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Y-Chromosome and its future implications: A Review

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ABSTRACT

Forensics has forever relied upon the various discrepancies in the Y-Chromosome in studying the human race. It may possess structural and compositional variety but this very fact has made it stand out in forensic studies. The contribution of the Y-chromosome in identifying sex, lineage is of course undeniable. By this paper, the author wishes to highlight the implementations of Y- Chromosome in Sex Determination, Lineage studies, Disease identification, and Migration pattern. Through the structural anomalies of the Y- chromosome and various testing methods developed over the years, forensics has developed Y into a tool of a human population study. All the markers indicate that they can be further used as foundational stones in improving human life and understanding of our past.

Keywords

Y- Chromosome, Amelogenin, Y-Deletion, Haplogroups.

Introduction

The chromosomal structure, differences, and implications have a major role to play in forensics and with everyday advances of our understanding of the butterfly effect of DNA through generations;races and regions have substantiated the role. In scientific casework, there is regularly a need to decide the sex of an individual dependent on DNA proof in cases like identification of survivors of the mass fiasco, missing people examinations, and rape cases. Examination of Y explicit arrangements on the Y chromosome is a generally successful technique for deciding the chromosomal sex of an individual and assessing the proportion of male-female DNA in a forensic sample. However, the males belonging to the same lineage on the father's side have Y-STR haplotypes in common. Therefore, questions that relate to paternity, lineage, and race can be answered by backtracking the Y-chromosome. This particular implication would not only help in establishing paternity but can also serve as important in determining migration through the decades. Various studies have likewise illustrated a relationship between Loss of Chromosome Y and the improvement of sicknesses like Alzheimer's, immune system infections (immune system thyroiditis and twofold cirrhosis), cardiovascular occasions, schizophrenia, and various malignancies like; prostate disease, intense myelogenous leukemia, gastric malignant growth, oesophageal carcinoma, testicular germ cell tumor, bladder malignant growth, renal cell carcinoma (1). Lastly, the future avenues where the prowess of Y-Chromosome can be used are multifold. Several studies are being conducted into finding out the projected use of Y implication, which have been discussed further.

Structure of Y-Chromosome

The Y chromosome takes account of about 2-3% of a haploid genome because it being the smallest chromosome present in the human body. As depicted in Figure 1 the different parts of the Y chromosome based on chromosome

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banding may be identified as follows: the Pseudo-autosomal parcel (partitioned within two parts: PAR1 and PAR2), heterochromatic, and the euchromatic areas. The PAR1 is positioned at the extreme end of the short arm (Yp) while PAR2 is found at the terminus of the long arm (Yq). PAR2 and PAR1 cover around 320 and 2600 kb of DNA, separately. When the male meiosis takes place, the (Yp) end combines with the pseudo-autosomal end of the X

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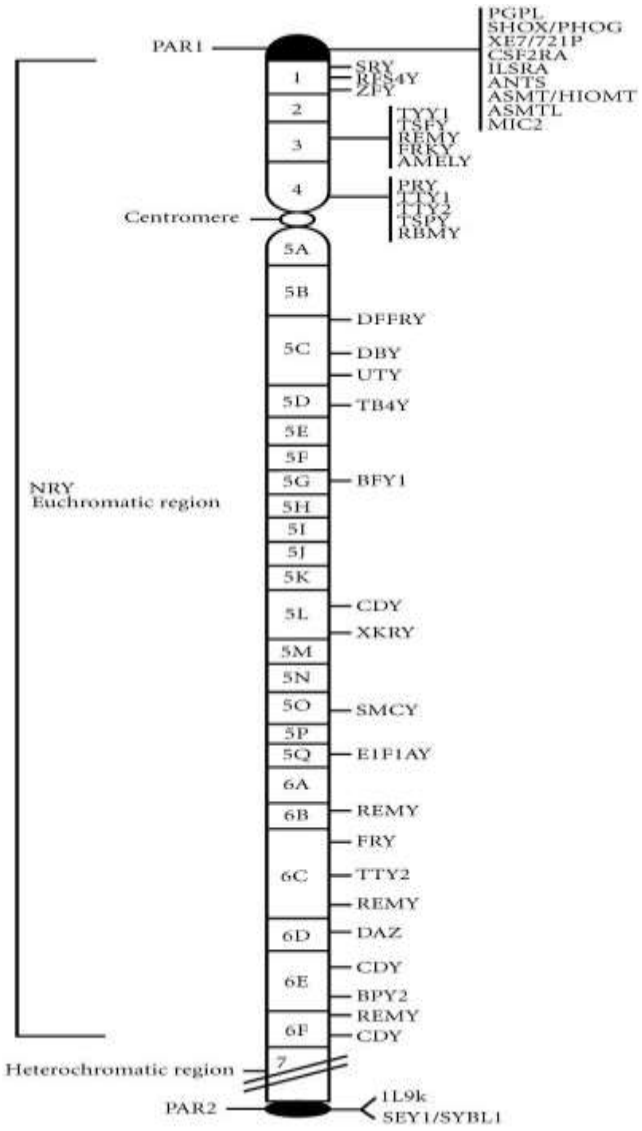

