p12) that also produces a tri-allelic pattern might be compatible with

a minimal influence on normal development (Bakker et al., 2001). In this context, Muna Al-Saffar et al. (2000), have shown a 7-month-old well-developed girl with the karyotype 46, XX, der(13) t(2;13)(p23; p11.2).ish der(13)(wcp2+) de novo. A chromosome painting strategy confirmed that the additional segment of chromosome 2 was on 13p, resulting in trisomy of 2p23–2pter. Megarbane et al. (1997) also demonstrated that the partial trisomy of 2p was compatible with adulthood. Another possibility is that the third TPOX allele may not be linked to chromosome 2. Lane showed that two thirds of the TPOX tri-allelic adults were females, and TPOX tri-allelic fathers only transmitted the TPOX tri-allelic genotype to their daughters (Lane, 2008). With this evidence, he suggested that the inserted allele was on an X chromosome. This report was enhanced by Díaz et al. (2009).

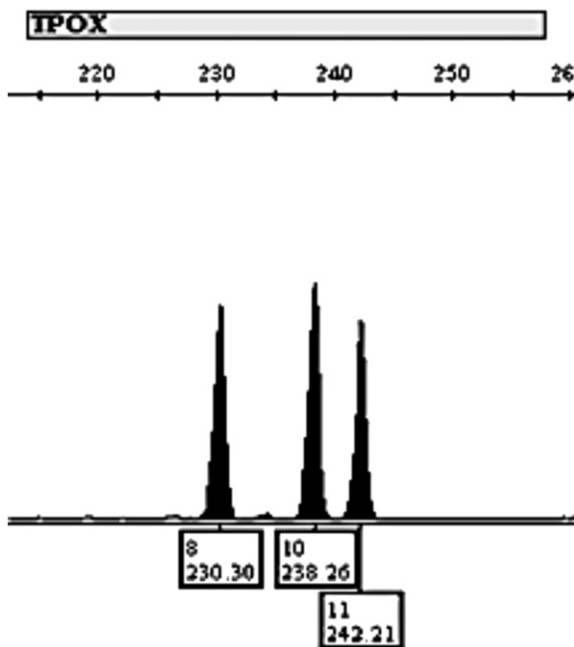
Despite the substantial frequency of the TPOX tri-allelic pattern, the nature of the third allele is still poorly understood. In this work we present data obtained from 45 individuals of the same family where there were cases of TPOX tri-allelic pattern, and employ these data to investigate the underlying inheritance of the third allele detected at this locus.

## 2. Material and methods

The 45 studied subjects, belonging to the same family pedigree, were born and are living in four different cities in the Rio Grande do Sul State, southern Brazil. The proband (or propositus) was a female called LTMV, she was the first tri-allelic family member who received attention for her genetic characteristic. The DNA profiles of her and her daughter were analyzed in a kinship lab routine. Then, a large number of her relatives were invited to participate in this study. This project was approved by the Research Ethics Committee of Pontifícia Universidade Católica do Rio Grande do Sul (PUCRS) (Protocol #09/04688-OfCEP943/29); and the informed written consent and assent to participate were obtained from all subjects or their surrogates.

All subjects participated in an interview on their own residence when they response a questioner about health and development conditions. Data about important medical disorders, syndromic conditions, typical diseases, pathological sickness, abnormal features, atypical appearances, distinctive symptoms, intellectual capacities, and other characteristics were enquired. No medical exams (biochemical or images) were evaluated.

Blood samples were collected on FTA cards and DNA was extracted from blood spots using the manufacturer's protocols. In all 45 subjects, we confirmed kinship between them, by using autosomal STRs (AmpF/STR® Identifier™ PCR Amplification Kit; Applied Biosystems; Life Technologies, USA), with paternity index values above 10,000. A total of 0.5–1.0 ng of DNA was used to amplify 15 autosomal STR loci (D8S1179,



**Fig. 2.** Tri-allelic TPOX genotype as depicted by the ABI GeneMapper3.2 software. The three TPOX STR peaks represent alleles 8, 10, and 11.



