Genetic, sex, and diet effects on body weight and obesity in the Berlin Fat Mouse Inbred lines

Asja Wagener, Armin O. Schmitt, Soner Aksu, Werner Schlotte, Christina Neuschl, and Gudrun A. Brockmann

Institute of Animal Sciences, Humboldt-Universität zu Berlin, Berlin, Germany

Submitted 6 September 2005; accepted in final form 1 August 2006

Wagener, Asja, Armin O. Schmitt, Soner Aksu, Werner Schlotte, Christina Neuschl, and Gudrun A. Brockmann. Genetic, sex, and diet effects on body weight and obesity in the Berlin Fat Mouse Inbred lines. Physiol Genomics 27: 264–270, 2006. First published August 15, 2006; doi:10.1152/physiolgenomics.00225.2005.—Mouse lines long-term selected for high fatness offer the possibility to identify individual genes involved in the development of obesity. The Berlin Fat Mouse (BFM) line has been selected for low protein content and afterward for high fatness. Three Berlin Fat Mouse Inbred (BFMI) lines, which are derivatives of the selection line BFM and an unselected control line (C57BL/6; B6) were systematically phenotyped between 3 and 20 wk. The body weights and body compositions were measured on a weekly basis. We demonstrated that the BFMI lines dispose of more body weight, body fat mass, and body lean mass than the control line B6 because of a better feed efficiency in these lines. In contrast to other growth-selected mouse lines, the BFMI lines exhibited a general increase in body fat mass but only a marginal increase in body lean mass. The three BFMI lines also showed line- and sex-specific patterns and varied in their response to high-fat diet. The phenotypic differences between the BFMI lines can be traced back to different sets of fixed alleles contributing to fat accumulation and diet-induced obesity. Our results demonstrate that the genetically related BFMI lines are novel models to study the genetic as well as the nutritional aspects of obesity.

SEVERAL SINGLE-GENE MUTATIONS causing obesity or obesity-related phenotypes have been identified in mice to date (11, 12, 22). However, monogenic types of obesity are likely to account for only a small fraction of human obesity. Most genetically controlled types of obesity seem to be influenced by multiple gene loci. Individual genes only have a small effect, but the interaction of many genes causes extreme phenotypes (3, 5). In humans, the genetic analysis of such polygenic traits is difficult because of the effects of the environmental and genetic background; therefore, polygenic mouse models are used to study the genetics of complex traits such as obesity. Mouse lines, long-term selected for the desired feature, and, more specifically, their inbred derivate offer the possibility to identify individual genes and to elucidate the complex network of interacting genes with regard to the interaction between genes and environment. Depending on the genetic variability in the particular founder population, the selected mouse lines differ not only in their phenotypes but also in their specific set of genes and alleles. Several different mouse lines derived from heterogeneous base populations have been selected either for body weight or fat content (9), for example, the lines LG/J, DU6, M16, New Zealand obese (NZO), KK, and F. The lines LG/J and DU6 were selected for high body weight (10, 19), whereas the mouse line M16 is a result of selection for rapid weight gain (15). The NZO line was bred for high body weight and obesity (4), while only the F line has been selected solely for high fat content (24). The KK line was originally established as a diabetic line developing moderate obesity (21). All of these mouse lines develop obesity on standard breeding diet, but in some lines the degree of body fat can be additionally increased by a high-fat diet. However, the specific genes that are responsible for determining sensitivity to dietary obesity are potentially different from those causing general obesity. Recently, interactions between genotype and diet composition have been detected in experiments with lean mouse lines where obesity was induced by high-caloric diets (13, 18, 25, 33). However, some of these mouse lines did not develop diet-induced obesity (DIO).

To study the genetic basis of obesity, the intercross of phenotypically different inbred mouse lines provides an excellent multigenic model. Crosses between diverse growth-selected mouse lines as well as between different inbred lines have revealed many quantitative trait loci (QTLs) for body weight and obesity (5, 22). However, crosses between different line pairs showed a diverse pattern of QTLs. This indicates that many different genes contribute to obesity and related traits. Moreover, most of the above-mentioned mouse lines were selected primarily for high body weight. High body weight consists not only of fat, but also of a considerable proportion of body lean mass. It is therefore very likely that many QTLs merely affecting fat accumulation are still unknown. Thus the development of new animal models to identify genes responsible for common obesity is still important.

To constitute a valuable model for studies of the genetic basis of fat accumulation, we have established the Berlin Fat Mouse Inbred (BFMI) lines BFMI856, BFMI860, and BFMI861, which are collectively termed BFMI lines in this article, as novel mouse models for obesity. In contrast to some of the above-mentioned models, the BFMI lines were generated from an outbred population selected for a high-fat phenotype with low body weight. The objectives of the primary experiment that we report here were 1) the phenotypic characterization of the genetically related BFMI lines as polygenic model for obesity and 2) the analysis of the response of the different BFMI lines to a high-fat diet. The genetic similarity between these lines on the one side and the different sensitivity to diet-induced obesity on the other make these mouse lines
valuable resources for further dissection of the involved genetic factors.

