 Int J Hum Genet, 6(3): 177-183 (2006)

Human Chromosomal Polymorphism in a Hungarian Sample

Kata Décsey[1], Orsolya Bellovits[2] and Györgyi M. Bujdosó[2]

1. Semmelweis University, Department of Forensic Medicine, Budapest, Hungary, 1091
2. Hungarian Academy of Sciences - Semmelweis University, Institute of Forensic Medicine, Budapest, Hungary, 1091
E-mail: bujgyo@igaz.sote.hu

KEYWORDS Chromosomal variation; banding; Hungarian population

ABSTRACT In the Department of Forensic Medicine of Semmelweis University, Budapest, Hungary we carried out a study about human chromosomal polymorphism in a Hungarian population. Q-band method was used for the analysis of chromosomes 3, 4, 13, 14, 15, 21, 22 and Y and C-band for chromosomes 1, 9, 16 and Y. The polymorphism of the representative Hungarian population was compared to the data of different ethnic groups found in the literature, such as Central-European, Italian, Indian and Turkish data. The result shows that there is a relatively small difference between the Hungarian and Indian group, the Central-Europeans differ more, and the most distant relatives are the Turks among the populations mentioned in this paper.

INTRODUCTION

Many researchers dealt with human chromosomal polymorphisms all over the word, so the distributions of the polymorphisms are known in many ethnic groups. In Hungary, there has not been data about this. In the Department of Forensic Medicine of Semmelweis University, Budapest, Hungary we carried out a study about human chromosomal polymorphism. The chromosomes of 1171 persons (563 females and 608 males) were analyzed by Q- and C-banding techniques. The investigated individuals were unrelated and they represented the common Hungarian population. The aim of our research was to determine the Hungarian chromosomal variation and to compare it with different ethnic groups found in the literature. We summarized a few studies that treat this subject. Our nation cross-bred with the Central-Europeans due to the historical and the geographical position. The Turkish population played an important role (migration of nations, the Turkish occupation) in the history of the Hungarian nation, so it is expected to appear in the genetics. The Indians are in relation with the Gypsies, who are the biggest ethnic group in Hungary. Molecular genetic methods supported our observations, that there is a relatively small difference between the Hungarian and Indian groups, the Central-Europeans differ more, and the most distant relatives are the Turks among the populations mentioned in this paper.

Correspondence Address: Györgyi M. Bujdosó
Hungary, Budapest, 1091, 93. Üllõi street
Telephone: 36-1-2157300
Fax: 36-1-2162676
E-mail: bujgyo@igaz.sote.hu

MATERIAL AND METHODS OF INVESTIGATION

One thousand one hundred and seventy-one unrelated persons of Hungarian origin were investigated. The data were collected from the reports of paternity cases carried out in the last 15 years and from azoospermic males. In paternity cases father-mother-child trios were examined, but in this study we did not take the children into consideration to avoid the duplication of the data. In azoospermic cases only chromosome Y was described with Q-banding. Chromosomes 1, 9, 16 and Y were taken into account with C-banding, in case of inversion we used up the data of a previous Hungarian study (Bujdosó 1985) also. We compared our Q-banded data with some study found in the literature (Schwanitz 1975; Buckton et al. 1976; Ibraimov and Mirrakhimov 1983; Kalz and Schwanitz 2004; Kalz et al. 2005). We made a comparison with the C-banded data also (Müller et al. 1975; Buckton et al. 1976; Verma et al. 1978; Berger et al. 1979; Sofuni et al. 1979; Simi and Tursi 1982; Hsu et al. 1987; Kalz and Schwanitz 2004; Kalz et al. 2005).

The chromosomes were obtained from the blood taken under sterile circumstances following a 72-hours culture. Two banding techniques were used. Chromosomes 1, 9, 16 and Y could be

examined with C-band staining (centromere staining) (Sumner 1972). There are 5 levels according to the length of the centromeric heterochromatin. Level 1: very-small; level 2: small, middle-small; level 3: middle; level 4: middle-large, large; level 5: very-large. In some cases partial or total pericentric inversion can be seen, and that is a very valuable feature in paternity testing. Q-band stained (Caspersson et al.1970) chromosomes were investigated with ultra violet light. There are five levels with Q-band staining. Level 1: no fluorescence; level 2: pale; level 3: medium; level 4: intensive; level 5: brilliant. The frequencies of brilliant bands were described for the chromosomes 3, 4, 13, 14, 15, 21, 22 and Y. In the acrocentrics two regions were distinguished: p11 (short arm) and p13 (satellite).

