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Chromosomal Q-Heterochromatin Polymorphism in Patients with Alimentary Obesity

Ibraimov AI*

Institute of Balneology and Physiotherapy, Bishkek and Laboratory of Human Genetics, National Center of Cardiology and Internal Medicine, Bishkek, Kyrgyzstan

***Corresponding author:** Ibraimov AI, Institute of Balneology and Physiotherapy, Bishkek and Laboratory of Human Genetics, National Center of Cardiology and Internal Medicine, Bishkek, Kyrgyzstan, Tel: +996 0700 30 56 20; E-mail: ibraimov_abyt@mail.ru

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Abstract

Variability of the amount of chromosomal Q-heterochromatin regions (Q-HRs) was studied in individuals with alimentary obesity and in controls from two ethnic groups living in Bishkek, Kyrgyzstan. It was shown that obese individuals differ from controls in the extremely low amount of Q-HRs in their genome. The question as to the possible role of the amount of Q-HRs in the genome in the susceptibility of man to the development of alimentary obesity is discussed.

Keywords: Alimentary obesity; Chromosomal Q-heterochromatin; Cell thermoregulation

Introduction

During the last decades obesity has become on extremely wide spread occurrence with serious medicosocial after-effects. Besides the detriment to health, such as hypertension and heart disease, obese people are often stigmatized socially. But despite the fact that substantial advances have been made towards identifying the components of the physiological system that regulates body weight, we are still far from the full understanding of the pathogenesis of obesity. That the existing methods of treatment and other forms of control of obesity are insufficiently effective is indicated by the following fact: more than 90% of individuals who lose weight by dieting eventually return to their original weight [1]. Although much remains to be uncovered, there is growing optimism that the causes of susceptibility to a positive energy balance will be identified. The bulk of the ongoing research in this field focuses on the molecular mechanisms of appetite and satiety regulation, energy metabolism, nutrient partitioning, and adipose cell differentiation and enlargement. It is supposed that this is likely to provide geneticists with a whole new generation of candidate genes to explore for DNA sequence variation and relationships with body fat content and proneness to become obese with age [2].

Without contesting the importance of these studies, we have chosen a somewhat different approach to the search for biological markers predisposing to the development of obesity. It is based on studying the phenomenon of wide quantitative variability of chromosomal Q-HRs in the human genome in certain purely human pathologies [3]. The point is that quantitative Q-HRs variability only exists in man, though this type of constitutive heterochromatin is present in the genome of two other higher primates: *Pan troglodytes* and *Gorilla gorilla* [4-6].

Materials and Methods

The group studied consisted of Kyrgyz and Russian females of reproductive age who had an alimentary form of obesity without clinically pronounced neurohormonal defects. All of them were residents of Bishkek, the capital of Kyrgyzstan.

The choice of representative of only the female sex was mainly due to two reasons: 1) although variability in the amount of chromosomal Q-HRs in the genome of females and males is only determined by seven Q-polymorphic autosomes, males, however, have a Y chromosome with the largest Q-HR segment in the human karyotype, which is characterized by extremely high polymorphism [4,7]; 2) males, at least those living in our country, do not pay too much attention to their body mass, and, as was rightfully noted by [1] "…this view is very dependent on cultural context. In many cultures, obesity is considered to be a sign of affluence and prestige, particularly among those cultures where food is less available", and this almost fully in keeping with the realities of the Kyrgyzstan of today.

Unfortunately, apart from the general medical examination and talks, we have not performed subtle laboratory and instrumental studies aimed at detecting latent forms of neuroendocrine disorders. Therefore, into our sample fell females with a weight that was 20% or higher than a normal one and was diagnosed from external clinical signs the alimentary form of obesity was diagnosed. The controls consisted of phenotypically healthy Kyrgyz and Russian females of reproductive age whose weight was normal.

Chromosomal preparations were made using short-term cultures of peripheral blood lymphocytes. The cultures were processed according to slightly modified [8] conventional methods [9]. The dye used was propyl quinacrine mustard. Calculation and registration of chromosomal Q-HR variability was performed using the criteria and methods described in detail elsewhere [10-14].

