**Mool1** obesity quantitative trait locus in BTBR T+ *Itpr3*ff/J mice increases food intake

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Karunakaran S, Manji A, Yan CS, Wu ZJ, Clee SM. **Mool1** obesity quantitative trait locus in BTBR T+ *Itpr3*ff/J mice increases food intake. Physiol Genomics 45: 191–199, 2013. First published January 22, 2013; doi:10.1152/physiolgenomics.00159.2012.—The rising prevalence of obesity is one of the greatest health challenges facing the world today. Discovery of genetic factors affecting obesity risk will provide important insight to its etiology that could suggest new therapeutic approaches. We have previously identified the Modifier of obese 1 (**Mool1**) quantitative trait locus (QTL) in a cross between leptin-deficient BTBR T+ *Itpr3*ff/J (BTBR) and C57BL/6J (B6) mice. Understanding the mechanism by which this locus acts will aid in the identification of candidate genes. Here we refined the location of this QTL and sought to determine the mechanism by which **Mool1** affects body weight. We found that the effects of **Mool1** also alter high fat diet-induced obesity in mice having functional leptin. In detailed metabolic analyses we determined that this locus acts by increasing food intake in BTBR mice, without affecting energy expenditure. The expression levels of the main molecular mediators of food intake in the hypothalamus were not altered, suggesting this locus affects an independent pathway, consistent with its identification in mice lacking functional leptin. Finally, we show that the increased adiposity resulting from **Mool1** is sufficient to affect glucose tolerance. These studies show that the **Mool1** obesity QTL affects food intake, likely through a novel mechanism, and indicate that modulation of the underlying pathway may not only ameliorate obesity but also its clinical consequences.

**Obesity is one of the largest health crises facing the world today** (44). While our increasingly “obesogenic” environment is driving this epidemic, individuals differ greatly in their susceptibility to obesity. The molecular etiology of obesity is largely unknown. Identification of factors affecting an individual’s risk of obesity could provide important new information about its pathogenesis and identify potential treatments.

Common obesity has a strong genetic component, due mainly to the net effects of numerous genetic variants, each of which has a modest effect on risk (3, 31, 38). Recent genome-wide association studies (GWAS) have identified numerous such variants (17, 39). However, given the genetic heterogeneity underlying the disease and the large effects of lifestyle and environmental factors, such as diet and exercise, on adiposity, the discovery of these genetic variants has required enormous cohorts and unprecedented international collaboration, and yet still the majority of the inherited contribution to obesity is unexplained (15).

Many obesity genes have been mapped in mouse models (33). The use of model organisms facilitates gene identification by reducing environmental variation, enhancing the observed genetic effects. Several genes underlying quantitative traits affecting body weight have been discovered by use of mouse genetics. Initial success came with single loci resulting in severe obesity, such as the obese (ob) and diabetes (db) loci, encoding the hormone leptin and its receptor, respectively (26, 48). In contrast to the severe obesity resulting from mutations such as ob, genes contributing to modest variation in body weight, such as those underlying strain differences, are likely to be more relevant to common human obesity. Recent advances in genomics technologies have accelerated gene discovery for loci differing between strains that have more subtle effects on metabolic phenotypes (6, 8, 9, 13, 23, 36, 46).

The BTBR T+ *Itpr3*ff/J (BTBR) inbred mouse strain is a model of increased obesity and Type 2 diabetes susceptibility (11, 32, 40, 41). We have shown that this strain has genetic variation that promotes insulin resistance and that, in the presence of the ob mutation in the leptin gene (BTBR*obob*), results in severe diabetes (11, 41). The BTBR strain also has alleles that increase body weight and body fat compared with the C57BL/6J (B6 strain), even in the absence of functional leptin (40). To identify the genetic causes of obesity susceptibility in these mice we previously performed genetic linkage analysis in a cross between B6*obob* and BTBR*obob* mice. Two loci influencing body weight were mapped in these studies: Modifier of obese 1 and 2 (**Mool1** and **Mool2**) (40). **Mool1**, the primary genetic determinant of the increased body weight in BTBR*obob* mice, mapped to murine chromosome 2 (40). The syntenic region in humans overlaps several obesity linkages, and supporting data from various GWAS suggest a potential association between genetic variation in the region and body weight, suggesting the gene or genes underlying **Mool1** may affect obesity in humans (1, 2, 18, 33, 35).