RESULTS

Q-Band: With Q-banding, chromosomes 3, 4, 13, 14, 15, 21, 22 and Y can be examined (Fig. 1). According to the fluorescence intensity, chromosomes are classified into 5 levels. In the Hungarian group intensive band was the most frequent (64.4%) and the frequency of pale or no fluorescence was low (Table 1) for chromosome Y. On the acrocentric chromosomes one satellite was observed in 0.3 %, two satellites in 0.21 % and three satellites in 0.22 %. The most brilliant bands (30.8 %) were on the 13p11 region, the least (0.1 %) on the 14p11 region (Table 2). The frequency of brilliant bands was 12 % of the total amount of the relevant chromosomes analyzed. There was no difference between sexes.

C-Band: After C-band staining, chromosomes 1, 9, 16 and Y were analyzed. Chromosome Y was examined with both two techniques, but in case of C-band staining it was only described only in some azoospermic cases, and when the child in the paternity test had a male karyotype. That is the reason why only 251 Y chromosomes were analyzed with C-banding (Table 1). In Hungary the large chromosome Y was more frequent than the small one, which was the least common. There was no difference in the distribution of the length of chromosomes Y between the azoospermic and healthy men. Our experience indicates that the length of chromosome Y does not influence the sexual capability. The small Y chromosomes with C-band (level 1 and level 2) are equivalent with Y chromosomes having not any or pale fluorescence intensity with Q-band.

Among women the frequency of very small centromere (level 1) on chromosome 1 was higher than among men. On the other hand, men had a larger frequency of small centromere region (level

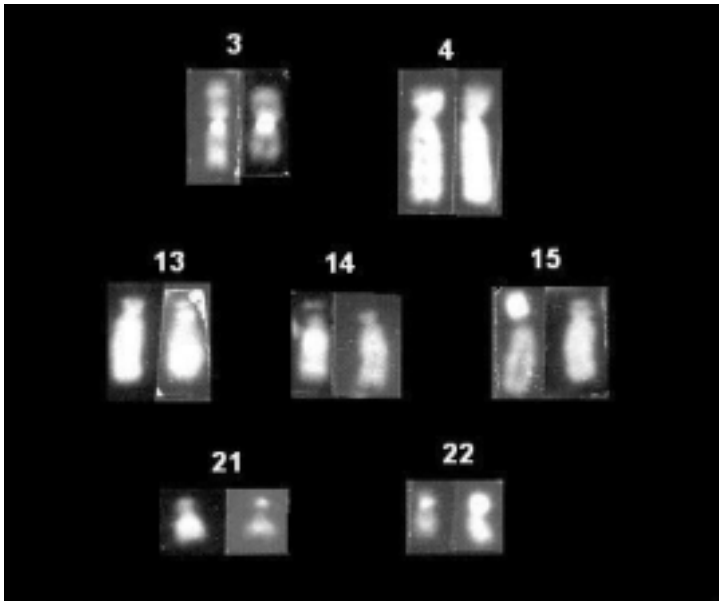

Fig. 1. Q-banded chromosomes

2) for chromosome 1 than women. Beyond that, there was no essential difference between sexes (Tables 3-4). We did not expect that difference, that can derive from the number of chromosomes examined.

During the description of inversion we added our data to a result of a previous Hungarian study (Bujdosó 1985), so the number of the examined chromosomes increased. The frequencies of partial inversion were 4.1 %, 11.41 % and 0.16 % for chromosomes 1, 9 and 16. The frequencies of total inversion were 0.03 %, 0.94 % and 0.03 % for chromosomes 1, 9 and 16 (Table 5).

DISCUSSION

Q-Band: The comparison of the frequencies of fluorescence intensity of different studies is based on the frequency of brilliant bands (level 5). We summarized some studies that dealt with chromosomal polymorphism.