To describe Q-HR variability in our samples we used only three main quantitative characteristics of this cytogenetic phenomenon: (1) the distribution of Q-HRs in the populations studied, i.e., the distribution of individuals having different numbers of Q-HR in the karyotype regardless of the location (distribution of Q-HRs), which also reflected the range of Q-HR variability in the population genome; (2) the derivative of this distribution, an important population characteristic, is the mean number of Q-HR per individual; (3) the frequency of Q-HRs in seven Q-polymorphic autosomes in the population.

The χ^2 test was used to compare distributions of Q-HRs. The mean numbers of Q-HRs per individual were compared using the Student t-test.

Results

Data on the distribution and mean number of Q-HRs per individual in the samples studied are presented in Table 1. As can be seen from this Table, females with obesity, regardless of their ethnic origin, are characterized by a consistently low value of the mean number and by narrow range of variability in the distribution of Q-HRs numbers in the samples as compared with controls. Their similarity in these two major quantitative characteristics of chromosomal Q-HRs variability allowed us to combine them into one group for subsequent comparative analyses.

Number of Q-HRs	Obese Females			Controls		
	Kyrgyz (N=56)	Russians (N=4)		Kyrgyz (N=100)	Russians (N=100)	
	I	II		III	IV	
0	11 (19.6)	5 (11.4)		2 (2.0)	4 (4.0)	
1	24 (42.9)	18 (40.9)		11 (11.0)	7 (7.0)	
2	19 (33.9)	19 (43.2)		32 (32.0)	24 (24.0)	
3	2 (3.6)	2 (4.5)		19 (19.0)	33 (33.0)	
4				22 (22.0)	31 (31.0)	
5				11 (11.0)	1 (1.0)	
6				2 (2.0)		
7				1 (1.0)		
Total number of Q-HRs	68	62		294	283	
	$\chi^2_{1,2}$=1.69	$\chi^2_{1,3}$=1.55	$\chi^2_{1,4}$=4.15	$\chi^2_{2,3}$=1.78	$\chi^2_{2,4}$=8.74	$\chi^2_{3,4}$=14.18
	df=2	df=2	df=2	df=2	df=2	df=2
	P>0.50	P<0.001	P<0.001	P<0.001	P<0.001	P>0.95
Mean number of Q-HRs	1.21 ± 0.11	1.41 ± 0.11		2.94 ± 0.14	2.83 ± 0.11	
	$t_{1,2}$=1.29	$t_{1,3}$=9.72	$t_{1,4}$=10.41	t2,3=8.59	$t_{2,4}$=9.13	$t_{3,4}$=0.62
	df=99	df=156	df=144	df=140	df=123	df=189
	P>0.20	P<0.000	P<0.000	P<0.000	P<0.000	P>0.50

Table 1: Distribution and mean number of Q-HR per individual in groups of obese females and in control samples.

Table 2 shows the values of absolute and relative Q-HRs frequencies on seven Q-polymorphic autosomes in studied and controls groups. Comparative analysis of our samples once again demonstrated our previous observations that on seven Q-polymorphic autosomes in the human genome the distribution of Q-HRs are not fortuitous. The greatest amount of Q-HRs, like in other previously examined populations, is located on autosomes 3 and 13 (more than half of all the Q-HRs), while the rest of the Q-HRs are more or less uniformly distributed on other Q-polymorphic autosomes, indicating, as we suppose, nonlocusspecificity of Q-HRs in the human genome [15-18]. Indeed, as can be seen from this Table, Q-HRs in obese individuals is encountered with an expected frequency on all the potentially Q-polymorphic autosomes [3].