Fig. 3. High-resolution karyotype analysis (>550 bands) of lymphocytes from female II-4 stained with Trypsin and Giemsa.

D21S11, D7S820, CSF1PO, D3S1358, TH01, D13S317, D16S539, D2S1338, D19S433, vWA, TPOX, D18S51, D5S818, and FGA) with the amplification kit, following the manufacturer's instructions, followed by analysis on a capillary ABI 3130xl Genetic Analyzer. All tri-allelic subjects were also tested by PowerPlex®21 System kits, to confirm the tri-allelic pattern in TPOX locus. To avoid the possibility of a false tri-allelic genotype caused by micro-variants (shorter alleles) of the adjacent bins (e.g.: D18S51 – AmpFISTR® Identifiler® or the FGA- PowerPlex®21), all TPOX tri-allelic subjects had their DNA amplified by the singleplex PCR-based analysis of the TPOX-locus; using primer forward 5'-GCACAGAAC AGGCACTTAGG-3' and primer reverse 5'-CGCTCAAACGTGAGGTTG-3' they had the TPOX tri-allelic pattern confirmed.

A high-resolution karyotype (>550 bands) was obtained from lymphocytes through the adapted from Yunis' technique (Yunis, 1981). Briefly, this includes a cell culture for 72 h of lymphocytes stimulated with phytohemagglutinin, synchronization with the use of methotrexate/thymidine and stained with Trypsin and Giemsa, producing G-banded chromosomes (GTG). Twenty five metaphase plates per case were analyzed with the aid of a Zeiss Axioskop microscope.

Based on Lane's (2008) suggestion, we considered the TPOX extra-allele as allele10 and cogitated that it was in X chromosome. To verify if there was linkage disequilibrium between the TPOX extra-allele (allele10) and the X-STR markers, we used a multiplex system that allows the simultaneous analysis of 12 STRs associated to the X chromosome; a multiplex PCR (Loci DXS9895, DXS7132, DXS6800, DXS9898, DXS6789, DXS7133, GATA172D5, DXS7130, HPRTB, GATA 31E08, DXS7423, and DXS10011) was performed based on Ribeiro-Rodrigues et al. (2008, 2009).

### 3. Results and discussion

The 45 studied subjects were apparently healthy and normally developed. Fig. 1 shows the family pedigree with the DNA profiles of the TPOX STR locus. The proband on this pedigree was the female LTMV (II-4) and it is noted with an arrow. In order to show the Clayton category of the tri-allelic pattern, we presented in Fig. 2 a TPOX STR profile of this II-4 woman (depicted by the GeneMapper® ID version 3.2 software of the ABI 3130xl Genetic Analyzer). The three peaks

**Table 1**  
Frequency of each allele in bi- and tri-allelic subjects in our pedigree and in Brazil, and tri-allelic/bi-allelic frequencies Ratio.

TPOX allele	Allelic frequency in tri-allelic subjects in the Pedigree	Allelic frequency in bi-allelic subjects in the Pedigree	Relative Ratio tri-allelic/bi-allelic in the Pedigree	Allelic frequency in bi-allelic subjects in Brazil	Relative Ratio tri-allelic subjects in the Pedigree/bi-allelic subjects in Brazil
	Subjects N = 6 TPOX alleles N = 18	Subjects N = 39 TPOX alleles N = 78		Subjects N = 123,102 <sup>a</sup> TPOX alleles N = 246,204	
6	0	0	0	0.018	0
7	0	0.026	0	0.008	0
8	0.333	0.359	0.928 (0.333/0.359)	0.456	0.730 (0.333/0.456)
9	0	0.115	0	0.124	0
10	0.333	0.089	3.741 (0.333/0.089)	0.067	4.970 (0.333/0.067)
11	0.333	0.385	0.865 (0.333/0.385)	0.275	1.211 (0.333/0.275)
12	0	0.026	0	0.048	0
13	0	0	0	0.002	0

<sup>a</sup> Aguiar et al. (2012): 123,102 individuals; N = 246,204 alleles.

shown here and in the other five tri-allelic subjects have similar areas which are compatible with Type 2 as defined by Clayton et al. (2004), which reflects the presence of three copies of the STR sequence in all cells, and not to the Type 1 pattern, that could result from a mutation in sporadic somatic cells. The age of all pedigree subjects ranged from 6 to 73 years. We noticed a total of six tri-allelic subjects in this family, and all of them were women. Analyzing the pedigree, it was observed that only the descendants of the generation I, who are located on the right side of the genealogy, had inherited of TPOX third allele.