Mikelsaar et al. (1974) investigated 207 unrelated individuals of Estonian nationality. The frequency of chromosomes having a brilliant band were 64.9 %, 27.6 % and 84.4 % respectively for chromosomes 3, 4 and 13. The distribution was described separately between men and women. Significant differences between sexes in the distribution of homo and heterozygotes for brilliant band in chromosome 3 were observed: among the women heterozygotes prevailed, among the men, homozygotes. A tendency toward distinction between sexes was also found for chromosome 4, but the difference was not statistically significant. No difference between sexes was found for chromosome 13. This peculiar distribution apparently indicates the relatively independent evolution of these chromosomes. Brilliant bands (A-T rich regions) may arise independently at various sites in the genome. However, we do not know yet why brilliant band prevail in chromosomes 3 and 13, but not in chromosome 4.

There is evidence that a difference exist in the proportion of specific chromosome variants between populations. Lubs et al. (1977a) found that the studied U.S. Black population had a greater preponderance of bright Q-band in comparison to the white population. Ibraimov and Mirrakhimov (1982) found differences in the frequency of the bright inverted Q-heterochromatin band in chromosome 3 between Russian (6.0 %) and Asian Mongoloid (0.3 % - 3.0 %) populations. The significance of these differences, as well as the role of heterochromatin in general, is unknown.

Kalz and Schwanitz (2004) investigated 600 unrelated persons of Central-European origin, 310 of which had a male, 290 a female karyotype. Hundred chromosome analyses used lymphocyte (Ly) cultures and 500 chromosome investigations derived from amniotic (A) fluid cultures. For each region, they documented fluorescence intensity (i5=brilliant), size deletion and total inversion and made statistical analysis. Duplications of the satellites (p13) of the acrocentric chromosomes had a frequeny of 0.8 % in group A and of 0.3 % in group Ly. The total frequencies of brilliant fluorescence intensity were 25.8 % in group A and 18.5 % in group Ly, and this proved to be statistically significant.

Kalz et al. (2005) analyzed the chromosomes of 3 ethnic groups. Chromosomes of 100 Central-Europeans (E) were compared with 100 Turkish (T) and 67 Southern-Indian (I) people. The individual polymorphic regions were documented according to size, localization and brilliant fluorescence intensity. The brilliant bands were determined in 18.5 % (E), 22.8 % (I) and 14.9 % (T) of the total amount of the relevant chromosomes analyzed. These differences proved to be statistically significant. In the Hungarian sample this ratio was less, only 12 %. Duplications of the satellites of the acrocentric chromosomes had a frequency of 0.3 % (E), 0.2 % (I) and 0.8 % (T). The Hungarian sample is in correlation with groups E and I. To sum up, they showed a closer relation between Central-Europeans and Indians, more distant ones between Central-Europeans and Turks and most distant relation between Indians and Turks; and this is in accordance with the anthropological and clinical findings.

Different authors found a high frequency of brilliant band on chromosome 3 (36.6 – 58.3 %) but in our study, it was only 17.2 %. The Hungarian sample is the biggest so it can be considered to the most representative. On the acrocentrics, the frequencies of brilliant bands were higher on the satellites, than on the p11 region.

Population genetic analyses of polymorphisms can reveal similarities or differences in ethnic groups. It is obvious, though, that the validity of comparisons of different studies is limited. The size of the groups and the ethnic

structure vary immensely. To get reliable facts it is advisable to use as large population as it is possible. The analysis of small population can give easily falsely high frequency in a case of a rare polymorphism. It is important to use the same cell system and the same method as well.

To sum up, it can be stated, that the frequency of polymorphism was higher in Hungary than in Scotland (Buckton et al. 1976), but lower than in the above mentioned Turkey and Central-Europe. The Hungarian data vary the most from the Turkish. Strangely there is a considerable difference between German (Schwanitz 1976) and Central-European (Kalz and Schwanitz 2004) populations.

C-Band: At the examination of C-banded chromosomes, it is hard to make an objective definition for the classes. When subjective or arbitrary relative forms of classification are used, the data from different workers have a very few points of comparability. In the interest of reducing the subjectivity to the minimum, different authors used different chromosomes as a reference size. Buckton et al. (1976) used subjective classification in Scotland. Müller et al. (1975) used the 21q region as relative C-band length and obtained a different distribution than Verma et al. (1978) and Sofuni et al. (1979) who used the 16p as reference size. Berger et al. (1979) used the same method but got different results. Simi and Tursi (1982) carried out a study on 469 individuals in Italy also using 16p as reference size. For chromosomes 1 and 9 level 2 was the most frequently represented. That is in accordance with our observations. In Table 6 the Hungarian data represent the mixed male and female population.