Location of Q-HR	Obese females	Controls (females)	
	(N=100)	Kyrgyz (N=100)	Russian (N=100)
	I	II	III
3	69 (0.345)*(53.1)**	83 (0.415) (28.2)	99 (0.495) (35.0)
4	6 (0.030) (4.62)	17 (0.085) (5.78)	9 (0.045) (3.18)
13	24 (0.120) (18.5)	100 (0.500) (34.0)	99 (0.495) (35.0)
14	7 (0.035) (5.38)	14 (0.070) (4.76)	15 (0.075) (5.30)
15	11 (0.055) (8.46)	27 (0.135) (9.18)	21 (0.105) (7.42)
21	21 (0.105) (7.42)	35 (0.175) (11.9)	17 (0.085) (6.01)
22	7 (0.035) (5.38)	18 (0.090) (6.12)	23 (0.115) (8.13)
Total number of Q-HRs	130	294	283
Mean number of Q-HRs	1.30 ± 0.08	2.94 ± 0.14	2.83 ± 0.11

Table 2: Q-HR frequencies in seven Q-polymorphic autosomes in obese females and in the control group.

* represents the Q-HR frequency from the number of chromosomes analyzed and ** represents the Q-HR frequency as percentage of the overall number of chromosomal Q-HR.

Discussion

As was neatly noted by Friedman [1]: "…because eating is an activity in which we all partake, it is not surprising that almost everyone has an opinion about this subject." Therefore, it is not surprising that the trends of fundamental studies devoted to obesity are extremely wide. The bulk of the ongoing research in this field focuses on the molecular mechanisms of appetite and satiety regulation, energy metabolism, nutrient portioning, and adipose cell differentiation and enlargement [2,19].

In contrast, little progress has been made during the same period of time with respect to the genetic basis of human obesity. Let us mention at once that a number of mendelian disorders are known to exist in humans, but no specific genes have yet been identified for them [20,21]. Although several single gene defects are known that produce obesity in animals and all of these have been cloned, providing a rich new base for understanding obesity [22-27].

From these studies the discovery of leptin has generated great excitement. It was shown, in particular, that mutations that result in leptin deficiency are associated with massive obesity in humans as well as rodent [28,29]. Leptin can also affect energy expenditure, which, in

other context, is regulated independently of food intake [20,30]. Mutation in the leptin receptor is also associated with extreme obesity [31]. It has served as a major piece of evidence that obesity is a serious disease and can be produced by genetic and molecular abnormalities.

It should be kept in mind, however, that the effects of leptin deficiency are critically dependent on adrenal glucocorticoids. Adrenalectomy in the ob/ob mouse, the db/db mouses, and all the other animal models in rodents will stop the development of obesity. Moreover, this steroid is essential for the development of insulin resistance, for the alterations in muscle function, and for the alterations in bone growth and hyperphagia these animals manifest [2].

Why then are some individuals obese and others not? The answer of authors studying neuroendocrine and molecular aspects of obesity is that the intrinsic sensitivity to leptin is variable and that, in general, obese individuals are leptin-resistant [20,30]. The molecular basis for leptin resistance has been explained in some instances [32-35]. But nevertheless, the range of the latest studies is outlined by the system of leptin and body-weight regulation. Though it is admitted that there is plasticity of this system and such factors as diet, environment, age and perhaps exercise are also important in the pathogenesis of obesity [36]. Environmental factors have been shown to affect leptin sensitivity, as a high-fat diet leads to leptin resistance, although the basis for this poorly understood [20].

The point is that there are a number of circumstances that are directly or indirectly indicative of the scantiness of molecular approaches of studies, including the search for a hypothetical gene (or genes) involved in the development of obesity in man. Thus, for instance: 1) the results of numerous epidemiological studies carried out in many countries and regions have unequivocally shown that the frequency of obesity in females is two times higher than in males; 2) the global medico social problem of obesity only arised in the last decades; and we consider the functional derangements in the neuroendocrine and central nervous system in preserving energetic homeostasis in the contemporary man very doubtful just because of an improved diet and life conditions despite the fact that corresponding homeostatic systems act in nature have been acting for a long time. Moreover, our bodies are better adapted to combat weight loss than to combat weight gain, since for thousands of years our species evolved in circumstances where nutrients were in short supply; 3) in the evolution of the species Homo sapiens there never was such a period of "prosperity" as in the present economically developed countries to produce in its genome serious changes capable of causing the appearance of a specific structural gene of obesity, and therefore, the increasing rates of obesity cannot be explained exclusively by changes in the gene pool. In connection of the aforementioned facts we suppose that possibly exist other biological factors predisposing to obesity in man.

