RELATIONSHIP OF HUMAN HETEROCHROMATIN AND CONGENITAL MALFORMATIONS

[1]Hasanova A.T., [2]Jafarova G.A.

[1]*Azerbaijan Medical University. Department of Medical Biology and Genetics. Baku, Azerbaijan*

[2]*Azerbaijan Medical University. I Department of Children's Diseases. Baku, Azerbaijan*

Publication date: December 2019

***Contact information:** AZE 1078. Baku, U.V.Chamanzaminli str. 9; e-mail: aytakin_hasanova@mail.ru

Aim. The variability of centromeric heterochromatin of the chromosome pairs 1,9 and 16 was studied in material provided by the Cytogenetic Counselling Centre.

Materials and methods. The size of bands 1q12, 9q12 and 16q11 was classified as normal**,** larger**,** very large, narrow and pericentric inversion. The karyotypes under study were divided into four groups: (I) from persons with abnormal karyotype and abnor-mal phenotype**,** (II) from persons with abnormal phenotype and normal karyotype, (III) from healthy nearest relatives (parents and sibs) of persons with abnormal phenotype and karyotype**,** (IV) from normal healthy persons with normal phenotype and karyotype without any congenital malformations in the family history.

Results. A different variability of centromeric hetero-chromatin of chromosomes 1, 9 and 16 was observed. Quite a low variability was found in chromosome 16, while chromosomes 9 and 1 showed a high degree of variability, which was more accentuated in chromosome 9 than in chromo-some 1.

Conclusions. In all four groups there was a similar pattern of variability with the only exception in the group of nearest relatives of children with abnormal phenotype and karyotype where an unusually narrow band 1q12 was more frequently detected.

Key words: centromeric heterochromatin, chromosome pairs 1, 9 and 16, congenital malformations

İNSANIN HETEROXROMATİNİ İLƏ ANADANGƏLMƏ İNKİŞAF QÜSURLARI ARASINDA QARŞILIQLI ƏLAQƏ

[1]Həsənova A.T., [2]Jəfərova G.A.

[1]*Azərbaycan Tibb Universiteti. Tibbi biologiya və genetika kafedrası. Bakı, Azərbaycan.*

[2]*Azərbaycan Tibb Universiteti. I uşaq xəstəlikləri kafedrası .Bakı, Azərbaycan*

Nəşr tarixi: Dekabr 2019

*Əlaqə üçün məlumatlar: AZE 1078. Baku, U.V.Çəmənzəminli küçəsi 9; e-mail: aytakin_hasanova@mail.ru

Tədqiqatın məqsədi sentromer heterochromatininin dəyişkənliyinin araşdırılması olmuşdur.

Material və metodlar. 1,9 və 16-cı xromosom cütləri Sitogenetik Məsləhət Mərkəzindən götürülmüş materialda tədqiq olunmuşdur.1q12, 9q12 və 16q11 bantlarının ölçüsü normal, daha böyük, çox böyük, dar və perisentrik inversiya kimi təsnif edilmişdir. Tədqiq olunan karyotiplər: (I) anormal karyotipi və anormal fenotipi olan insanlar; (II) anormal fenotipi (çoxsaylı qüsurlar) və normal karyotipi olan insanlar; (III) anormal fenotipi və karyotipi olan şəxslərin sağlam yaxın qohumları (valideynlər və bacı-qardaşlar) ; (IV) ailə tarixçəsində heç bir anadangəlmə qüsuru olmayan normal fenotipi və karyotipi olan sağlam insanlar aid olan qruplar olmaqla dörd qrupa bölündü.

Nəticələr. 1, 9 və 16 saylı xromosomların sentromer heteroxromatininin müxtəlif dəyişkənliyi müşahidə edildi. 16-cı xromosomda az dəyişkənlik nəzərə çarpdığı halda, 9-cu və 1-cı xromosomlarda bu dəyişkənlik daha çox olmuşdur. Xüsusi ilə 1 saylı xromosomda dəyişkənliyin yüksək dərəcəsi qeydə alınmışdır.

Yekun.Qeyri-adi dar 1q12 bantının daha tez-tez tapıldığı, (III) anormal fenotipi və karyotipi olan uşaqların sağlam yaxın qohumları olan qrup istisna olmaqla dəyişkənliyin oxşar mənzərəsi bütün dörd qrupda müşahidə edildi.