We generated a congenic strain, designated Moo1-C, in which B6 alleles of murine chromosome 2 just telomeric to the linkage peak were substituted into the BTBR strain background (40). BTBR*obob* mice with B6 alleles in this region replacing those of BTBR weighed less than littermate BTBR*obob* mice (40), localizing an obesity quantitative trait locus (QTL) to this region. In contrast, two other congenic strains, Moo1-A and Moo1-B, with congenic segments outside this region did not show differences in body weight. To facilitate the identification of the gene underlying **Mool1**, it is important to understand the mechanism by which this locus affects obesity. We examined how B6 alleles in the Moo1-C congenic strain affect the development of obesity. The **Mool1** obesity QTL was mapped and initially localized in mice lacking functional leptin (40). Here we show that the effects of **Mool1** are evident in high fat-fed mice with functional leptin, where they affect obesity predominantly by altering food intake. Furthermore, we show that the effects of **Mool1** are sufficient not only to alter obesity,
but also its clinical consequences, such as impaired glucose tolerance.

EXPERIMENTAL PROCEDURES

Animal procedures. The Moo1-C congenic strain was generated as previously described (40). Experimental animals were bred in-house from heterozygous mice to generate litters of all three genotypes (Moo1-C-B6, Moo1-C-BT, and Moo1-C-BT). Male offspring were used for these studies. The animals were housed in an environmentally controlled facility with 12-h light cycles (0700–1900). The mice were fed a high-fat diet (HFD) containing 60% calories from lard and 20% calories from sugar (D12492; Research Diets, New Brunswick, NJ) from weaning at 19 days of age. All procedures were performed on age-matched mice at the specified age ± 3 days. All procedures were performed according to the Canadian Council on Animal Care guidelines and were approved by the University of British Columbia Committee on Animal Care.

Genotyping. DNA was extracted from ear notches with a commercially available kit (Puregene Core Kit A; Qiagen, Toronto, ON Canada) according to the manufacturer’s directions. All animals were genotyped for the first and last marker known to be derived from the B6 strain (changed over time as the strain boundaries were refined), either by microsatellite analysis as previously described (12) or by high-resolution melt curve (HRM) analysis of single nucleotide polymorphism (SNP) markers. HRM was performed using Type-it HRM PCR kit (Qiagen) on a Rotorgene Q machine, according to the manufacturer’s directions.

Assessment of obesity. Weekly body mass measurements were made from 3 to 10 wk of age. Ano-nasal length was measured on briefly anaesthetized mice at 10 wk of age. Body mass index (BMI), was calculated as the body mass (g) divided by the square of body length (cm) and was used to normalize body mass by body size. As an alternate method, the Lee Index was calculated as the cube root of body weight (g) divided by the body length (cm) (28). Body composition was determined using dual-energy X-ray absorptiometry (DEXA) with a PIXImus Mouse Densitometer (Inside Outside Sales, Madison, WI) at 10 wk of age. All procedures were performed at a standardized time of day.

Metabolic analyses. Measurement of energy expenditure by indirect calorimetry, physical activity (beam breaks), and food intake was performed at 11 wk of age with metabolic cages (PhenoMaster; TSE Systems, Bad Homburg, Germany), as previously described (18). This system records these parameters continually, without investigator interruption. Calorimetric and physical activity measurements were obtained every ~15 min, while the amount of food consumed was recorded in 10 s intervals. In brief, the mice were first acclimatized to single housing, the procedure room, and the cages for 4 days. The mice were then placed in the experimental system housed inside a climatic chamber held at 21°C for 3 days. Data from the first (partial) light and first dark cycles were discarded, and the remaining days averaged. There were no obvious genotypic differences in the adaptation to the metabolic cages system.

Biochemical measurements. Intraperitoneal glucose tolerance tests (GTT) were performed at 8 wk of age on mice at fasting 4 h (8 AM–noon) as previously described (27). Blood samples were collected from the saphenous vein into EDTA-containing tubes prior to and at 15, 30, 60 and 120 min postglucose (2 g/kg body wt) injection. Plasma was obtained by centrifugation (10 min, 10,000 g, 4°C), and samples were stored at −80°C until analysis. These tests were performed at 8 wk of age. Glucose was measured with a commercially available kit (Autokit Glucose; Wako Diagnostics, Richmond VA). We quantified the total glucose clearance by calculating the area between the normalized (baseline subtracted) glucose curve and the x-axis [area under the curve (AUC)] between 0 and 120 min. Insulin was measured by ELISA, as previously described (20). Plasma triglyceride levels were measured with the Infinity TM Triglycerides Reagent (Thermo Scientific, Middletown, VA).