A remarkable feature of human chromosomal Q-heterochromatin regions (Q-HRs) is their wide quantitative variability characterized by the fact that individuals in a population differ in the number, location, size and intensity of fluorescence of these specific fluorescence areas [4,37]. The existence of population Q-HRs variability in twelve polymorphic loci of seven autosomes and on the distal portion of the long arm of chromosome Y is well-established fact [7,38-46].

By studying chromosomal Q-HRs variability in the human populations permanently living in various climatic-and-geographic conditions of Eurasia and Africa, in norm and pathology we have obtained the data indicating possible participation of chromosomal Q-HRs in cell thermoregulation (CT). We have checked this hypothesis on the level of human organism assuming that CT is the basis for heat conductivity of whole cell part of body [3,47].

In the present study we found that in individuals with obesity the amount of Q-HRs in their genome proved to be extremely low. We once again feel that the reason for this difference lies in the features of cell thermoregulation. Thus, in patients with alimentary obesity and therefore with a low BHC (even assuming that they use the same amount of calories as people with normal weight), we believe that a part of the calories accumulates in the body in the form of adipose deposits due to inadequate heat loss. The point is that alimentary obesity mainly occurs in people living in temperate, more often in northern but economically developed countries. Surplus heat is not completely removed from the body due to good heat insulation (comfortable habitation and life) and body insulation in the form of modern clothes that are warm but do not adequately contribute to heat loss. If we also take into account the use of high-caloric, easily assimilable food-stuffs, hypodynamia and, possibly, the use of power consuming beverages (alcohol), ineffective heat loss in alimentary obesity become evident.

And finally, the answer to the raised question: "Why are some individuals lean or some obese?" instead of the existing points of view that obesity is either the result of fundamental lack of discipline on the part of affected individuals or that the answer to this question will be found by the identification of genes that a responsible for human obesity, we would answer that obesity is not simply a personal failing or the result of abnormal functioning of some structural genes (here we mean only alimentary obesity). We suppose that in a human population there is a very great variety in the functioning of the system of energy homeostasis involved in the regulation of food intake, fat stores and energy expenditure related to the amount of Q-HRs in the genome. In individuals with a low BHC, even with a same consumption of food as in people with a normal weight, in comfortable conditions of life, more fat will be deposited than in individuals with a medium or high BHC, as their heat losses are lower due to a lesser BHC [48,49]. In any event the study factors implicated in weight gain and obesity is crucial for predictions about the future impact of the global epidemic of obesity, and provides a unique opportunity for the implementation of preventive actions [50].

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References

1. Friedman JM (2000) Obesity in the new millennium. Nature 404: 632-634.
2. Bray G, Bouchard C (1997) Genetics of human obesity: research directions. FASEB J 11: 937-945.
3. Ibraimov AI, Kazakova AK, Moldotashev IK, Sultanmuratov MT, Abdyev KS (2010) Variability of Human Body Heat Conductivity in Population II. Diseases of Civilization. J Hum Ecol 32: 69-78.
4. Paris Conference (1971) and Supplement (1975) Standartization in human cytogenetics. Birth Defects, France.
5. Pearson PL (1973) Banding patterns chromosome polymorphism and primate evolution. Progress in Medical Genetics 2: 174-197.
6. Pearson PL (1977) The uniqueness of the human karyotype. In: Chromosome identification: technique and applications in biology and medicine. Academic Press, New York, London.