Podugolnikova et al. (1979) analyzed the chromosomes of 100 children by quantitative methods. Chromosome 1 had the largest C segment, while the length and variability of C segments on chromosomes 9 and Y were identical and the C segment length and its variability on chromosome 16 was the smallest. There was no difference between sexes.

Ibraimov et al. (1982) did not found any statistically significant difference in the frequency of C-band classes in four Mongolian groups living under different ecological conditions.

Cavalli et al. (1985) compared Caucasians and Japanese living in Brazil. They made a quantitative analysis of C-bands using densitometric measurement. Sixty normal, unrelated people (30 males and 30 females) were studied in each racial group. No sex difference was detected. Caucasians presented C-bands of chromosomes 1, 9 and 16 larger than Japanese, but, on average, only the difference of chromosome 9 was statistically significant. Inversions were detected only among the Caucasians. Their data indicates, that, beside the differences regarding the amount of constitutive

Table 1: Frequencies of C- and Q-bands on chromosome Y in Hungary.

Method	*n*	*level*				
		1	*2*	*3*	*4*	*5*
Q-band	608-*	1.5	4.4	18.6	64.4	11.1
C-band	251	0.4	5.2	21.9	51.4	21.1

*In one case without Y chromosome

Table 2: Comparison of the frequency of brilliant bands.

Group	*n*	*Chromosome*											
		3	*4*	*13*		*14*		*15*		*21*		*22*	
				p11	*p13*	*p11*	*p13*	*p11*	*p13*	*p11*	*p13*	*p11*	*p13*
Germany Schwanitz, 1975	81	38.3	1.9	16.6	0.6	-	2.5	-	1.9	-	1.2	-	1.9
Scotland Buckton et al., 1976	149	58.3	18.1	21.2	11.2	-	6.0	-	10.5	0.3	4.9	1.0	11.6
USSR, Turkmen Ibraimov and Mirrakhimov 1983	116	36.6	6.5	33.2	3.9	10.3	8.6	15.1	4.3	13.4	6.0	10.3	3.0
Central-Europe Kalz and Schwanitz, 2004	100	39.5	6.5	63.5	11.5	1.0	21.0	0.5	23.5	0.5	20.5	9.0	23.5
India Kalz et al., 2005	100	33.0	12.5	44.5	15.0	0.5	12.5	-	12.5	-	21.0	4.0	24.0
Turkey Kalz et al., 2005	67	43.3	10,5	68.7	21.7	1.5	20.2	2.2	21.6	1.5	32.8	19.4	30.6
Hungary *2005*	1131	17.2	2.1	30.8	5.5	0.1	11.0	0.6	14.6	0.75	10.1	16.0	18.6

Table 3: Frequency of C-band size among women in Hungary.

Chromosome	n	level				
		1	2	3	4	5
1	563	13.85	39.25	33.21	13.14	0.53
9	563	1.69	31.08	34.28	29.22	3.73
16	563	0.80	35.97	41.21	20.07	1.95

Table 4: Frequency of C-band size among men in Hungary.

Chromosome	n	level				
		1	2	3	4	5
1	598	7.19	46.24	33.95	11.79	0.83
9	598	1.75	33.20	32.11	29.26	3.68
16	598	1.34	36.79	44.23	16.05	1.59

Table 5: Incidence of partial and total inversion heteromorphisms of chromosomes 1, 9 and 16.

