SPECIAL ARTICLE

Current Status of the Human Obesity Gene Map

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Abstract

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An overview of the status of the human obesity gene map up to October 1995 is presented. The evidence is drawn from several lines of clinical and experimental research. First, 12 loci linked to Mendelian disorders exhibiting obesity as one clinical feature are reviewed. Second, six loci causing obesity in rodent models of the disease are considered. Third, eight chromosomal regions where quantitative trait loci, identified by crossbreeding experiments with informative strains of mice, are defined. Fourth, 10 candidate genes exhibiting a statistical association with BMI or body fat are introduced. Fifth, nine loci found to be linked to a relevant phenotype are listed and the four cases for which the evidence for linkage is strongest are emphasized. The latter are mapped to 2p25, 6p21.3, 7q33 and 20q12-13.11. Finally, the studies that have concluded that there was no association or linkage with a marker or gene are also reviewed. It is recommended that a system be developed by the obesity research community to ensure that an accurate and easily accessible computerized version of the human obesity gene map becomes available in the near future.

Key words: adiposity, mapping, Mendelian disorders, animal models, linkage, association, locus, chromosome

Introduction

A first paper on the status of the human obesity gene map as of August 1994 was presented by us at the Toronto 7th International Congress on Obesity and will appear in the proceedings of the meeting (35). This second paper provides an overview of the human obesity gene map at the time of the October 1995 meeting of the North American Association for the Study of Obesity. It does not include the findings reported at that meeting held at the Pennington Biomedical Research Center in Baton Rouge, Louisiana. Support for a role of a gene in human obesity or variation in body fat content has been obtained from the six lines of evidence identified in Table 1. All of them will be addressed in turn in this paper with the exception of the evidence accumulated from transgenic rodent models and gene knockout experiments. Although these studies provide support for the potential role of a gene in body fat content fluctuation when it is overexpressed in some or all tissues or when the gene is inactivated or results in a nonfunctional peptide, the true contribution of these genes to human obesity remains to be clarified. The present review also addresses only the issue of excess body mass for height (BMI) or body fat content (percent fat, fat mass, sum of a number of skinfolds) and does not deal with fat distribution phenotypes. More can be found in previous reviews on these topics (3-5).

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Mendelian Disorders

Genetic syndromes characterized by the presence of obesity could be useful in the identification of loci contributing to obesity. A search on the Online Mendelian Inheritance in Man (OMIM) computerized data base for syndromes in which the word "obesity" appears in the field "clinical synopsis," reveals that a total of 24 Mendelian disorders have obesity as one of their clinical features. Among these disorders, nine are autosomal dominant, 10 are autosomal recessive and five are X-linked. As shown in Table 2, nine of these Mendelian disorders have been mapped to eight different chromosomes (3,4,8,11,15,16,20 and X). With the Bardet-Biedl syndrome alone having been linked to four different chromosomal regions, a total of 12 loci are linked to these Mendelian disorders. Although these disorders account for a very small fraction of the obese population, they illustrate that single gene defects could lead to the development

Table 1. Human obesity gene map: lines of evidence

- MENDELIAN DISORDERS (MIM)
- SINGLE GENE RODENT MODELS
- QTL FROM CROSSBREEDING EXPERIMENTS
- TRANSGENIC AND KNOCKOUT MODELS
- ASSOCIATION STUDIES
- LINKAGE STUDIES

of human obesity. Fifteen of these syndromes have not been mapped yet to specific genomic regions.

In order to determine whether these loci contribute to obesity in otherwise clinically normal people, Reed et al. (37) tested for linkage relationships between 17 genetic markers spanning the regions of the Prader-Willi, the Bardet-Biedl (BBS1, 2 and 3), the Cohen, the Borjeson and the Wilson-Turner syndromes and the body mass index measured in subjects from 44 families with obese probands. Analyses based on a total of 207 pairs of siblings revealed no evidence of linkage between any of the markers and obesity in these families (see Table 7). These results suggest that the genetic loci contributing to obesity in these families are not the same as those involved in the Mendelian disorders reported above. However, before excluding these chromosomal regions as potential carriers of loci predisposing to obesity in clinically normal subjects, other studies with a larger number of genetic markers will have to be performed. Furthermore, these negative results do not exclude the possibility that individuals carrying one copy of a gene responsible for an autosomal recessive disorders are at a greater risk of becoming obese than individuals with no copy of the defective gene. For example, it has recently been shown that the prevalence of obesity was significantly higher among heterozygous carriers (parents of affected individuals) of a gene responsible for the Bardet-Biedl syndrome compared to age- and sex-matched normal noncarriers, suggesting that this gene may predispose to obesity in the general population (11).

