

## Human Chromosomal Polymorphism in a Hungarian Sample

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**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 world, 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.

### 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

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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

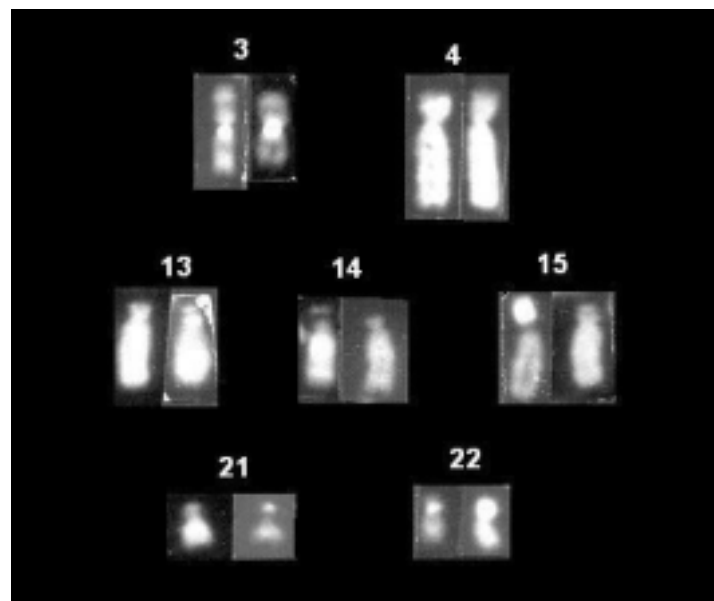


Fig. 1. Q-banded chromosomes

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 frequency 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



**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
<b>Hungary</b> 2005	3093	0.03	0.94	0.03	4.1	11.4	0.16
<b>Scotland</b> Buckton et al., 1976	1854	-	0.9	-	1.2	1.4	-
<b>Italy</b> Simi and Tursi, 1982	930	-	0.7	-	-	1.8	-
<b>USA, Afro-Americans</b> Hsu et al., 1987	3590	-	3.6	-	-	-	-
<b>USA, Hispanics</b> Hsu et al., 1987	3474	-	2.4	-	-	-	-
<b>USA, Asians</b> Hsu et al., 1987	768	-	0.3	-	-	-	-
<b>USA, white Americans</b> Hsu et al., 1987	4668	-	0.7	-	-	-	-
<b>Central-Europe</b> Kalz and Schwanitz, 2004	200	-	0.5	-	-	-	-
<b>India</b> Kalz et al., 2005	200	-	1.5	-	-	-	-
<b>Turkey</b> 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 find 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 Schwantz (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, Iranians, 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.

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