Lukka et al. (2006) show evidence that the tri-allelic pattern should be due to the duplication in chromosome 2 containing the TPOX STR Locus. Thus, since partial isodisomy for chromosome 2p might be compatible with minimal influence on normal development and/or compatible with adulthood (Al-Saffar et al., 2000; Bakker et al., 2001; Megarbane et al., 1997), we carried out a karyotype analysis in the cells of female II-4 (proband) to test a probable partial trisomy of chromosome 2. A partial 2p duplication, located on the same chromosome 2 or elsewhere in the genome, should be clearly viewable with a karyotype assessment. However, no partial trisomy of the 2p segment was apparent in the GTG-Banded karyotype of this female (Fig. 3).

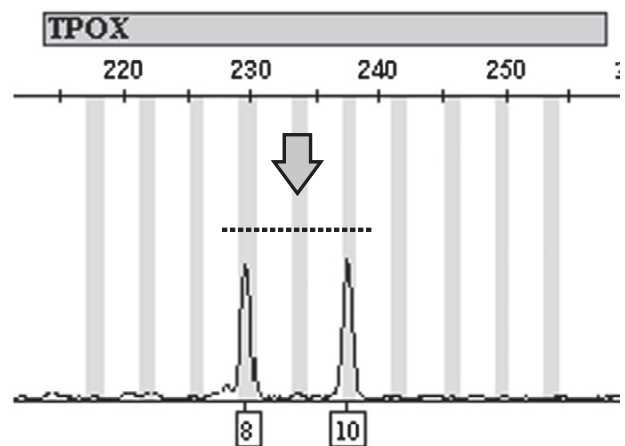
Forty five family members are no large enough to make some conclusions with statistical significance, nevertheless, when we compared the allele frequencies among bi and tri-allelic subjects, we observed that the frequencies of the alleles 8 and 11 were similar, but the allele 10 frequency in tri-allelic subjects was four (3.741) and five (4.970) times higher than in bi-allelic subjects in pedigree members' and in Brazilian global population, respectively (Table 1). With these results, it was possible to strengthen the hypothesis that the third-extra allele would be the allele 10.

Our six tri-allelic females had alleles 8–10–11. Due to the presence of those alleles we focused our investigation on the analysis of the transmission and the segregation of them. Based on previous suggestion (Lane, 2008 and STRBase data), we presumed the third TPOX extra-allele as the allele 10. Analyzing the descendants III-7 (11–11; son of II-4 and II-5), III-13 and III-11 (11–11; descendants of II-6 and II-7), and III-14 (9–11; daughter II-10 and II-11) we observed that the allele 11 was transmitted as a regular allele; i.e. as an ordinary TPOX allele on chromosome 2. These results also indicated that this allele 11 segregated independently from the supposed extra-allele-10. About the allele 8, observing the man II-12 (8–8; brother of II-4, II-6, II-8, and II-10), we detected that allele 8 was also transmitted as a regular allele, as well as it had an independent segregation from the extra-allele-10. We believe that our data were able to maintain the supposition previously assumed for allele 10 as the TPOX extra-allele. We examined the DNA profile of subject IV-6 since this boy could have three TPOX alleles with a possible concomitant homozygosity of alleles 8 or 10. Fig. 4 shows that his DNA yielded two even TPOX peaks which indicate that he has equal doses of alleles 8 and 10 and not a double dose of either. It is possible that his mother III-9 transmitted allele 8 and the father transmitted his normal allele 10. All these data

may indicate that the TPOX extra-allele segment is not necessarily closely linked to a chromosome 2 regular TPOX locus. This data corroborate with Lane (2008) and Díaz et al. (2009).