Açar sözlər: Sentromer heteroxromatini, 1, 9 və 16-cı xromosom cütləri, anadangəlmə qüsurlar

Heterochromatin of centromeric chromosome regions contains late replicating, largely repetitive DNA. It is suggested that heterochromatin participates in chromosome pairing, crossing-over and in chromosome disjunction control (1,3).

Centromeric heterochromatin, a variety of heterochromatin, is a tightly packed form of DNA. Centromeric heterochromatin is a constituent in the formation of active cenromeres in most higherorder organisms; the domain exists on both mitotic and interphase chromosomes [4,5,6,8]

Centromeric heterochromatin is usually formed on alpha satellite DNA in humans; however, there have been cases where centric heterochromatin and centromeres have formed on originally euchromatin domains lacking alpha satellite DNA; this usually happens as a result of a chromosome breakage event and the formed centromere is called a neo-centromere. Centromeric heterochromain domains are flanked by pericentric heterochromatin. (Fig. 1).

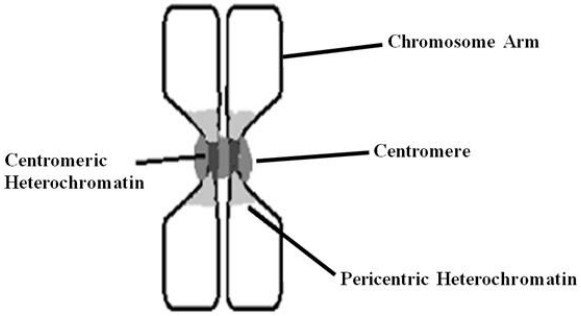

Fig. 1 Centromeric heterochromatin

Human chromosomes 1, 9 and 16 possess relatively higher amounts of centric heterochromatin varying in size. Individuals with extremely polymorphous heterochromatic regions may show a decreased relative reproductive fitness and there may be an increased risk of chromosome abnormalities for the progeny [2,7,9,10].

Our study of varying centromeric heterochromatin of the chromosome pairs 1, 9 and 16. was based on data provided by the Cytogenetic Counselling Centre of the AF-GEN Genetik Laboratory in Baku. Preliminary results of this study will be presented below.

Material and methods. The short-term cultivation of human peripheral lymphocytes (60 hours) and trypsin-banding technique were used to prepare the cells for cytogenetic analysis. The bands on chromosomes were marked according to the *International System for Human* Cytogenomic *Nomenclature* (ISCN 2016). The size of 1q12, 9q12 and 16q11 bands under study (Fig.2) were classified from the photographs, using the classic Smarttype Karyotyper method. Two cytogeneticists classified the size of each band independently, and in case of disagreement a third one decided the final classification.

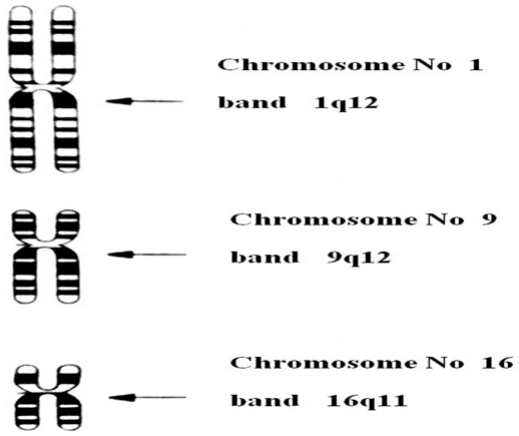

Fig. 2 Human chromosomes Nos 1, 9 and 16 according to the *International System for Human Cytogenomic Nomenclature* (ISCN 2016)

The bands were classified as: normal (+), larger (+ +), very large (+ + +), narrow (±) and pericentric inversions (p.c.i.) The karyotypes were divided into four groups: (*I*) from persons with abnormal phenotype and abnormal karyotype, (*II*) from persons with abnormal phenotype (multiple congenital malformations) and normal karyotype, (*III)* from healthy nearest relatives (parents and sibs) of persons with abnormal phenotype and karyotype, *(IV)* from normal healthy persons with

genital malformations in family history.

Abnormal karyotypes here mean inborn chromo-somal aberrations (trisomy, deletion, unbalanced translocation), multiple congenital malformations mean abnormalities of at least two organs combined with mental deficiency.