Single Gene Rodent Models

Because of the high degree of homology in the genomes of mammalian species, it is possible to use rodent models of obesity to identify genes potentially involved in the etiology of human obesity. Several different single-gene mutations have been shown to cause obesity in rodents: diabetes (*db*), fat (*fat*), obese (*ob*), tubby (*tub*), adipose (*Ad*) and Yellow (A^y) in the mouse, and fatty (*fa*) in the rat (16). Although all these mutations result in obesity in the animals, the time of onset and the severity of obesity vary among the various mutations. Furthermore, the obesity phenotype is frequently associated with metabolic abnormalities including insulin resistance, hyperinsulinemia, NIDDM,

Table 2. Obesity-related Mendelian disorders with known map location

MIM number	Disorder	Locus
Autosomal Dominant		
100800	Achondroplasia (ACH)	4p16.3
122000	Posterior Polymorphous Corneal Dystrophy (PPCD)	20q11
176270	Prader-Willi Syndrome (PWS)	15q11.2-12
Autosomal Recessive		
	Bardet-Biedl Syndrome (BBS)	
209901	BBS1	11q13
209900	BBS2	16q21
600151	BBS3	3p13-12
600374	BBS4	15q22.3-23
216550	Cohen Syndrome (CHS1)	8q22-23
X-LINKED		
301900	Borjeson-Forssman-Lehmann Syndrome (BFLS)	Xq26-q27
303110	Choroideremia with deafness and obesity	Xq21
309585	Wilson-Turner Syndrome (WTS)	Xq21.1-22
312870	Simpson-Golabi-Behmel (SGBS)	Xq25-27

Adapted from OMIM (Online Mendelian Inheritance in Man) computerized data base. MIM = Mendelian Inheritance in Man.

Table 3. Possible synteny between rodent obesity genes and human chromosome regions

Locus	Transmission	Mouse chromosome	Human chromosome
Mouse			
Diabetes (*db*)	Recessive	4	1p35-31
Fat (*fat*)	Recessive	8	4q21
Obese (*ob*)	Recessive	6	7q31
Tubby (*tub*)	Recessive	7	11p15.1
Yellow (A^y)	Dominant	2	20q12-13.11
Rat			
Fatty (*fa*)	Recessive	5	1p35-31

hyperglycemia, hypertension and hyperlipidemias (21). Six of these seven mutations, listed in Table 3, were found to have homologous regions in the human genome. The obesity phenotype caused by the *db* mutation in mice is very similar to the phenotype observed in the fatty (*fa*) rat. It has been shown that these two mutations are likely in homologous genes (39) and both are syntenic to human chromosome 1p35-31 region (24,40). The chromosomal locations of the rodent obesity genes have been determined, and the genes responsible for three of these mutations have been cloned, including the A^y mutation in the agouti locus (28) and the *ob* mutation (55). Recently Naggert et al. (30) reported that the *fat* mutation on mouse chromosome 8 mapped very closely to the gene for carboxypeptidase E (Cpe), which encodes an enzyme involved in the processing of the insulin prohormone into an active hormone. Homozygous *fa/fa* mice, which have no *in vitro* enzymatic activity due to a mutation in the Cpe gene, develop hyperproinsulinemia. Treatment with insulin was shown to suppress obesity and hyperglycemia in these animals. The Cpe gene in humans is located on 4q21.

QTL From Crossbreeding Experiments

Another method originally developed for plant genetics is now commonly used with rodents to identify loci that influence quantitative phenotype such as obesity. It is known as the quantitative trait locus mapping method or the QTL. The method was fully described recently by Warden et al. (46) and it has been used to identify loci that are linked with body fat in rodents.