Group	number of chromosomes	Total Inversion Chromosome			Partial Inversion Chromosome		
		1	9	16	1	9	16
Hungary 2005	3093	0.03	0.94	0.03	4.1	11.4	0.16
Scotland Buckton et al., 1976	1854	-	0.9	-	1.2	1.4	-
Italy Simi and Tursi, 1982	930	-	0.7	-	-	1.8	-
USA, Afro-Americans Hsu et al., 1987	3590	-	3.6	-			
USA, Hispanics Hsu et al., 1987	3474	-	2.4	-			
USA, Asians Hsu et al., 1987	768	-	0.3	-			
USA, white Americans Hsu et al., 1987	4668	-	0.7	-			
Central-Europe Kalz and Schwanitz, 2004	200	-	0.5	-			
India Kalz et al., 2005	200	-	1.5	-			
Turkey Kalz et al., 2005	134	-	0.5	-			

Table 6: Comparison of frequencies of sizes on the chromosomes 1, 9, 16 and Y according to studies from the literature.

n / Level	Buckton et al., 1976 801 Chromosome			Müller et al., 1975 376 Chromosome			Verma et al., 1978 80 Chromosome			Simi and Tursi, 1982 469 Chromosome			
	1	9	16	1	9	16	1	9	16	1	9	16	Y
1	-	-	-	1	<1	24	10	24	48	11.1	35.6	77.1	8.0
2	3	5	3	33	46	70	44	53	44	75.2	57.3	22.9	81.4
3	93	93	95	57	46	6	45	21	8	13.7	4.5	-	10.5
4	3	2	2	7	7	-	1	2	-	-	-	-	-
5	<1	<1	<1	2	1	-	-	-	-	-	-	-	-

n / Level	Sofuni et al., 1979 93 Chromosome			Berger et al., 1979 236 Chromosome			Bhasin et al., 1981 200 Chromosome			Hungary, 2005 1161 Chromosome			
	1	9	16	1	9	16	1	9	16	1	9	16	Y
1	4	8	77	14	33	85	1.2	-	0.9	10.4	1.7	1.1	0.4
2	67	86	23	67	56	14	38.0	60.5	56.7	42.9	32.2	36.4	5.2
3	26	6	<1	19	11	1	52.5	38.5	39.2	33.6	33.2	42.8	21.9
4	3	<1	-	-	-	-	7.7	1.0	2.92	12.4	29.2	18.0	51.4
5	<1	-	-	-	-	-	0.5	-	0.17	0.7	3.7	1.7	21.1

heterochromatin between the autosomes and chromosome Y in samples from different populations, the total amount of constitutive heterochromatin remains constant due to the interchromosomal compensation. It suggests the existence of a powerful control on the nature of distribution.

Erdtmann et al. (1981) measured the size of C-

band in chromosomes 1, 9 and 16 of 394 natives of various Southern-American tribes and 40 Brazilian Caucasians. They found a minimal difference between them.

Zenenga et al. (1984) compared the chromosomes 1, 9, 16 and Y of 38 Blacks and 38 Caucasians in Brazil. The C-band in chromosomes 1, 9 and 16 of the Blacks were smaller than in the Caucasians but of similar size for chromosome Y of both group. Lubs et al. (1977b) and Verma and Dosik (1981) did not found any difference between the Caucasians and the Blacks living in the USA. This all suggests that the constitutive heterochromatin must have some function. According to Hsu (1975), this is a so called bodyguard function. Recent investigations revealed the fact that constitutive heterochromatin is important in gene regulation. On the autosomes the band variability is relatively stable and the mutation rate is low, while chromosome Y has great differences in length among populations even of the same race. There are different explanations about the origin of repeated DNA sequences: for example unequal crossing over (Smith 1976), translocation between chromosome Y and the autosomes (Britten and Kohne 1968). The most extensive comparative study about human population cytogenetics was made by Bhasin (2005), it is now a guideline in this field.

Beside the variations of length, the localization can be altering as well. Normally the C-band is located on the q (long) arm; if it is also situated on the p (short) arm it is called translocation. The inversion is a relatively rare feature. Its frequency in international studies is 1-3% on chromosome 9. The clinical significance of this heteromorphism is unknown. The heterochromatin of chromosome 9 has a bit different staining, but even now it is hard to pull a border between normal and abnormal chromosomal polymorphism.

Hsu et al. (1987) analyzed the chromosomes of 6250 persons belonging to 4 different ethnic groups. They used amniotic culture and found differences in the frequency of pericentric inversion of chromosome 9. Kalz and Schwanitz (2004) found total pericentric inversions in group A in 0.1 %, 1.1 %, 0 % for chromosomes 1, 9 and 16, and in group Ly in 0 %, 1.5 %, 0 % for chromosomes 1, 9 and 16. Kalz et al. (2005) made a comparison between 3 ethnic groups: Central-Europeans (E), Turks (T) and Indians (I). Similarities were found between the European and white-American, and between the Turkish and Asian populations apart from the fact that different cell systems may give different results (Verma 1988).