Figure1: Diagrammatic exhibition of the Y chromosome depicting the pseudo-autosomal areas (PAR1 and PAR2) and the non-recombining region (NRY) and the genes occurring in them (2).

chromosome, and genetic information owing to hereditary is exchanged between the two. Subsequently, qualities situated inside the PAR are acquired similarly to autosomal qualities. The euchromatic locale comprising of three distinct portions by the names of and comprises of the paracentromeric area (short arm), the centromere, and the paracentromeric area (long arm) is distal to the PAR1.

At last, the heterochromatic locale contains distal Yq relating to Yq12. Since, it is made of exceptionally redundant succession groups- DYZ2 & DYZ1, in around 2000 to 5000 replicates of each, the heterochromatic locale is considered hereditarily dormant and polymorphic long in various male populaces. The “Recombining Y” so to say is addressed by PAR1 and PAR2, which is 5% of the whole chromosome, whereas “Non-Recombining Y" (NRY) covers the major portion of the Y – Chromosome i.e. (95%). This incorporates the heterochromatic and euchromatic areas of the chromosome. While the latter is considered to be inactive by the hereditary point of view, the former has

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various exceptionally rehashed groupings yet additionally contains a few qualities liable for significant natural capacities that we will audit here (2).

Sex Determination through Amelogenin

The amelogenin sex determination is based on the presence of two comparable of the protein, i.e. AMELY & AMELX, both of which show length polymorphism. Their differentiation in size and arrangements tends to give different sex determinations. In contrast with AMELY, AMELX has a 6bp deletion adding to the distinction in proportions between these two homologous qualities. PCR enhancement utilizing the ordinarily utilized groundwork sets produces sections of 112 and 106 bp long for AMELY and AMELX individually (3).

Along these lines, in females just X explicit pieces can be noticed, though, in men, both X and Y explicit pieces are seen after electrophoretic partition (4). Consequently, the male and female can be recognized based on the number of sections distinguished in them (5,6). Scientists at first built up a solitary arrangement of preliminaries traversing part of the intron 1 of Amelogenin quality for a quantitative appraisal of sex at DNA level utilizing less than 1 ng DNA layout. Systematically, to oblige the amelogenin marker in multiplexing frameworks, shifted preliminary sets have been created focusing on various parts of the quality and flanking districts. In this unique circumstance, intron 3 of the Amelogenin quality has been investigated extraordinarily to plan preliminary sets focusing on the 6 bp distinction in amplicons among AMELY and AMELX (7).

Discrepancies and Alternatives

Amelogenin has been utilized for quite a long time for sex assurance at the atomic level in crime scene investigation just as for hereditary and atomic profiling in pale history and human sciences. In non-human investigations, this marker is valuable in different areas like the proliferation field, archaeozoology, meat creation, and test identification (8). The potency of the amelogenin marker was questioned when mentions of men being identified as women falsely, came to light (9). The amelogenin marker has experienced various failures around the world however; the Indian population has been subjected to major letdowns in studies regarding Y deletion as reported by scientists (10-12). In the table (Table 1) below a summarized version of all the alternative techniques and sex-markers are put together and their subsequent advantages and disadvantages have also been projected.

