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Review

Y-Chromosome short tandem repeat, typing technology, locus information and allele frequency in different population: A review

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Chromosome Y microsatellites seem to be ideal markers to delineate differences between human populations. They are transmitted in uniparental and they are very sensitive for genetic drift. This review will highlight the importance of the Y- Chromosome as a tool for tracing human evolution and describes some details of Y-chromosomal short tandem repeat (STR) analysis. Among them are: microsatellites, amplification using polymerase chain reaction (PCR) of STRs, separation and detection and advantages of X-chromosomal microsatellites.

Key words: Forensic, population, review, STR, Y- chromosome.

INTRODUCTION

Microsatellites are DNA regions with repeat units that are 2 to 7 bp in length or most generally short tandem repeats (STRs) or simple sequence repeats (SSRs) (Ellegren, 2000; Imad et al., 2014). The classification of the DNA sequences is determined by the length of the core repeat unit and the number of adjacent repeat units. It may contain several hundred to thousands (Butler, 2012) of these. Tandem repeats occur in the form of iterations of repeat units of almost anything from a single base pair to thousands of base pairs. Mono-, di-, tri- and tetranucleotide repeats are the main types of microsatellite, but repeats of five (penta-) or six (hexa-) nucleotides are usually classified as microsatellites as well. DNA can be used to study human evolution. Besides, information from DNA typing is important for medico-legal matters with polymorphisms leading to more biological studies (Walkinshaw et al., 1996). Since the STR markers are important for human identification purposes (Rui et al., 1996) the number of repeats can be highly variable among individuals and can be used for identification purposes. There are three types of repeat patterns for STRs. Two or more adjacent simple repeats

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Abbreviations: STR, Short tandem repeat; **PCR,** polymerase chain reaction; **SSRs,** simple sequence repeats; **PAGE,** polyacrylamide gel electrophoresis; **CE,** capillary electrophoresis; **SNP,** single nucleotide polymorphism; **Y-DNA,** Y-chromosome DNA; **mtDNA,** mitochondrial DNA.

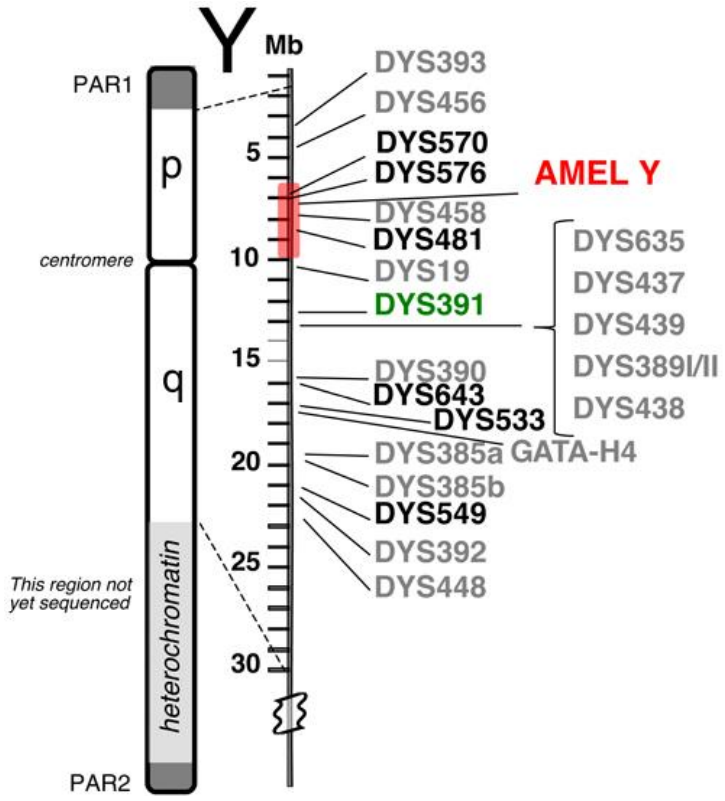

Figure 1. Relative positions of 23 Y-STR loci available in the PowerPlex® Y23 System. The six new loci are shown in bold font. PAR1 and PAR2 are pseudo-autosomal regions on the tips of the Y chromosome that recombine with the X chromosome. The shaded region around AMEL Y can sometimes be deleted, causing loci such as DYS458 to be missing from an otherwise full Y-STR profile. DYS391 is located a sufficient distance away to avoid deletions affecting AMEL Y (Butler, 2012).

are considered a compound repeat. Units of similar length are called simple repeats (Budowle, 1995; Butler et al., 2009; Mohammed and Imad, 2013).