Comparing the Hungarian and international data it can be seen that there are similarities in the frequency of pericentric inversion for chromosomes 9 between the Hungarian, white American, Turkish, Central-European, Italian and Scottish groups (Table 5). Beside us, only Buckton et al. (1976) and Simi and Tursi (1982) reported data about the frequency of partial inversion among the authors mentioned above.

Molecular cytogenetic studies suppose that the breakpoints are at repetitive sequences. The inversion has been reported as familiar, but Betz et al. (2005) gave an account of two cases of de novo inversion. Both two patients had a neoplasia. The proximal short arm of chromosome 9 take part in several malignant disorders, so the breakpoints may potentially be involved in the pathogenesis of these disorders.

The studies that use gene frequencies are more suitable to compare international data. Guglielmino et al. (2000) collected and compared the available gene frequencies of Hungarian (8 ethnic groups, and non-Hungarian populations (Slavs, Germans, Iranins, Finns, Turks, Orientals, Uralics). They made a cluster analysis and they pointed out, that the Slavs are the closest relatives of the mixed Hungarians, than the Germans, Iranians and Turks.

SUMMARY

With the comparison of different ethnic groups, we can draw a conclusion about their relationship. It is a problem that the authors work with populations of different size. The frequency of polymorphism of the Hungarian population diverges from all the groups mentioned above. Some authors used a relatively small number of participants, contrarily to the Hungarian study, where we included the highest number of subjects. Keeping this in view, the smallest difference is between the Hungarian and the Indian groups, while the Central-Europeans differ more. The biggest difference is between the Hungarians and the Turks, so they seem to be the most distant relatives.

The molecular genetic study of Guglielmino et al. confirmed our observations.

REFERENCES

Berger R, Brenheim A, Coniat M, Vecchione D 1979. C-banding studies in various blood disorders. *Cancer Genet Cytogenet,* **1:** 95-102.

Betz JL, Behairy AS, Rabionet P, Tirtorahardjo B, Moore MW, Cotter PD 2005. Acquired inv(9): what is its significance? *Cancer Genet Cytogenet,* **160:** 76–78.

Bhasin MK 2005. Human population cytogenetics: A review. *Int J Hum Genet,* **5(2):** 83-152.

Britten RJ, Kohne DE 1968. Repeated sequences in DNA. *Science*, **161:** 529-540.

Buckton KE, O'Riordan ML, Jacobs PA, Robinson JA, Hill R, Evans HJ 1976. C- and Q-band polymorphism in the chromosomes of three human populations. *Ann Hum Genet,* **40:** 99-112.

Bujdosó Gy 1985. *X vagy Y, apaságvizsgálat, igazságszolgáltatás*. Budapest: Medicina Könyvkiadó

Caspersson T, Zech L, Johannson C 1970. Quinacrine mustard fluorescence of human chromosomes. *Exp Cell Res,* **61:** 474-475.

Cavalli IJ, Mattevi MS, Erdtmann B, Sbalqueiro IJ, Maia NA 1985. Equivalence of the total constitutive heterochromatin content by an interchromosomal compensation in the C band sizes of chromosomes 1, 9, 16, and Y in Caucasian and Japanese individuals. *Hum Hered,* **35:** 379-387.

Erdtmann B, Salzano FM, Mattevi MS, Flores FZ 1981. Quantitative analysis of C-bands in chromosomes 1, 9, and 16 of Brazilian Indians and Caucasoids. *Hum Genet,* **57:** 58-63.

Guglielmino CR, De Silvestri A, Beres J 2000, Probable ancestors of Hungarian ethnic groups: an admixture analysis. *Ann Hum Genet,* **64:** 145-159.

Hsu LYF, Benn PA, Tannenbaum HL , Perlis TE, Carlson AD 1987. Chromosomal polymorphisms of 1, 9, 16, and Y in 4 major ethnic groups: A large prenatal study. *Am J Med Genet,* **26:** 95-101.

Hsu TC 1975. A possible function of constitutive heterochromatin: The bodyguard hypothesis. *Genetics,* **79 (Suppl.):** 137-150.