Gene expression. Tissues were collected from mice at death at 10 wk of age, flash-frozen in liquid nitrogen, and stored at −80°C until analysis. RNA extraction and cDNA synthesis were performed as previously described (47). Gene expression was measured by quantitative RT-PCR using SYBR Green incorporation (Rotor-Gene SYBR Green PCR Kit, Qiagen). Gene expression was normalized to the level of Cyclophilin b (Ppib) mRNA, which did not differ between genotypes, and analyzed by comparing these ΔCT values. The primers used were as follows: Ppib [forward (for): TGAGAGCCACAAAGACAGAC, reverse (rev): TGCCGGAGTGCACAATTG, Npy for: ATATGGCAAGAGATCTCAGCC, rev: ATACGGAGGGTCTTTACAGG, Cart for: CTGGACCAGGATTCTT, Agapr for: ATGGCTCTAAAGAACATTGCAG, Agrp for: ATGGGCCTCAGAAAGACATTGC, ACGAGACTCTGGCTTGTTG, Ghsr for: GGGACCTGTCTGCAAAACTC, SCGATG-GGAATAGGCGCT, Pome for: CATCCTGGCATTGCAAACATT, rev: ACCATGGACGTACTTCCGGA, and Ucp1 for: ACACCTGCTCTCTCAACCC, rev: TGCATTCTGACCTCCAG].

Statistical analyses. Unless otherwise described, comparisons between genotypes were made by t-test or ANOVA, as appropriate. The growth curves were compared by two-way (repeated-measures) ANOVA. Food intake and energy expenditure data were compared by ANOVA with lean and fat mass as independent covariates (7, 14, 42). Data are shown as means ± SE.

RESULTS

Genomic and bioinformatic refinement of the Moo1-C strain. We previously generated the Moo1-C congenic strain, and found that BTBR<sub>ob/ob</sub> mice having this segment replaced...
by the corresponding segment from the B6 genome had reduced weight gain (40). Taking advantage of the publicly available mouse SNP data (http://www.jax.org/Phenome), we precisely defined the boundaries of the Moo1-C strain. These data refined the location of this congenic replacement to a 5.7 Mb segment of mouse chromosome 2 (Fig. 1). The Moo1-C region contains 71 genes and 12,000 SNPs known to differ between B6 and BTBR.

**Association of Moo1 with diet-induced obesity.** As few individuals are leptin deficient, we examined whether the effects of the Moo1 QTL also affect HFD-induced obesity in Moo1-C mice with normal leptin. Moo1-C mice were fed an HFD from weaning, and their body weights measured weekly. To account for any differences in initial weight (e.g., due to differences in litter size), we examined their increase in body weight from weaning. Moo1-C mice homozygous for B6 alleles (Moo1-C<sup>B6/B6</sup>) had reduced weight gain compared with their littermates homozygous for BTBR alleles (Moo1-C<sup>BT/ BT</sup> Fig. 2A). Weight gain became significantly lower in Moo1-C<sup>B6/B6</sup> mice by 10 wk of age (Fig. 2B), the same age at which body weights were different in the ob/ob mice (40). High-fat-fed heterozygous congenic mice (Moo1-C<sup>B6/BT</sup>) had intermediate weight gain (Fig. 2, A and B). These data confirm that the effects of Moo1 are not compensated for or overcome by the presence of functional leptin.

The body weights of the Moo1-C mice at weaning were not different (Fig. 2C), indicating that initial body size is not affected by Moo1. Similarly, body lengths at 10 wk of age were not different between Moo1-C<sup>B6/B6</sup> and Moo1-C<sup>BT/ BT</sup> mice (Fig. 2D), indicating that the Moo1-C<sup>BT/ BT</sup> mice didn’t simply

![Graph A](image1.png)