Such failure cases have only risen so much rather recently. The reason why the amelogenin marker may give bogus adverse outcomes is allele dropouts coming due to discrepancies in similar areas. Males holding erasures and transformations in the AMELY area would be identified as females in the nonattendance of some other substantiating confirmations. In the figure (Fig.2) below, it is shown how disparities in the test marker because of the allele dropout can either give positive or adverse results. In fact, X- Chromosome has less deletion in the amelogenin areas as compared to the Y- chromosome.

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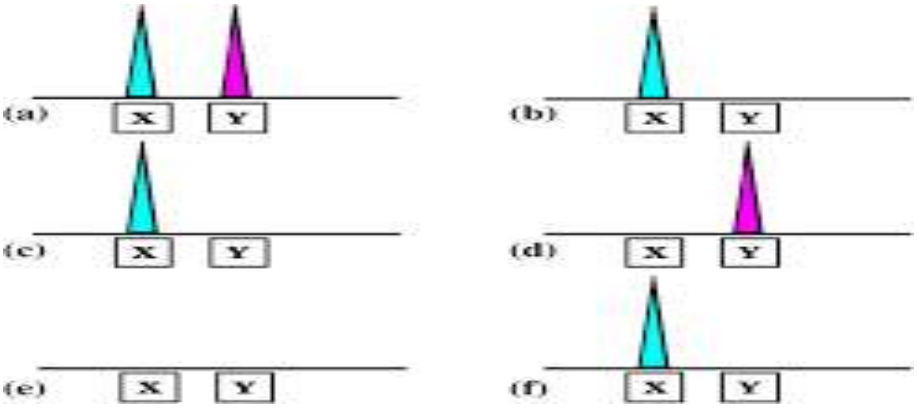

Figure 2. Plausible outcomes and issues occurring with amelogenin typing in both fit and unfit specimens; a) Ordinary Male sample, b) Standard Female sample, c). Deletion of Y in a male sample, d).A Male sample without X, e).Deletion of X in a female specimen at both the chromosomes, f). A female sample with X deletion in any one of the chromosome (13)

Y-Chromosome in Disease detection

The Y-chromosome is not only responsible for male gonad development but also maintains fertility and male traits linked to the Y-phenotype (14-15). Other than that, its contribution to bone growth, size of teeth, right or left-handedness, and cerebral lopsidedness is noticeable (16-18). The Y-chromosome gonadal diseases(Y-GD) characterized by testicular immature development are also seen (19). Such patients also develop gonadoblastoma, which is proposed to be concerned with the centromere of Y (20-21). Various other viral infections and cardiovascular diseases including increased blood pressure, arterial infections, and strokes have been associated with the Y chromosome (22-23).

Since, only the male genealogies can carry the Y-chromosome, in most examinations various groups of Y haplotypes can be identified pointing towards variation in hereditary happening in the MSY district of the chromosome. The significant Y haplogroups are A&B, CT, C, D, E, F, G, H, I, J, K, L&T, K2, K2a, K2a1, K2b1, NO and NO1, N, O, M&S, P, Q, and R. Y haplogroups have often been linked to various sicknesses of which the Y haplogroups-I is one of the most detailed models. This particular haplogroup has been responsible for the faster widespread of AIDS, but protection from HAART in these patients and coronary infections. The Y chromosome seems to be connected with major illnesses seen worldwide and can be attributed to the overall life expectancy of people and various differences seen amongst individuals.

Future Implications of Y-Chromosome

Commercially viable Y-STR kits have rather expanded the paternal lineage identification goal. It is difficult to separate random men in a given demographic and segregation of related men is not possible. The future commercial Y-STR kits are expected to have more and more markers, specifically when it comes to RM Y-STRs. Be that as it may, counting more RM Y-STRs will prompt a further expanding issue of putting a factual load on a noticed haplotype match given the super high variety of RM Y-STR haplotypes requiring incredibly enormous reference information bases for assessing a to some degree solid recurrence of the coordinating haplotype required for assessing the match likelihood, except if new measurable arrangements will be created (24). For parentage testing utilizing Y-chromosome markers, future work needs to give more information about the geographic dissemination of large numbers of the as of late found Y-SNPs, to build up how valuable they are for improving the geographic goal