Ibraimov AI, Mirrakhimov MM 1982. Human chromosomal polymorphism. IV. Chromosomal Q polymorphism in Russians living in Kirghizia. *Hum Genet,* **62:** 258-260.

Ibraimov AI, Mirrakhimov MM 1983. Human chromosomal polymorphism. VI. Chromosomal Q polymorphism in Turkmen of the Kara-Kum desert of Central-Asia. *Hum Genet,* **63:** 380-383.

Ibraimov AI, Mirrakhimov MM, Nazarenko SA, Axenrod EI 1982. Human chromosomal polymorphism. II Chromosomal C polymorphism in Mongoloid populations of central Asia. *Hum Genet,* **60:** 8-9.

Kalz L, Kalz-Füller B, Hegde S, Schwanitz G 2005. Polymorphisms of Q-band heterochromatin: qualitative and quantitative analyses of features in 3 ethnic groups (Europeans, Indians, and Turks). *Int J Hum genet,* **5(2):** 153-163.

Kalz L, Schwanitz G 2004. Characterization of constitutive heterochromatin, in particular of fluorescence polymorphisms, in a Central European population. *Int J Hum Genet,* **4(1):** 1-10.

Lubs HA, Kimmerling WJ, Hecht F, Patil SR, Brown J, Gerald P, Summit RL 1977a. Racial differences in the frequency of Q and C chromosomal heteromorphisms. *Nature*, **268:** 631-633.

Lubs HA, Patil SR, Kimberling WJ, Brown J, Cohen M, Gerald P, Hecht F, Myrianthopoulos N, Summitt RL 1977b. Q and C banding polymorphisms in 7- and 8-year-old children: racial differences and clinical significances. In: EB Hook, IH Porter (Eds) *Populational Cytogenetic Studies in Humans*. Academic Press: New York, pp. 133-159.

Mikelsaar AVN, Viikmaa MH, Tüür SJ, Käosaar ME 1974. Human karyotype polymorphism. II. The distribution of individuals according to the presence of brilliant bands in chromosome 3, 4, and 13 in a normal adult population. *Humangenetik,* **23:** 59-63.

Müller H, Klinger HP, Glasser M 1975. Chromosomal polymorphism in a human newborn population. II. Potential of polymorphic chromosome variants for characterizing the ideogram of an individual. *Cytogenet Cell Genet,* **15:** 239-255.

Podugolnikova OA, Sushanlo HM, Parfenova IV, Prokofieva-Belgovskaja AA 1979. The quantitative analysis of polymorphism on human chromosomes. 1, 9, 16, and Y. II. Comparison of the C segments in male and female individuals (group characteristics). *Hum Genet,* **49:** 251-260.

Schwanitz G 1976. *Die Normvarianten menschlicher Chromosomen*. Erlangen: Perimed Verlag.

Simi S, Tursi F 1982. Polymorphism of human chromosomes 1, 9, 16, Y: Variations, segregation and mosaicism. *Hum Genet,* **62:** 217-220.

Smith GP 1976. Evolution of repeated DNA sequences by unequal crossover. *Science,* **191:** 528-535.

Sofuni T, Naruto J, Awa A 1979. Quantitative analysis of C-bands on area measurement. *Jpn J Hum Genet,* **24:** 194-195.

Sumner AT 1972. A simple technique for demonstrating centromeric heterochromatin. *Exp Cell Res,* **75:** 304-306.

Verma RS 1988. Heteromorphisms of heterochromatin. In: *Heterochromatin Molecular and Structural Aspects.* RS Verma (Ed.). New York: Cambridge University Press pp. 276-292.

Verma RS, Dosik H 1981. Human chromosomal heteromorphism in American Blacks. V. Racial differences in size variation of the short arm of acrocentric chromosomes. *Experientia,* **37:** 241-243.

Verma RS, Dosik H, Lubs HA 1978. Size and pericentric inversion heteromorphisms of secondary constriction regions (h) of chromosomes 1, 9 and 16 as detected by CBG technique in Caucasians: classification, frequencies and incidence. *Am J Med Genet,* **2:** 331-339.

Zanenga R, Mattevi MS, Erdtmann B 1984. Smaller autosomal C band size in Blacks than in Caucasoids. *Hum Genet,* **66:** 286.