7. Ibraimov AI, Mirrakhimov MM (1985) Q-band polymorphism in the autosomes and the Y chromosome in human populations. In Progress and Topics in Cytogenetics. The Y chromosome. Basic Characteristics of the Y chromosome. Alan R Liss Inc, New York.
8. Ibraimov AI (1983) Chromosome preparations of human whole blood lymphocytes: an improved technique. Clin Genet 24: 240-242.
9. Hungerford DA (1965) Leukocytes cultured from small inocula of whole blood and the preparation of metaphase chromosomes by treatment with hypotonic KCl. Stain Technol 40: 333-338.
10. Ibraimov AI, Mirrakhimov MM (1982) Human chromosomal polymorphism. III. Chromosomal Q polymorphism in Mongoloids of northern Asia. Hum Genet 62: 252-257.
11. Ibraimov AI, Mirrakhimov MM (1982) Human chromosomal polymorphism. IV. Chromosomal Q polymorphism in Russians living in Kirghizia. Hum Genet 62: 258-260.
12. Ibraimov AI, Mirrakhimov MM (1982) Human chromosomal polymorphism. V. Chromosomal Q polymorphism in African populations. Hum Genet 62: 261-265.
13. Ibraimov AI, Mirrakhimov MM, Nazarenko SA, Axenrod EI, Akbanova GA (1982) Human chromosomal polymorphism. I. Chromosomal Q polymorphism in Mongoloid populations of Central Asia. Hum Genet 60: 1-7.
14. Ibraimov AI, Kurmanova GU, Ginsburg EKh, Aksenovich TI, Aksenrod EI (1990) Chromosomal Q-heterochromatin regions in native highlanders of Pamir and Tien-Shan and in newcomers. Cytobios 63: 71-82.
15. Ibraimov AI (1993) The origin of modern humans: a cytogenetic model. Hum Evol 8: 81-91.
16. Ibraimov AI, Mirrakhimov MM, Axenrod EI, Kurmanova GU (1986) Human chromosomal polymorphism. IX. Further data on the possible selective value of chromosomal Q-heterochromatin material. Hum Genet 73: 151-156.
17. Ibraimov AI, Aksenrod EI, Kurmanova GU, Turapov OA (1991) Chromosomal Q-heterochromatin regions in the indigenous population of the northern part of West Siberia and in new migrants. Cytobios 67: 95-100.
18. Ibraimov AI, Karagulova GO, Kim EY (1997) Chromosomal Q-heterochromatin regions in indigenous populations of the Northern India. Ind J Hum Genet 3: 77-81.
19. Schwartz MW, Woods SC, Porte D Jr, Seeley RJ, Baskin DG (2000) Central nervous system control of food intake. Nature 404: 661-671.
20. Friedman JM, Halaas JL (1998) Leptin and the regulation of body weight in mammals. Nature 395: 763-770.
21. Arner P (2000) Obesity--a genetic disease of adipose tissue? Br J Nutr 83 Suppl 1: S9-16.
22. West DB, Goudey-Lefevre J, York B, Truett GE (1994) Dietary obesity linked to genetic loci on chromosomes 9 and 15 in a polygenic mouse model. J Clin Invest 94: 1410-1416.
23. Dragani TA, Zeng ZB, Canzian F, Gariboldi M, Ghilarducci MT, et al. (1995) Mapping of body weight loci on mouse chromosome X. Mamm Genome 6: 778-781.
24. Warden CH, Fisler JS, Shoemaker SM, Wen PZ, Svenson KL, et al. (1995) Identification of four chromosomal loci determining obesity in a multifactorial mouse model. J Clin Invest 95: 1545-1552.
25. Chagnon YC, Bouchard C (1996) Genetics of obesity: advances from rodent studies. Trends Genet 12: 441-444.
26. Gauguier D, Froguel P, Parent V, Bernard C, Bihoreau MT, et al. (1996) Chromosomal mapping of genetic loci associated with non-insulin dependent diabetes in the GK rat. Nat Genet 12: 38-43.
27. Galli J, Li LS, Glaser A, Ostenson CG, Jiao H, et al. (1996) Genetic analysis of non-insulin dependent diabetes mellitus in the GK rat. Nat Genet 12: 31-37.
28. Zhang Y, Proenca R, Maffei M, Barone M, Leopold L, et al. (1994) Positional cloning of the mouse obese gene and its human homologue. Nature 372: 425-432.