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of fatherly heritage deduction. Normally, such information will permit fatherly bio-geographic heritage surmising to be moved from the current degree of generally mainland goal to a substantially more definite geographic goal. Just like the Y-STRs, the Y-SNPs, all the constraints used in genotyping innovations must be survived utilized in legal DNA, to take full benefit of the huge number of Y-SNPs required for construing bio-geographic parentage on a

Markers/techniques	Advantages	Disadvantages

point-by-point level. At last, a few authors have proposed other scientific uses of the human Y-chromosome than talked about above, for example anticipating a man's last name from his Y-chromosome DNA (25-26).

Table 1. Alternative sex determiners and their pros and cons in forensic application (13)

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STS	Y homologue will function as an inner control Disparities in X linked icthyosis victims	Marker's size is large Discrepancies in results from unfit samples
SRY	Immediate link with male phenotype Smaller in size Works even if sample is degraded	Instances of translocation of SRY to X chromosome
TSPY	Highly delicate Favorable results from depraved samples Subtle work for mixture analysis	Negative internal control
DXYS156	Has some internal control Multi-allelic penta nucleotide repeat marker Helps identifying race of sample	No distinction between X and Y homologue
SNPs	Works fine with degraded DNA Establishes lineage Automation is helpful Helps where no suspect is available	Limited discriminatory power 15 STRs are equivalent to 50–100 SNPs
YZ1/Alu	High replicates in males Helps in distinguishing monozygotic twins Uses RT PCR method	No internal control Results are obtained relative to each other

Conclusion

Y is unusual in many respects. It is in a continuous haploid position and is loaded with a redesigned array. However, it is responsible for significant biological functions, for example, sexual stability and fertility in men. Besides, the Y chromosome is a wonderful property to explore the human race. Y maintains a record of contact with male offspring through the development of the unconnected area, which is because the meiosis is holoandrically communicated from father to child, without being reconnected. As a result, the investigation of the various changes that this particle has collected with its progress may be deeply enlightening in concluding the accounts of the human population. Overall, it is time to change the value of this individual chromosome.

Though the Y- chromosome has been studied for over 30 years, it is acknowledged important by various individuals, except in exceptionally prohibited conditions. Y does not seem only to have incredible teaching in unraveling the historical background of the human race; it additionally has basic natural functions that make this chromosome a significant part of the human gene.

Reference

1. Barros, B., Morais, M., Teixeira, A. L., & Medeiros, R. (2020).Loss of Chromosome Y and Its Potential Applications as Biomarker in Health and Forensic Sciences. *Cytogenetic and Genome Research*, *160*(5), 225-237.
2. Murci, L. Q., & Fellous, M. (2001).The human Y- Chromosome: the biological role of a "functional wasteland".*Journal of Biomedicine and Biotechnology*,*1:1*, 18–24.
3. Masuyama, K., Shojo, H., Nakanishi, H., Inokuchi, S., &Adachi, N. (2017) Sex determination from fragmented and degenerated DNA by amplifed product length polymorphism bidirectional SNP analysis of Amelogenin and SRY genes. PLOS ONE 12(1):e0169348.
4. Dutta, P., Bhosale, S., Singh, R., Gubrellay, P., Patil, J., Sehdev, B., Bhagat, S., Bansal, T. (2017) Amelogenin gene: the pioneer in gender determination from forensic dental samples.*Journal of Clinical and Diagnostic*,*11(2)*:ZC56–ZC59.
5. Nakahori, Y., Takenaka, O., &Nakagome, Y. (1991) A human X-Y homologous region encodes "amelogenin". *Genomics, 9(2)*,264–269
6. Sasaki, S., &Shimokawa, H. (1995).The amelognin gene.*International Journal of Developmental Biology*, *39*(1),127-133.
7. Sullivan, K.M,,Mannucci, A., Kimpton, C.P., &Gill, P. (1993). A rapid and quantitative DNA sex test: fuorescence-based PCR analysis of X-Y homologous gene amelogenin. *Biotechniques*, *15(4*), 636–638.
8. Fontanesi, L., Scotti, E., &Russo, V. (2008).Diferences of the porcine amelogenin X and Y chromosome genes (AMELX and AMELY) and their application for sex determination in pigs.*Molecular Reproduction and Development, 75*(11),1662–1668.
9. Zehethofer, K., &Rolf, B. (2011).A molecular analysis of three amelogenin negative males in two routine paternity tests.*Forensic Science International: Genetics*, *5(5), 550–551.*
10. Santos, F.R., Pandya, A., &Tyler-Smith, C. (1998). Reliability of DNAbased sex tests. *Nature Genetics*, 18,103.