TABLE 1
Variability of bands 1q12, 9q12, 16q11

Grop No.of subject		1q12					9q12					16q11				
		+	++	+++	±	p.c.i	+	++	+++	±	p.c.i	+	++	+++	±	p.c.i
(I)	No.	45	2	1	0	0	44	2	1	1	0	48	0	0	0	0
24	%	93.5	4.5	2.0	0	0	92.0	4.0	2.0	2.0	0	100.0	0	0	0	0
(II)	No.	65	6	0	3	0	62	9	3	0	0	71	1	1	1	0
37	%	88.0	8.0	0	4.0	0	84.0	12.0	4.0	0	0	94.5	1.5	1.5	1.5	0
(III)	No.	41	3	0	8	0	42	7	2	0	1	52	0	0	0	0
26	%	79.0	6.0	0	15.	0	80.5	13.5	4.0	0	2.0	100.0	0	0	0	0
(IV)	No.	152	7	0	3	0	132	27	0	2	1	159	2	0	1	0
81	%	94.0	4.0	0	2.0	0	81.5	17.0	0	1.0	0.5	98.0	1.5	0	0.5	0
∑	No.	303	18	1	14	0	280	45	6	3	2	330	3	1	1	0
	%	90.2	5.4	0.3	4.1	0	83.3	13.4	1.8	0.9	0.6	99.2	0.9	0.3	0.3	0

(I) Persons with abnormal phenotype and abnormal karyotype
(II) Persons with abnormal phenotype (multiple congenital malformations) and normal karyotype
(III) Healthy nearest relatives (parents and sibs) of persons with abnormal phenotype and karyotype
(IV) Normal healthy persons with normal phenotype and karyotype without congenital malformations in family history

Classification of centromeric heterochromatin of chromosomes Nos 1, 9 and 16:"+" normal, "++" larger, "+++" very large,"±" narrow, "p.c.i." pericentric inversion

Results and discussion. Our results are presented in Table I. A different variability of centromeric hetero-chromatin of chromosomes 1, 9 and 16 was observed. Quite a low variability was found in chromosome 16, while chromosomes 9 and 1 showed a high degree of variability, which was more accentuated in chromosome 9 than in chromo-some 1.

In all four groups of persons there was a similar pattern of variability with the only exception mentioned below.

On the whole, band 1q12 was either enlarged or diminished, while band 9q12 was most frequently enlarged. Pericentric inversions were observed very rarely and only on chromosome 9.

The only exception was found in the nearest relatives of children with abnor-mal phenotype and karyotype: an unusually narrow band 1q12 was frequently detected, often on both members of the chromosomal pair.

Source of finance: None.
Conflict of interest: None.

References.

1. *Comings D.E.* The structure and function of chromatin. In: Advances Inhuman genetics3. Editors: Harris, H. and Hirschhorn, K. Plenum Press, New York-London, 1972; 237-432.
2.*Holbek, S., Friedrich,U., Lauritsen, J.G. Et al.* Marker chromosomes in parents of spontaneous ahortuses. Huniangenetik, 1974; *25:* 61-64.
3. *Babu A., Verma R.S.,* Characterization of human chromosomal constitutive heterochromatin. Can. J. Genet. Cytol. 1986; 28: 631– 644.
4. *Gardner R.J., Sutherland G.R.* Chromosome Abnormalities and Genetic Counselling, third ed. Oxford University Press, Oxford. 2004.
5. *Nanko, S., Kunugi, H., Sasaki, T. et al*. Pericentric region of chromosome 9 is a possible candidate region for linkage study of schizophrenia. Biol. Psychiatry. 1993; 33: 655–658.
6. *Mc. Kinlay Gardner R., Sutherland, G.* Chromosome Abnormalities and Genetic Coun-selling, third ed. Oxford University Press, Oxford. 2004.
7. *Schaffer, L., Mc. Gowan-Jordan, J., Schmid, M.,* An International System for Human Cytogenetic Nomenclature, Karger, Basel. 2012.
8. *Wyandt H., Tonk V.,* Atlas of Human Chromosome Heteromorphisms, Kluwer, Dordrecht. 2004.
9. *Yilmaz Z, Sahin F, Tarim E, et al.* Triploides In first and second trimester pregnancies in Turkey. Balkan J. Med Genet 2007; 10(2): 71–75.
10. *Codina-Pascual M, Navarro J, Oliver-Bonet M, et al.* Behaviour of human heterochromatic regions during the synapsis of homologous chromosomes. Hum Reprod 2006; 21(6): 1490–1497.