Briefly, QTL mapping requires two key resources: two inbred strains and a detailed genetic map of the animal genome. The procedure requires the following steps (46): a) two inbred strains divergent for the phenotype under consideration are crossed to produce F_1 and then F_2 or backcross progeny; b) the animals are individually genotyped for markers to span the entire genome at close intervals; c) the animals are appropriately phenotyped ; and d) QTLs are located by an interval mapping approach such as that provided by the program Mapmaker (26). Mapmaker uses genetic markers and quantitative phenotypes to identify QTLs with a LOD score. Because of the density of the genetic map of the mouse genome, mice are at present the preferred species for QTL studies. Moreover, regions of homology between mouse and human chromosomes have been extensively defined and this allows quite often for the identification of the approximate location of a putative gene linked to the phenotype of interest on the human gene map. It is important to recognize that when a QTL on a given chromosome has been found with an acceptable LOD score, considerable work is needed before the true nature of the gene involved is identified. To date, eight QTLs have been identified by this method and they are summarized in Table 4. Fisler et al. (15) obtained a backcross between the strains *Mus Spretus* and C57BL/6J, which they called the BSB mouse. BSB exhibits a wide range of carcass lipid, from 1 to 50 % and more. On the basis of the QTL approach with a large number of markers, Warden et al. (44,45) identified four "multigenic obesity" (Mob) loci on four different mouse chromosomes. A first locus (Mob-1) on BSB chromosome 7 determines the lipid content of the carcass (LOD score of 3.8). A second locus (Mob-2), on chromosome 6, affected only subcutaneous fat pads (LOD = 2.8). A third locus (Mob-3), encoded on chromosome 12, was linked to percentage lipid in the carcass (LOD = 4.8) while Mob-4 (chromosome 15) was linked primarily to mesenteric fat (LOD = 3.8). Syntenic regions with these four mouse QTLs are on human chromosomes 10q21-26, 11p14-ter and 16p13-11 for Mob-1, 7q22-36 for Mob-2, 14q13-32 for Mob-3 and 5q11-13 for Mob-4 (Table 4).

A mouse polygenic model of differential susceptibility to dietary fat has been developed by crossing a dietary-lipid-sensitive strain (AKR/J) with a resistant strain (SWR/J). After 12 weeks of feeding on a moderately

high fat diet, the AKR/J strain had approximately six-fold higher carcass fat than the SWR/J strain (52). F2 animals and backcross data were used and, to date, three QTLs have been identified (50,51). Do1 (chromosome 4), Do2 (chromosome 9) and Do3 (chromosome 15) are linked to the level of adiposity and, in the case of Do2, also to mesenteric fat. Although regions of homology in the human genome have not been described, it appears likely that syntenic areas can be found on human chromosome 1p36-32 for Do1, 3p21 for Do2, and 5p14-12 for Do3.

Finally, one QTL on mouse chromosome 2 was uncovered in a cross between mouse NZB/B1NJ and SM/J strains (14). The human equivalent of this locus appears to be on human chromosomes 20p11.2-q13.2 and 17. Other loci have been reported recently for the various QTL experiments defined above but they are unpublished at this time and are not reported herein.

Association Studies

Association and linkage studies are important tools for the delineation of the genetic basis of overweight and obesity. However, association and linkage are not the same and cannot be used interchangeably. The concept of association refers to a situation in which the correlation of a genetic polymorphism with a phenotype is investigated. Such studies are generally carried out on samples of unrelated individuals. They may take several forms including comparison of cases versus controls (e.g. obese versus lean subjects), analysis of variance across genotypes for the locus under consideration and comparison of carriers versus noncarriers of a given allele. If a significant association is observed with a polymorphism at a candidate gene locus, there are two likely explanations: either the locus is causally related to the phenotype or the locus is in linkage disequilibrium with another polymorphism of relevance as a result of natural selection or chance. Association studies may provide important information on genes with a major or a minor contribution to a phenotype; the method is particularly useful for the identification of genes that make only a minor contribution (18).

It is important to recognize that the strength of an association is critical in the appraisal of its relevance as a marker for the susceptibility to obesity. Although there are no commonly agreed upon standards, we like to qualify an association as strong when the p value < 0.001 or when the mutation accounts for at least 10 percent of the phenotype variance adjusted for the proper concomitants. In contrast, a weak association, in our judgment, is one characterized by a p value < 0.05 or with the locus asso-