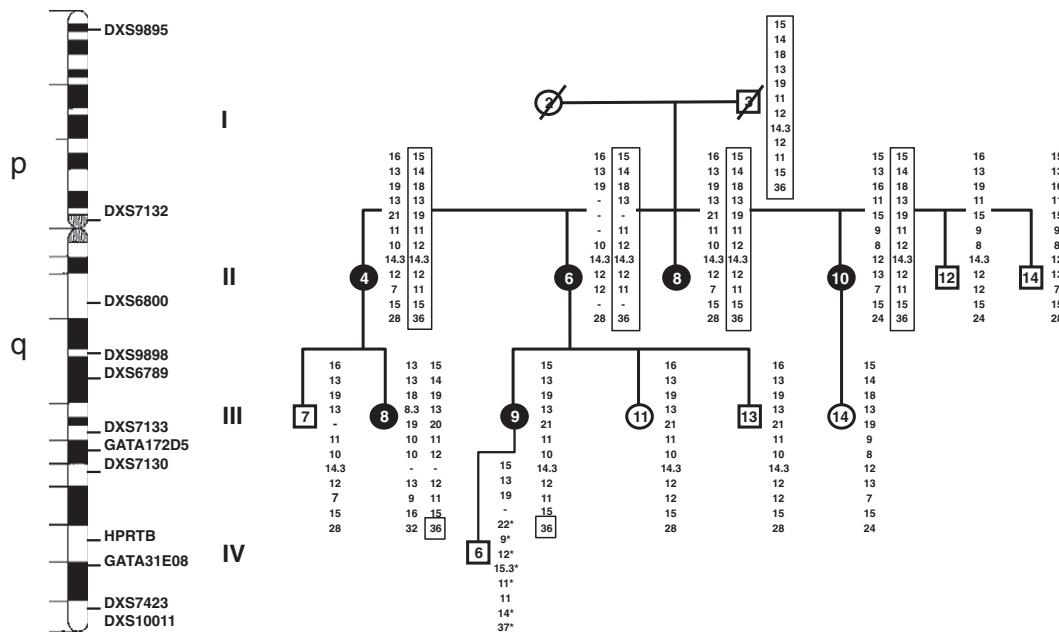
Lane's study suggested that the extra-allele-10 was inserted on an X chromosome (Lane, 2008). However the results in this pedigree neither support nor refute this hypothesis, since there is the possibility of segregation of the extra-allele-10 either as X-linked or as an autosomal chromosome. If the extra-allele-10 is located on an X chromosome then Fig. 1 suggests that the father I-3 may have been the transmitter parent because all his daughters have the tri-allelic genotype and neither of his two sons has. To support or reject the hypothesis that the third extra-allele is X-linked, we conducted a study with specific X-linked markers. In an attempt to identify linkage disequilibrium between the extra-allele-10 and X-chromosome markers, we evaluated 12 X-STRs in all subjects of the II-4 female family. Based on X-STRs present in individuals of generation II, it was possible to reconstruct the X-haplotype of the father I-3 (Fig. 5). Considering the occurrence of events of crossing-over between X chromosomes in females from generations III and IV, we evaluated if the transmission of the extra-allele-10 would be linked to some of the 12 X-STR alleles. We performed an association analysis with each pedigree member presented on Fig. 5 considering the presence/absence of each allele per loci and presence/absence of extra-allele 10; the analysis showed that only the allele 36 of the DXS10011 locus was statically significant ( $p = 0.0022$ ; Fisher exact test, two-tailed) and it would be linked to extra-allele-10. In this analysis, none of the other alleles were associated with extra-allele-10.

However, it was not possible to reach a conclusion about linkage disequilibrium in loci DXS7423, DXS9898 and HPRTB loci because there was homozygosity. According to the result we can infer that the extra-allele-10 could be located near the telomeric region of this Xq.