**Fig. 2.** High fat diet-induced obesity in Moo1-C mice. **A:** increase in body weight from weaning in Moo1-C<sup>B6/B6</sup>, Moo1-C<sup>B6/BT</sup>, and Moo1-C<sup>BT/ BT</sup> mice. The significantly reduced weight gain in Moo1-C<sup>B6/B6</sup> mice confirms the localization of a body weight quantitative trait locus to this region (40). **B:** weight gain at 10 wk of age in Moo1-C mice. Body weight at weaning (C) and body length (10 wk of age) (D) did not differ between genotypes. E: body mass index (BMI) at 10 wk of age. F: the Lee Index (cube root of body weight divided by body length) at 10 wk of age. n > 35 for all measurements and groups except weight gain at 3 wk of age in Moo1-C<sup>B6/B6</sup> mice where n = 25. The P value by ANOVA is shown on each graph, when significant. *P < 0.05, **P < 0.01, ***P < 0.001 vs. Moo1-C<sup>BT/ BT</sup> by subsequent Tukey pair-wise comparison.
grew more to account for their increased weight. Consistent with this, their growth curves remained similar throughout the initial rapid growth phase, until ~5 wk of age (Fig. 2A). By 10 wk of age, both the BMI (body weight/body length²) and Lee Index (cube root of body weight/body length) of both Moo1-C<sup>B6/B6</sup> and Moo1-C<sup>B6/BT</sup> mice were significantly reduced compared with Moo1-C<sup>Bt/Bt</sup> mice (Fig. 2, E and F), suggesting Moo1 primarily affects adiposity. To determine directly whether Moo1 affects obesity, we assessed body composition by DEXA, focusing on the two homozygous genotypes that have the largest difference in body weight. These data confirmed that lean mass was not different between Moo1-C<sup>B6/B6</sup> and Moo1-C<sup>B6/BT</sup> mice (Fig. 3A). Total fat mass tended to be increased in Moo1-C<sup>Bt/Bt</sup> mice (Fig. 3B), and the difference in weight gain between genotypes is due to differences in percentage body fat (Fig. 3C).

**Moo1 QTL affects obesity by altering food intake.** Next we sought to understand the mechanism by which B6 alleles protect Moo1-C mice from the development of obesity. We examined energy balance in Moo1-C<sup>B6/B6</sup> and Moo1-C<sup>B6/BT</sup> mice (Fig. 4). Moo1-C<sup>B6/B6</sup> mice tended to have reduced daily food intake compared with Moo1-C<sup>Bt/Bt</sup> mice (Fig. 4A, P < 0.1). As mice are more active and eat more during the dark cycle, we examined food intake in the light and dark cycles separately (Fig. 4B). Moo1-C<sup>B6/B6</sup> mice had significantly reduced food intake compared with Moo1-C<sup>Bt/Bt</sup> mice in the dark cycle, while no difference was seen during the less active light cycle. This difference in the amount of food consumed was similar in magnitude to that observed on a daily basis, suggesting the reduced intake of Moo1-C<sup>B6/B6</sup> mice during the dark cycle accounts for the difference in daily intake. Neither physical activity (Fig. 4C) nor total daily energy expenditure was different between Moo1-C<sup>B6/B6</sup> and Moo1-C<sup>Bt/Bt</sup> mice (Fig. 4D). Similar results were observed for these parameters in both the light and dark cycles (not shown). Thus, Moo1 affects the development of obesity by altering food intake.

To gain possible insight into the mechanism by which food intake is altered, we examined the feeding patterns of Moo1-C mice. These data showed that Moo1-C<sup>Bt/Bt</sup> mice tend to eat more per meal during the dark cycle (Fig. 4E), suggesting that pathways regulating meal cessation may be altered by Moo1. The number of meals consumed did not differ between the genotypes in either the dark or light cycles (Fig. 4F). Thus, the higher food intake in Moo1-C<sup>Bt/Bt</sup> mice during the dark cycle results from larger meals, not more frequent meals. The lack of difference in meal size or frequency during the light cycle is consistent with the lack of difference in total food intake during this cycle.

None of the genes contained in the region of chromosome 2 encompassed by the Moo1-C strain are known to affect food intake. We hypothesized Moo1 may reduce food intake through mechanisms that affect the major molecular pathways and neurons known to regulate food intake. We examined the expression of the canonical genes defining these neurons in the hypothalamus but did not detect any significant differences (Fig. 5), suggesting Moo1 may affect novel pathways regulating food intake. Similarly, no differences in the expression of any of these genes were observed in the remainder of the brain (not shown). Consistent with the lack of differences in metabolic energy expenditure between Moo1-C<sup>B6/B6</sup> and Moo1-C<sup>Bt/Bt</sup> mice, we did not find differences in *Ucp1* expression in either brown adipose tissue or white adipose tissue from these mice.