Table 4. Quantitative trait loci (QTL) linked to body fat phenotypes

Mouse cross	Locus	Lod score	Effect on adiposity	Mouse chromosome	Human location	Reference
AKR/J X SWR/J	Do1	4.5	NA	4	1p36-p32	50
	Do2	4.8	7% adiposity 47% mesenteric fat	9	3p21	51
	Do3	3.9	4% adiposity	15	5p14-12	51
C57BL/6J X Mus Spretus	Mob-1	4.2	7% percent fat	7	10q21-26 11pter-14 16p13-11	44
	Mob-2	4.8	7% femoral fat	6	7q22-36	44
	Mob-3	4.8	7% percent fat	12	14q13-32	44
	Mob-4	3.4	6% mesenteric fat	15	5q11-13	44
NZB/B1NJ X SM/J	D2Mit22 D2Mit28		36% percent fat	2	20p11.2-q13.2	14

Do = dietary obese; Mob = Multigenic obesity; NA = Not available

ciated with less than 5 percent of the phenotype variance. In all cases, replication studies are highly desirable.

The evidence for the presence of a significant association between a candidate gene and BMI or body fat phenotypes is summarized in Table 5. The listing reveals that only five markers had an association which reached a p level of 0.01 or better. These genes were Apo B, Apo D, TNF-α (a closely linked marker of the gene), DRD2 and LDLR. Among those genes, only one (Apo B) was confirmed in an independent study albeit at a lower p level (0.05). In the case of the D2 dopamine receptor, an independent study found no relationship with BMI (31). On the other hand, the weak associations observed with 3β-HSD or UCP were only with the changes in fatness over time in the Quebec Family Study adults and not with body fat content at a given point in time (33,42).

It should be noted that the table does not include the significant associations reported previously with the ABO (9q34) blood group and the human leukocyte antigens (HLA) systems. A review of these studies (23) suggest that the results are rather ambiguous, some studies finding association of ABO with body weight, while others did not. The few studies that used BMI or skinfold thicknessess as phenotypes reported negative results. In an attempt to further clarify the issue, the association between ABO blood type and body weight was recently investigated in four culturally distinct population samples and it was concluded that there is no evidence to support an association between ABO blood types and body weight (22). A few studies have also looked at association between obesity and class-I HLA markers. Although frequencies of the HLA B18, Bw35 and Cw4 antigens were found to be significantly higher

Table 5. Evidence for the presence of an association with BMI or body fat phenotypes

Gene	Location	Evidence			
		N cases	phenotype	p value	Reference
HSD3B1	1p13.1	132	12-year changes in sum of 6 skinfolds	0.04	42
ATP1A2	1q21-23	122	Percent fat	0.05	12
Apo B	2p24-23	132	BMI	0.005	36
		181	BMI	0.05	38
ACP1	2p25	75	BMI in children	0.02	27
Apo D	3q26-ter	114	BMI	0.006	41
UCP	4q28-31	123	High fat gainers over 12 years	0.05	33
TNF-α	6p21.3	304	BMI but not percent fat	0.01	32
LPL	8p22	24	Gains in fat mass with overfeeding	0.05	6
		236	BMI	0.05	20
DRD2	11q23.1	392	Relative weight	0.002	10
LDLR	19p13	84	BMI in hypertensives	0.004	56

Gene abbreviations and their chromosomal location are from the Human Genome Data Base.
HSD3B1 = 3-beta hydroxysteroid dehydrogenase; ATP1A2 = sodium potassium adenosine triphosphatase alpha-2 subunit; Apo B = apolipoprotein B; ACP1 = acid phosphatase; Apo D = apolipoprotein D; UCP = uncoupling protein; TNF-α = tumor necrosis factor alpha; LPL = lipoprotein lipase; DRD2 = Dopamine D_2 receptor; LDLR = Low-density lipoprotein receptor.

Table 6. Evidence for the presence of linkage with BMI or body fat phenotypes based on the sib-pair method

Gene or marker	Location	Evidence			
		N pairs	Phenotype	p value	Reference
D1S202	1q31-32	3-generation pedigree	BMI	LOD = 3.6 at $\theta = .05$	29
ACP1	2p25	> 300	BMI	.004	1
BF	6p21	> 168	triceps, subscapular and suprailiac skinfolds	.01<p<.03	54
GLO1	6p21	> 168	Suprailiac skinfold and relative weight	.004<p<.05	54
TNF-α	6p21.3	304	% body fat	.002	32
KEL	7q33	402	BMI and sum of 6 skinfolds	< .0001	2
ESD	13q14.1-14.2	194	%body fat and sum of skinfolds	< .04	2
ADA	20q12-13.11	428	BMI and sum of 6 skinfolds	.02<p<.001	2
P1	22q11	> 168	Relative weight	.03	54

See previous tables for abbreviations of loci already referred to.
Gene abbreviations and their chromosomal location are from the Human Genome Data Base.
BF = properdin factor B; GLO1 = glyoxylase I; KEL = blood group Kell; ESD = esterase D; ADA = adenosine deaminase; P1 = blood group P.

in obese subjects compared to controls in some reports (13,17), no association between HLA antigens and percent body fat or subcutaneous fat could be found in a larger population (7).