11. Kashyap, V.K., Sahoo, S., Sitalaximi, T., &Trivedi, R. (2006). Deletions in the Y-derived amelogenin gene fragment in the Indian population. *BMC Medical Genetics, 7*:37.
12. Thangaraj, K., Reddy, A.G., &Singh, L. (2002). Is the amelogenin gene reliable for gender identification in forensic casework and prenatal diagnosis?.*International Journal of Legal Medicine, 116,*121–123.
13. Dash, H.R., Rawat, N. & Das S. (2020).Alternatives to amelogenin markers for sex determination in humansand their forensic relevance.*Molecular Biology Reports,47(3),*2347-2360.
14. Affara, N., Bishop, C., Brown, W., Cooke. H., Davey, P., et al. (1995).Report of the Second International Workshop on Y chromosome Mapping.*Cytogenetic and Cell Genetics, 73(1-2),*33-76.
15. Jobling, M.A., &Tyler-Smith, C. (2000).New uses for new haplotypes - the human Y chromosome, disease and selection.*Trends in Genetics, 16*(8),356-362.
16. Crow, T.J. (2002).Handedness, language lateralisation and anatomical asymmetry: relevance of protocadherin XY to hominid speciation and the aetiology of psychosis.Point of view,*British Journal of Psychiatry, 181,*295-297.
17. Ginalski, K., Rychlewski, L., Baker, D., &Grishin, N.V. (2004).Protein structure prediction for the male-specific region of the human Y chromosome.*Proceedings of the National Academy of Sciences of the United States of America, 101(8):*2305-10.
18. Singh, N.P.,Madabhushi, S.R., Srivastava, S., Senthilkumar, R., Neeraja, C., et al. (2011).Epigenetic profile of the euchromatic region of human Y chromosome.*Nucleic Acids Research, 39(9),* 3594-3606.
19. Berberoglu, M., &Siklar, Z. (2018).Ankara University DSD Ethics Committee: The evaluation of cases with Y-chromosome gonadal dysgenesis: clinical experience over 18 years.*Journal of Clinical Researchin Pediatric Endocrinology, 10(1),*30-37.
20. Lau, Y.F., Li, Y., &Kido, T. (2011).Role of the Y-located putative gonadoblastoma gene in human spermatogenesis.*Systems Biologyin Reproductive Medicine, 57(1-2*):27-34.
21. Knauer-Fischer, S., Besikoglu, B., Inta, I., Kneppo, C., Vogt, P.H., &Bettendorf, M. (2015).Analyses of gonadoblastoma Y (GBY)-locus and of Y centromere in Turner syndrome patients.*Experimentaland Clinical Endocrinology Diabetes, 123(1),*61-65.
22. Case, L.K., &Teuscher, C. (2015).Y genetic variation and phenotypic diversity in health and disease.Case and Teuscher Biology of Sex Differences,6:6.
23. Johansson, M.M. (2015).The human Y-chromosome and its role in the developing male nervous system.Digital Comprehensive Summaries of Uppsala Dissertations from the Faculty of Science and Technology 1285, ActaUniversitatis, Upsaliensis, Uppsala.
24. Kayser, M. (2017).Forensic use of Y-chromosome DNA: a general overview, *Human Genetics, 136*(125–33).
25. Calafell, F., &Larmuseau, M.H.D. (2016). The Y chromosome as the mostpopular marker in genetic genealogy benefits interdisciplinary research. Human Genetics,136(5),559–573.
26. King, T.E., & Jobling, M.A. (2009).What's in a name? Y chromosomes, surnames and the genetic genealogy revolution. *Trends in Genetics, 25(8),*351-60.