**Fig. 4.** Normal bi-allelic TPOX genotype of boy IV-6 depicted by ABI GeneMapper3.2 software. No homozygosity in alleles 8 or 10 was observed.





**Fig. 5.** Family pedigree with the DNA profiles of the X-STR loci. Roman numerals show the five generations of this family. Females are represented by circles. Males are represented by squares. Shaded circles indicate women with tri-allelic TPOX genotype. Numbers within the symbols (circles and squares) indicate each subject. Numbers outside the symbols (left) indicate the X-STR haplotypes. The symbol “-” indicates locus where the allele designation was not possible. Based on the X-STR haplotype in subjects of generation II, it was possible to reconstruct the haplotype of the X chromosome of the father I-3, which is shown within the box. In women III-9, III-11, and III-14 parental haplotypes were removed to clarify the transmission of maternal X-chromosome. The alleles marked with asterisk (boy IV-6) are confirmed in the X-maternal of his grandfather. The allele 36 (locus DXS10011; inside the box in generation III), has been shown in linkage disequilibrium with allele-extra-10 present in tri-allelic females (black circles).

With our study on this pedigree, we cannot speculate about the origin of the TPOX extra-allele, but the possible mechanism for the origin of the third allele was discussed by Lane (2008) suggesting that a duplication/insertion could take place before the start of the Bantu expansion; it might be possible that slaves, who were drawn from both Western and Eastern Bantu groups, led the African tri-allelic genotype with them to the New World. So, according to Lane, the relatively common X-linked extra-allele-10 found in South African populations must have arisen before the start of the Bantu expansion. The same case was verified in other more recent population originated from African slaves (Díaz et al., 2009). Although the Southern Brazilian population has some African genetic component, the woman I-2 seems to have a full European origin. Her ethnic characteristic was typically Caucasian (e.g., thin nose, and white skin, eyes, and hair). The subjects of generation II also reported having Italian Matrilineal Ancestry, but there is no information about the father I-3. Brazil was discovered and colonized by the Portuguese at the beginning of the 16th century. In the same century, the slavery of African (mainly Bantu and Yoruba) individuals was introduced. After the eighteenth century, other people have migrated to Brazil, mainly from Portugal, Italy, and Germany. Nowadays, the general Brazilian genetic structure is considered to be quite complex and different population groups can be classified according to their ethnicity in European-derived, African-derived, Brazilian Mulattos and Asian-derived (IBGE, 2000). The admixture process happened diversely in different geographic regions, with a most pronounced Native American contribution in the North, a high African contribution in the Northeast and a relatively low Native American and African contributions in the South.

**4. Conclusion**

We presented a genealogy with TPOX tri-allelic subjects where the tri-allelic pattern is due to three copies of STR sequence in all cells (Type 2) and is not the result of overt visible partial 2p trisomy. Six tri-allelic subjects were women and all had genotype 8–10–11. We presented evidences to assume the TPOX third extra-allele as the allele

10. The alleles 8 and 11 appeared segregating independently from this extra-allele. Thus, our results allowed to support that insertion of extra-allele-10 is placed far from the main TPOX locus. We show evidences of a potential linkage of the TPOX extra-allele-10 with Xq.

**Conflict of interest**

The authors hereby declare that there are no conflicts of interest which may have affected the results and discussion provided herein.

**Acknowledgments**

We thank AB Lane for the suggestions, and for Tricia K. Albuquerque on behalf of the “Instituto Geral de Pericias do Rio Grande do Sul (IGP)” and the Applied Biosystems Company for supporting the analysis.

**References**

Aguiar, V.R., et al., 2012. Updated Brazilian STR allele frequency data using over 100,000 individuals: an analysis of CSF1PO, D3S1358, D5S818, D7S820, D8S1179, D13S317, D16S539, D18S51, D21S11, FGA, Penta D, Penta E, TH01, TPOX and vWA loci. *Forensic Sci. Int. Genet.* 504–509.