**Impaired fasting glucose and glucose tolerance in Moo1-C mice.** BTBR is a diabetes-susceptible strain (11). To examine whether the difference in body weight attributable to the Moo1 locus affected their diabetes risk, we examined the glucose tolerance of Moo1-C mice. Moo1-C<sup>Bt/Bt</sup> mice had significantly impaired glucose tolerance of an intraperitoneal glucose challenge (Fig. 6A), resulting in an approximate doubling of the area under the glucose clearance curve from baseline compared with Moo1-C<sup>B6/B6</sup> mice (Fig. 6B). Although plasma insulin levels were higher at all times during the GTT (Fig. 6C) in Moo1-C<sup>Bt/Bt</sup> mice, insulin secretion (changes in insulin from baseline) was similar between the genotypes (data not shown). This suggests that the impaired glucose tolerance in Moo1-C<sup>Bt/Bt</sup> mice results from increased insulin resistance, consistent with their increased adiposity. Also consistent with this, fasting insulin levels tended to be higher in Moo1-C<sup>Bt/Bt</sup> mice, although these did not reach statistical significance (time 0 in Fig. 6C). Fasting glucose levels (time 0) were significantly higher in Moo1-C<sup>Bt/Bt</sup> mice compared with their littermates (Fig. 6A). Fasting plasma triglyceride levels were not different between genotypes of Moo1-C (not shown). These data suggest that the decreased adiposity of Moo1-C<sup>B6/B6</sup> mice is sufficient to have beneficial effects on complications of obesity such as impaired glucose tolerance and insulin sensitivity.

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**Fig. 3.** Body composition of Moo1-C<sup>B6/B6</sup> and Moo1-C<sup>Bt/Bt</sup> mice. Lean mass (A), and fat mass (B), and percentage of body mass that is fat (C) obtained by dual-energy X-ray absorptiometry analysis. n = 25 and 36 for Moo1-C<sup>B6/B6</sup> and Moo1-C<sup>Bt/Bt</sup>, respectively.

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DISCUSSION

These studies have confirmed that a gene (or genes) underlying the Moo1 obesity QTL lie(s) within a 5.7 Mb region of chromosome 2. Within this region are >70 genes, many of which are potentially interesting candidates, including several transcription factors. As there are many known genetic variants between the strains in this region, further genetic localization will be needed to identify the causative gene. Importantly, these studies showed that Moo1 promotes obesity in HFD-fed animals, a more common form of obesity than that arising due to leptin deficiency. As we have not yet examined in these mice consuming other diets such as normal mouse chow, these studies do not preclude the possibility that this locus may affect adiposity even on normal diets. The fact that this locus was first identified in leptin-deficient ob/ob mice (40), however, indicates that the causative gene acts independently of leptin.

The body weights of Moo1-CB6/B6 mice at 10 wk of age were ~7% lower than their Moo1-CBT/BT littermates, and their body weights continue to diverge over time (e.g., 9% lower by 16 wk of age, not shown). Weight loss of this amount is sufficient to have therapeutic benefit. A 5% reduction in body weight is the threshold by which new therapeutics are considered effective (24, 34, 43). Thus, mimicking the effects of the underlying gene (e.g., inhibiting it to the same degree as a reduction in its expression), assuming the appropriate tissue(s) can be targeted, is likely to produce significant reductions in body weight and body fat. Furthermore, pharmacological modulation of the underlying gene may have larger effects on the

Fig. 4. Food intake and energy expenditure in Moo1-CB6/B6 and Moo1-CBT/BT mice. Average daily food intake (A) and average food intake during the light and dark cycles (B) (n = 14, 19 for Moo1-CB6/B6 and Moo1-CBT/BT, respectively). Food intake was excluded for mice from cages in which crumbled food was observed. C: average daily physical activity (beam breaks; n = 19, 28 for Moo1-CB6/B6 and Moo1-CBT/BT, respectively). D: average daily energy expenditure (n = 21, 26 for Moo1-CB6/B6 and Moo1-CBT/BT, respectively). Average meal size during the light and dark cycles (E) and average number of meals during the light and dark cycles (F) (n = 12, 16 for Moo1-CB6/B6 and Moo1-CBT/BT, respectively). Due to random sensor failures during various runs, some data were unavailable for some mice. Thus the numbers for each measurement differ.
activity of the protein and consequently on body weight than that due to the subtle allelic difference(s) in the gene between individuals or strains (10).