29. Montague CT, Farooqi IS, Whitehead JP, Soos MA, Rau H, et al. (1997) Congenital leptin deficiency is associated with severe early-onset obesity in humans. Nature 387: 903-908.
30. Pelleymounter MA, Cullen MJ, Baker MB, Hecht R, Winters D, et al. (1995) Effects of the obese gene product on body weight regulation in ob/ob mice. Science 269: 540-543.
31. Clément K, Vaisse C, Lahlou N, Cabrol S, Pelloux V, et al. (1998) A mutation in the human leptin receptor gene causes obesity and pituitary dysfunction. Nature 392: 398-401.
32. Stunkard AJ, Harris JR, Pedersen NI, McClearn GA (1990) The body-mass index of twins who have been reared apart. N Engl J Med 322: 1483-1487.
33. Erickson JC, Hollopeter G, Palmiter RD (1996) Attenuation of the obesity syndrome of ob/ob mice by the loss of neuropeptide Y. Science 274: 1704-1707.
34. Fan W, Boston BA, Kesterson RA, Hruby VJ, Cone RD (1997) Role of melanocortinergic neurons in feeding and the agouti obesity syndrome. Nature 385: 165-168.
35. Vaisse C, Clement K, Guy-Grand B, Froguel P (1998) A frameshift mutation in human MC4R is associated with a dominant form of obesity. Nat Genet 20: 113-114.
36. James W (1996) In: The Origins and Consequences of obesity. Wiley, Chichester.
37. McKenzie WH, Lubs HA (1975) Human Q and C chromosomal variations: distribution and incidence. Cytogenet Cell Genet 14: 97-115.
38. Geraedts JP, Pearson PL (1974) Fluorescent chromosome polymorphisms: frequencies and segregations in a Dutch population. Clin Genet 6: 247-257.
39. Müller H, Klinger HP, Glasser M (1975) Chromosome polymorphism in a human newborn population. II. Potentials of polymorphic chromosome variants for characterizing the idiogram of an individual. Cytogenet Cell Genet 15: 239-255.
40. Buckton KE, O'Riordan ML, Jacobs PA, Robinson JA, Hill R, et al. (1976) C- and Q-band polymorphisms in the chromosomes of three human populations. Ann Hum Genet 40: 99-112.
41. Lubs HA, Kinberling WJ, Hecht F, Patil SR, Brown J, et al. (1977) Racial differences in the frequency of Q and C chromosomal heteromorphisms. Nature 268: 631-633.
42. Yamada K, Hasegawa T (1978) Types and frequencies of Q-variant chromosomes in a Japanese population. Hum Genet 44: 89-98.
43. Al-Nassar KE, Palmer CG, Conneally PM, Yu PL (1981) The genetic structure of the Kuwaiti population II: The distribution of Q-band chromosomal heteromorphisms. Hum Genet 57: 423-427.
44. Stanyon R, Studer M, Dragone A, De Benedictis G, Brancati C (1988) Population cytogenetics of Albanians in Cosenza (Italy): frequency of Q- and C-band variants. Int J Antropol 3: 19-29.
45. Kalz L, Kalz-Fuller B, Hedge S, Schwanitz G (2005) Polymorphism of Q-band heterochromatin; qualitative and quantitative analyses of features in 3 ethnic groups (Europeans, Indians, and Turks). Int J Hum Genet 5: 153-163.
46. Décsey K, Bellovits O, Bujdoso GM (2006) Human chromosomal polymorphism in Hungarian sample. Int J Hum Genet 6: 177-183.
47. Ibraimov AI, Akanov AA, Meimanaliev TS, Sharipov KO, Smailova RD, et al. (2014) Human Chromosomal Q-heterochromatin Polymorphism and Its Relation to Body Heat Conductivity. Int J Genet 6: 142-148.
48. Ibraimov AI (2003) Condensed chromatin and cell thermoregulation. Complexus 1: 164-170.
49. Ibraimov AI (2004) The origin of condensed chromatin, cell thermoregulation and multicellularity. Complexus 2: 23-34.
50. Lima-de-Faria A (1983) Molecular Evolution and Organization of the chromosome. Elsevier, New York.