Chromosome Y microsatellites or short tandem repeats (STRs) seem to be ideal markers to delineate differences between human populations for several reasons: (i) They are transmitted in uniparental (paternal) fashion without recombination, (ii) they are very sensitive for genetic drift, and (iii) they allow a simple highly informative haplotype construction (Kayser et al., 1997). Also for forensic applications, this ability to differentiate distinct Y chromosomes makes Y- STRs an advantageous addition to the well characterized autosomal STRs. For a number of forensic applications, Y- STRs could be preferred to autosomal STRs. Especially in rape cases where (i) the differential extraction was unsuccessful, (ii) the number of sperm cells is very low, (iii) due to vasectomy epithelial cells instead of sperm cells from the ejaculate of the perpetrator have to be analyzed, and (iv) the perpetrator, due to a familial relationship shares many autosomal bands with the victim, Y- STRs could provide crucial evidence. Also, in the case of male-male rape or rape cases with multiple perpetrators Y- STRs could lead to essential qualitative evidence. In all such cases Y- STRs facilitate a simple and reliable exclusion of suspects.

Unlike autosomal STR markers, Y-STR markers are linked on the same chromosome and there is no genetic recombination between the markers (Figure 1). Therefore, unlike for autosomal STRs, the Hardy-Weinberg equation is not suitable for determining the frequency of a genotype from the frequency of the alleles at each locus (Beleza et al., 2003; Dupuy et al., 2004; Imad et al., 2015a; Mohammed et al., 2015). To determine the frequency of a particular Y-STR profile, the profile must be searched against different databases for a possible match, and these databases must be large enough to accurately represent the frequencies of the haplotypes present in the population of interest. Thus, as more Y-STR samples are typed and contributed to a database the more useful the database will become. However, at present, the databases are much too small to enable forensic scientists to attain the level of

discrimination provided by autosomal STR analysis (Ballantyne et al., 2010; Imad et al., 2015b; Muhanned et al., 2015).

AMPLIFICATION USING POLYMERASE CHAIN REACTION OF STRs

A billion copies of a given target sequence can be provided by Polymerase Chain Reaction (PCR) in a fast *in vitro* DNA synthesis process. A DNA polymerase may duplicate to result in specific DNA markers to be surfaced. dNTPs, Mg++ and a thermal stable DNA polymerase, (usually Taq polymerase) are five main chemical components. During the cycling of temperatures, the primers are designed to hybridize to the specific markers (e.g. STR loci) along the length of the template. A special DNA polymerase that is heat stable is used to copy and amplify the genetic markers using the remaining components after the DNA strands are separated and the primers bind to the template. This happens for a given thermal cycle (Del et al., 2009; Nadine et al., 2010). To analyze the DNA, the process of 28 to 32 heating and cooling cycles, is increased. The amplification of multiple samples can be done at one time. In fact in 3 h 96 samples can be amplified in this manner. The thermal samples contain many sample wells that allows this to happen when several different loci are simultaneously amplified in a single tube when multiple PCR occurs. It has been found lately that even 15 autosomal short tandem repeats (STRs) have been done at one time using DNA from a very small amount of contaminated sample.

SEPARATION AND DETECTION

After PCR there must be a process of separation and detection of the amplified products. A number of ways can be used to carry out the typing. Among them are (1) PolyAcrylamide Gel Electrophoresis (PAGE) followed by silver staining or if the primers are fluorescently tagged, detection by fluorescent gel scanners and (2) Capillary Electrophoresis (CE) with laser induced fluorescence. Based on the fact that it is automated this method has become popular. No gel is used and samples can be inserted mechanically. The resolution of the higher molecular weight loci is usually better than in the PAGE methods since the DNA traverses the entire length of the capillary. There are several components that impact DNA separations within CE systems. Among these are the polymer used for enabling the separation, the capillary, the electrophoresis buffer, and the field strength (John et al., 2004). The objective of the exercise is to introduce a different dye onto the 5'-(nonreactive) end of each primer or set of primers (Giusti and Adriano, 1993). The properties of these dyes are quite unusual. Although fluoresce in different regions of the spectra they all excited by a single argon-ion laser tuned to 488 nm. To determine which dye is present, based on the emission of each fragment as it passes the detector window, a multiwavelength analyzer, such as a charged coupled device (CCD) camera, can then be used. The advantage of this method allows the analysis of fragments of DNA that overlap in size as long as they are labeled with different colors, which fluoresce at different wavelengths.