Linkage Studies

When a gene influences a given phenotype to a large extent then both will be transmitted together across generations. This concept is referred to as linkage. Linkage analysis can be performed with candidate gene markers or with a variety of other polymorphic markers such as microsatellites. Evidence for linkage becomes more apparent as the marker loci get closer to the true locus that co-segregate with the phenotype. The procedure can be undertaken with large pedigrees or with panels of nuclear families. It is commonly used for complex multifactorial phenotypes which are characterized by the presence of a segregating major gene. However, it is not always appropriate to use a parametric linkage analysis procedure with LOD scores.

An alternative and practical method is the single locus sib-pair linkage method which allows to screen for potential linkage relationships between a quantitative phenotype and a genetic marker (19). The method is based on the notion that sibs who share a greater number of alleles (at a given locus) identical by descent at a linked locus should also share more alleles at the phenotype locus. Thus these sibs should have more similar phenotypes than pairs of sibs who share fewer marker alleles. The slope of the regression of squared sib-pair phenotype differences on the proportion of genes identical by descent is expected to be negative when linkage is present. An important advantage of the method is that it is not necessary to specify the mode of inheritance for the phenotype being considered. The method has been extended recently to include the information at all loci

Table 7. Evidence for absence of association or linkage with BMI or body fat

Gene or marker	Chromosome	Association		Linkage	
		N cases	Reference	N pairs	Reference
RHC, RHD					
RHE	1p36.2-34			420	2
GLUT1	1p35-31.3	52	49	55 families	9
PGM1	1p31			380	2
ATP1A1	1p13	122	12	110	12
HSD3B1	1p13.1	132	42		
FY	1q21-22			310	2
ATP1A2	1q21-23			110	12
ATP1B	1q22-25	122	12	110	12
BBS3 (D3S1254,1595, 1302)	3p13-12			207	37
UCP	4q28-31	123	33	90	33
MNSs	4q28.2-31.1			330	2
GRL	5q31-32	55	47		
ADRB2	5q32-34	142	34	70	34
ADRB3	8p12-11.1	642	43		
		251	53		
		185	8		
CSH1 (D8S270,257,281)	8q22-23			270	37
ABO	9q34.1-34.2			410	2
AK1	9q34.1			430	2
ADRA2A	10q24-26	142	34	70	34
INS	11p15.1-15.5	35	48		
BBS1 (D11S905,913)	11q13			207	37
DRD2	11q23.1	73	31		
PWS	15q11.2-12			207	37
BSS2	16q21			207	37
GLUT4	17p13	48	48		
JK	18q11-12			160	2
INSR	19p13.3	35	48		
WTS	Xq21.1-22			207	37
BFLS	Xq26-27			207	37

See previous tables for abbreviations of loci already referred to.
Gene abbreviations and their chromosomal location are from the Human Genome Data Base.
RH = blood group Rhesus; GLUT1 = glucose transporter-1; PGM1 = phosphoglucomuatse-1; ATP1A1 = sodium potassium adenosine triphosphatase alpha-1 subunit; FY = blood group Duffy; ATP1B = sodium potassium adenosine triphosphatase beta-1 subunit; MNSs = blood group MN and Ss loci; GRL = glucocorticoid receptor; ADRB2 = beta-2 adrenergic receptor; ADRB3 = beta-3 adrenergic receptor; ABO = blood group ABO; AK1 = adenylate kinase-1; ADRA2A = alpha-2A adrenergic receptor; INS = insulin; GLUT4 = glucose transporter-4; JK = blood group Kidd; INSR = insulin receptor;

available in a mutipoint linkage strategy based on pairs of sibs and other relatives (25). No linkage results have been reported to date with the multipoint sib-pair linkage strategy and very few with the parametric approach based on pedigrees or nuclear families.