Al-Saffar, M., Lemyre, E., Koenekoop, R., Duncan, A.M.V., Der Kaloustian, V.M., 2000. Phenotype of a patient with pure partial trisomy 2p(p23-pter). *Am. J. Med. Genet.* 94, 428–432.

Anker, R., Steinbrueck, T., Donis-Keller, H., 1992. Tetranucleotide repeat polymorphism at the human thyroid peroxidase (hTPO) locus. *Hum. Mol. Genet.* 1, 137.

Bakker, B., Bikker, H., Hennekam, R.C.M., Lommen, E.J.P., Schipper, M.G.J., Vulsma, T., 2001. Maternal isodisomy for chromosome 2p causing severe congenital hypothyroidism. *J. Clin. Endocrinol. Metab.* 86, 1164–1168.

Clayton, T.M., Guest, J.L., Urquhart, A.J., Gill, P.D., 2004. A genetic basis for anomalous band patterns encountered during DNA STR profiling. *J. Forensic Sci.* 49, 1207–1214.

Crouse, C.A., Rogers, S., Amriott, E., Gibson, S., Masibay, A., 1999. Analysis and interpretation of short tandem repeat microvariants and three banded allele patterns using multiple allele detection systems. *J. Forensic Sci.* 44, 87–94.

Díaz, V., Rivas, P., Carracedo, A., 2009. The presence of tri-allelic TPOX genotypes in Dominican population. *Forensic Sci. Int. Genet. (Suppl. 2)*, 371–372.

Freeman, J.L., Perry, G.H., Feuk, L., Redon, R., McCarroll, S.A., Altshuler, D.M., 2006. Copy number variation: new insights in genome diversity. *Genome Res.* 16, 949–961.

- Fridman, C., Santos, P.C.C., Kohler, P., Garcia, C.F., Lopez, L.F., Massad, E., 2008. Brazilian population profile of 15 STR markers. *Forensic Sci. Int. Genet.* 2, e1–e4.
- Huel, R.M., Basic, L., Madacki-Todorovic, K., Smajlovic, L., Eminovic, I., Berbic, I., 2007. Variant alleles, tri-allelic patterns, and point mutations observed in nuclear short tandem repeat typing of populations in Bosnia and Serbia. *Croat. Med. J.* 48, 494–502.
- Instituto Brasileiro de Geografia Estatística (IBGE), 2000. *BRASIL 500 Anos de Povoamento*. IBGE, Rio de Janeiro.
- Lane, A.B., 2008. The nature of tri-allelic TPOX genotypes in African populations. *Forensic Sci. Int. Genet.* 2, 134–137.
- Lukka, M., Tasa, G., Ellonen, P., Moilan, K., Vassiljev, V., Ulmanen, I., 2006. Triallelic patterns in STR loci used for paternity analysis: evidence for a duplication in chromosome 2 containing the TPOX STR locus. *Forensic Sci. Int.* 164, 3–9.
- Megarbane, A., Souraty, N., Prieur, M., Theophile, D., Chedid, P., Auge, J., 1997. Interstitial duplication of the short arm of chromosome 2: report of a new case and review. *J. Med. Genet.* 34, 783–786.
- Poiares, L.A., Osorio, P.S., Spanhol, F.A., Coltre, S.C., Rodenbusch, R., Gusmão, L., 2010. Allele frequencies of 15 STRs in a representative sample of the Brazilian population. *Forensic Sci. Int. Genet.* 4, e61–e63.
- Ribeiro Rodrigues, E.M., Leite, F.P., Hutz, M.H., Palha, T.J., Ribeiro dos Santos, A.K., dos Santos, S.E., 2008. A multiplex PCR for 11 X chromosome STR markers and population data from a Brazilian Amazon Region. *Forensic Sci. Int. Genet.* 2, 154–158.
- Ribeiro-Rodrigues, E.M., et al., 2009. An INDEL polymorphism at the X-STR GATA172D05 flanking region. *Int. J. Legal Med.* 123, 89–94.
- Yunis, J.J., 1981. New chromosome techniques in the study of human neoplasia. *Hum. Pathol.* 12, 540–549.