The STR fragments in the sample are amplified using primers with fluorescent tags in the most commonly used analytical method for detecting STRs. There is fluorescent dye in every new STR fragment made in a PCR cycle. When light is shown over it, each dye will emit a different color. Using electrophoresis in automated "genetic analyzer" machinery the fragments are separated according to their length. This technology is developed as a by-product of the technology developed for the Human Genome Project. That first carried out to sequence most of the entire genome. In these machines an electric field is used to extract DNA fragments placed at one end of the tube through the entangled polymer or comparable sieving medium. This is done using a long, narrow tube (a "capillary"). The bigger or bulkier fragments move slowly in the medium as compared to the smaller ones. Sending a laser beam through small glass window in the tube causes it to fluoresce at specific wavelength as the tagged fragments pass under the light. A kind of electronic camera records the intensity of light emitted by the dye. This can be translated into a graph, which shows a peak as an STR flashes by. Firstly, a short allele will pass by the window and fluoresce first. Later a longer fragment will come by, and this will show another peak on the graph.

HAPLOTYPE DIVERSITY FOR Y-CHROMOSOMAL STR IN DIFFERENT POPULATIONS

Observed Alleles, PCR Product Sizes, Repeat Structure and PCR Primer Sequences have been tabulated (White et al., 1999). The observed numbers of haplotypes and their frequencies have been tabulated (Table 1). Haplotypes detected in this study group have been compared with seven other populations: German (n = 88), Indian (n = 25), Chinese (n = 36), Italians (n = 100) (Manfred et al., 2001), Mozambican (n = 112) (Alaves et al., 2003), Japanese (n = 161) (Hara et al., 2007) and Turkish (n = 280) (Henke et al., 2001). Our data have also provided additional information to the framework of variation involving seventeen Y-STR loci as well as a further contribution to the Y-STR database for Iraq population. This supports the observations by others (Jorde et al., 2000) that, especially among European populations. Y-STRs are very powerful in the detection of genetic differences between male populations, compared with autosomal STRs. This can be attributed to the

Table 1. Comparison of the haplotypes and haplotype diversity in different human population groups.

Parameter	Iraq[1]	Tunis[2]	German[3]	Italy[4]	China[5]	India[6]	India[7]
Individuals number	320	105	88	100	36	25	154
Haplotypes number	276	81	77	82	34	16	152
Unique haplotypes	256	67	39	53	28	13	150
Proportion of unique haplotypes	0.93	0.83	0.51	0.65	0.82	0.81	0.98
Non-unique haplotypes	20	14	38	29	6	3	2
Proportion of non-unique haplotypes	0.07	0.17	0.49	0.35	0.18	0.19	0.01
Ratio (unique : non-unique)	13.2	4.88	1.03	1.83	4.67	4.33	98
Haplotypes diversity	0.8392	0.9932	0.9963	0.9941	0.9968	0.950	0.9935

[1]References: (Imad et al., 2013), [2]Reference: (Imen et al., 2005), [3]Reference: (Manfred et al., 2001), [4]Reference: (Manfred et al., 2001), [5]Reference: (Manfred et al., 2001), [6]Reference: (Manfred et al., 2001), [7]Reference: (Kuppareddi et al., 2010).

greater sensitivity of nonrecombining Y-chromosomal markers to founder effects and genetic drift. A similar conclusion was reached by Forster et al. (2000), on the basis of a phylogenetic approach only. The use of Y-STRs allows the simple construction of highly variable haplotypes. With these haplotypes, it is possible to analyze differences in population structure by a comparison of haplotype diversity and of the number of population-specific haplotypes.

In the study of molecular evolution, a haplogroup is a group of similar haplotypes that share a common ancestor with a single nucleotide polymorphism (SNP) mutation. Haplogroups pertain to deep ancestral origins dating back thousands of years. The most commonly studied human haplogroups are Y-chromosome or (Y-DNA) haplogroups and mitochondrial DNA (mtDNA) haplogroups, both of which can be used to define genetic populations. Y-DNA is passed solely along the patrilineal line, from father to son, while mtDNA is passed down the matrilineal line, from mother to both daughter and son. The Y-DNA and mtDNA may change by chance mutation at each generation. Therefore pattern H77 shared in three unrelated males in this study may be descended from same ancestry.

According to a 2000 study of Y-chromosome sequence variation human Y-chromosomes trace ancestry to Africa, and the descendants of the derived lineage left Africa and eventually were replaced by archaic human Y-chromosomes in Eurasia. The study also shows that a minority of contemporary East Africans and Khoisan are the descendants of the most ancestral patrilineages of anatomically modern humans that left Africa 35,000 to 89,000 years ago (Collins et al., 1998). Other evidence supporting the theory is that variations in skull measurements decrease with distance from Africa at the same rate as the decrease in genetic diversity. Human genetic diversity decreases in native populations with migratory distance from Africa, and this is thought to be due to bottlenecks during human migration, which are events that temporarily reduce population size (Manica et al., 2007; Phillips et al., 2011). Regarding forensic applications, the unique pattern of Y-DNA in the rest of samples in present study makes it useful as powerful tool for discrimination individuals in crimes, rapes and paternity or log dead people such as in mass graves.

Conflict of interests

The authors did not declare any conflict of interest.

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