Since most of the results summarized in Table 6 were derived from the single locus sib-pair linkage method, it is useful to consider the issue of the strength of evidence for such data. Common wisdom suggests that a linkage can be considered as strong if the p value

Table 8. A summary of the rodent (human homologous regions) and human loci potentially associated or linked with obesity or body fat

Human Chromosome	Locus	Human Chromosome	Locus
1p36-32	mouse Do1	11p15.1	mouse Tubby
1p35-31	mouse Db	11pter-14	mouse Mob-1
1p35-31	rat Fa	11q13	BBS1
1q31-32	D1S202	13q14.1-14.2	ESD
2p24-23	Apo B	14q13-32	mouse Mob-3
2p25	**ACP1**	15q11.2-12	PWS
3p21	mouse Do2	15q22.3-23	BBS4
3p13-12	BBS3	16p13-11	mouse Mob-1
4p16.3	ACH	16q21	BBS2
4q21	mouse Fat	20p11.2-q13.2	NZB QTL
5p14-12	mouse Do3	20q11	PPCD
5q11-13	mouse Mob-4	20q12-13.11	**ADA**
6p21	BF	20q13	mouse Yellow
6p21	GLO1	22q11	P1
6p21.3	**TNF-α**	Xq21	Choroideremia
7q31	mouse Ob	Xq21.1-22	WTS
7q22-36	mouse Mob-2	Xq25-27	SGBS
7q33	**KEL**	Xq26-27	BFLS
8q22-23	Cohen syndrome		
10q21-26	mouse Mob-1		

See previous tables for abbreviations. Highlighted loci are those showing the strongest evidence of linkage in human studies.

attains 0.001 and less and preferably with a replication. A weak linkage ($p < 0.05$) may be relevant if the finding is replicated by a few other laboratories. From Table 6, it is obvious that only a few of the linkages reported have a reasonable degree of robustness. ACP1 (2p25), TNF-α (closely linked marker) (6p21.3), KEL (7q33) and ADA (20q12-13.11) are the only markers exhibiting such a linkage relationship. The others are supported by weaker evidence at this time. One marker on 1q31-32 was shown to be linked with a LOD score of 3.6 at a recombination fraction of 0.05 in a 3-generation pedigree in which the prevalence of obesity was high (29). Since these findings are sensitive to the assumptions made about mode of transmission, penetrance and other characteristics, we need more information before concluding on the presence of a linkage with a marker on 1q.

Negative Results

Association and linkage studies which have generated negative results are numerous. Table 7 presents a listing of these studies as it could be established from the literature. Again we are in need of replication studies in order to ensure that the findings are not false negative. The only clear case appears to be that of the ADRB3 gene for which the same mutation was shown to be independent of BMI in three different studies (also percent fat in one study) (8,43,53). Note also that most association studies are based on small sample sizes.

Conclusions

Several genes are known to cause obesity or to be linked with body fat content in animals. Table 8 lists those genes, loci or markers for which the evidence of an association or a linkage with obesity, BMI, or body fat content is more robust. The list includes the loci from single gene rodent models, QTL from crossbreeding experiments, Mendelian disorders exhibiting obesity as one of the clinical features, and genes supported by robust evidence from association and linkage studies conducted on human populations. Four chromosomal arms (2p, 6p, 7q and 20q) are of particular interest as strong evidence for linkage with a marker in each of these regions has been reported. However, to date, no study has replicated the linkage for any of the four chromosomal areas.

Other regions of considerable interest include 1p, 3p, 11p, 15q and perhaps Xq. The compendium of markers and genes related to obesity or body fat is likely to grow significantly in the coming years. Despite the costs

involved in the publishing enterprise, journal space should be offered to those reporting negative findings if a comprehensive picture of the human obesity gene map is to emerge. Journal editors should be encouraged to develop a formula (perhaps a one journal page paper) allowing to report such findings in a timely but economically viable fashion. The other side of this argument is obviously that authors with positive findings for a gene or markers should experience no difficulty publishing their results in obesity or nonspecialty journals.

Finally, even though the human obesity gene file can still be managed by a small group of investigators or a single laboratory, the situation is likely to change dramatically in the coming years. The geneticists, molecular biologists and informatic specialists working in this area, with the support of NIH, NAASO and other organizations, should devise a mechanism by which a computerized version of the human obesity gene map can be maintained and be made easily accessible to interested individuals and laboratories.

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