We determined that the Moo1 QTL acts by affecting food intake, primarily during the dark/active cycle. A difference in intake of a similar magnitude was observed on a daily basis, although this did not reach significance. The daily difference in food intake that we observed (Fig. 4A) corresponds to a difference of \(-0.7\) Kcal per day. If all stored as fat, this difference would be expected to result in a \(3.9\) g difference in weight gain observed in the Moo1-C mice. The increased food intake during the dark cycle was likely due to increased meal size, as we found no difference in the number of feeding episodes. Interestingly, increased meal size itself, even in the absence of differences in total intake, may promote obesity. It has recently been shown that increased meal sizes are associated with increased postprandial plasma insulin AUC (16), and we have recently shown that increased plasma insulin drives obesity (30). Thus, it is possible that both the increased total intake and increased meal size contribute to the obesity in these mice.

We examined the expression of the neuropeptide genes defining the major neurons known to be involved in the regulation of food intake within the hypothalamus. None of these genes themselves are located within the Moo1 confidence region and are thus not expected to directly contribute to Moo1. However, there are many transcription factors in the Moo1-C region. Thus we hypothesized that they may affect the expression of the predominant players regulating food intake, but the expression of these genes involved in the canonical pathways regulating food intake in the hypothalamus or remainder of the brain did not differ. These data do not exclude the possibility that these pathways could be affected at a posttranscriptional level, e.g., the regulation of their release or their signaling. However, as none of the \(\sim 70\) genes in the region of the Moo1-C congenic region are known to affect food intake or the regulation of these pathways, this suggests discovery of the underlying gene(s) will reveal a novel mechanism regulating food intake and meal cessation.

Obesity is a major risk factor for Type 2 diabetes (22). We determined that the difference in obesity resulting from the Moo1 QTL, even just at 10 wk of age, is sufficient to alter their risk of Type 2 diabetes. Moo1-\(C^{\text{BT/WT}}\) mice had elevated fasting glucose levels and tended to have increased plasma glucose homeostasis in Moo1-\(C^{\text{BT/WT}}\) and Moo1-\(C^{\text{BT/WT}}\) mice. A: intraperitoneal glucose tolerance test. B: area under the glucose clearance curve of each animal from its baseline (t = 0) value. C: plasma insulin levels in response to the intraperitoneal glucose challenge. \(n = 7\) and 13 for Moo1-\(C^{\text{BT/WT}}\) and Moo1-\(C^{\text{BT/WT}}\), respectively. *\(P < 0.05\), **\(P < 0.01\), ***\(P < 0.001\) vs. Moo1-\(C^{\text{BT/WT}}\) at each time point.
insulin levels and impaired glucose tolerance. Thus, the increased adiposity in BTBR mice due to Mool1 is sufficient to increase their risk of Type 2 diabetes. This suggests that therapeutic modulation of the underlying pathway may have clinical benefit not only to reduce obesity but also to protect against some of its severe clinical complications. Although the preceding is the most common interpretation of these findings, it is alternatively possible that the underlying gene(s) affects both body weight and insulin sensitivity independently (25) or that the gene predominantly affects insulin sensitivity of the brain, which has been shown to result in obesity and glucose intolerance, while not affecting insulin signaling in adipose tissue, which must remain intact to promote fat storage (5, 21, 29, 37).

Discovery of the genes underlying QTLs affecting metabolic disease in mice is possible, and there have been many recent successes. We recently identified two Type 2 diabetes susceptibility loci in these strains (4, 12). Several others have identified genes underlying obesity and Type 2 diabetes-related traits in other strains (6, 8, 9, 13, 23, 36, 46). Identification of the gene(s) underlying Mool1 will provide novel insight into leptin-independent mechanisms regulating food intake. Knowledge of the mechanism by which Mool1 affects body weight will assist with the identification of candidate genes, for example, by knowing what pathways may be affected, where the gene might be expressed, or what it might do. These data may also be useful for investigators studying the many overlapping obesity-related QTLs in mice and humans (35, 45), providing a hint about how other QTLs may act, if they are in fact due to the same gene.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS


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