**MATERIALS AND METHODS**

**Mouse Populations**

Founder animals of the Berlin Fat Mouse lines were originally purchased in several pet shops in Berlin, Germany. The selection process comprised several distinct phases. In the first phase, animals were sib-selected over 23 generations for low protein content of the carcass at the age of 60 days (2, 32). In the second phase, the mice were selected for low body weight and high fat content at 42 days (31). In the fourth generation of this selection period, some mice exhibited a phenotype of high fatness. Beginning with these mice, during the third phase of the line history, animals were selected for phenotypic high fatness at 9 wk. The new line was named the Berlin Fat Mouse (BFM) line. This line was consolidated with about 20 families per generation at a mating ratio of one male to three females for 10 generations. Subsequently, 40 families per generation were reproduced with a mating ratio of one male to two females. Forty breeding pairs were maintained per generation in the BFM line from generation 24 to 50, and from generation 51 onward, thirty breeding pairs were kept per generation. After 58 generations of selection in the BFM line, inbred derivates (BFMI lines) have been generated. Distinct inbred lines have been obtained by brother-sister mating from randomly chosen founder sib-pairs of the selection line. For the phenotypic characterization, we used the inbred lines BFMI856, BFMI860, and BFMI861 after six generations of inbreeding. Although inbreeding was avoided during the selection process because of the family structure, the inbreeding coefficient of the outbred population was ~0.45 after 58 generations of selection and rose to 0.85 after an additional six generations of inbreeding (unpublished data, calculated according to Ref. 17). To ensure a high genetic homogeneity of the animals of the BFMI lines in the different diet groups, four male and four female full sibs of each litter were equally assigned to two dietary conditions. Two litters of every line were used for our experiment. As a control line, we used C57BL/6NCrl (B6) (Charles River Laboratories, Sulzfeld, Germany), which were reproduced in our mouse facility. Nine to ten males and females of B6 were taken for either standard breeding or high-fat diet conditions. The number of animals in the different diet groups is shown in Table 1.

**Feeding Conditions**

After weaning at the age of 3 wk, animals were fed ad libitum with either a rodent standard breeding diet (SBD) or a high-fat diet (HFD). The SBD (Altromin breeding diet no. 1314, Lage, Germany) derived its fat from soy oil, whereas the HFD (Altromin breeding diet no. 1314 with 18.5% fat, Lage, Germany) derived its fat from coconut oil.

**Table 1. Origin and no. of animals in different feeding groups of BFMI lines and B6**

<table>
<thead>
<tr>
<th>Line</th>
<th>SBD</th>
<th>HFD</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>BFMI856</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>BFMI860</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>BFMI861</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>B6</td>
<td>10</td>
<td>9</td>
</tr>
</tbody>
</table>

Within Berlin Fat Mouse Inbred (BFMI) lines, 8 full sibs were assigned to standard breeding (rodent standard breeding diet; SBD) and high-fat diet (HFD) feeding groups; 2 full sib males and 2 full sib females were assigned to each diet group. B6, C57BL/6NCrl. *One animal died during the experiment.

The composition of the two diets is given in Table 2. The diets were formulated to be as equivalent as possible in their ingredients with the exception of fat content. Water was given ad libitum. Food intake was estimated as the difference between the offered and the remnant amount of food for 7-day intervals from week 8 onward. Food pellets were especially pressed for low spillage by the food-providing company; possible residual spillage was not considered. Energy intake was determined from the energy content in each diet. Food and energy intake were calculated on a per day basis. Feed efficiency was determined as the ratio of body weight gain and body fat weight gain in grams to consumed energy in kilojoules, respectively. For the comparison between lines, energy intake, feed efficiency, and body fat gain per energy intake, weekly measurements of food intake were averaged over the period between 8 and 20 wk.

**Body Weight and Body Composition**

For the phenotypic characterization of the BFMI lines and B6, animals were systematically analyzed between 3 and 20 wk. We considered body weight, body fat weight, and body fat percentage as indicators of obesity. Body lean weights and body lengths were measured as general growth parameters. Body weight, body fat mass, body lean mass, and body length (nasal-anal) were measured weekly on the basis of day of birth. Body fat mass and body lean mass were determined in nonanesthetized animals by quantitative magnetic resonance (QMR) analysis using the EchoMRI whole body composition analyzer (Echo Medical Systems, Houston, TX) (27, 30). Animals were measured twice, and the mean was used for further analyses. Body fat percentage was calculated as the proportion of the body fat mass (measured by QMR) to body weight, weighed before the QMR measurements. Growth rates were determined as the differences of the weekly measured body weights.

At 20 wk, mice were killed by decapitation using surgical scissors after a fasting period of 2 h. After bleeding, all white fat tissues (reproductive fat pad, renal fat pad, subcutaneous fat pad as well as the residual fat tissue containing all visible remaining white fat tissues) and the brown adipose tissue were dissected and weighed. The sum of all white fat tissues is termed “total white fat tissue” here. Additionally, weights of liver, heart, spleen, kidney, quadriiceps, and the carcass (body without head, inner organs, fat tissues, quadriiceps, gut, and tail) were recorded.

The animals were treated in accordance with the National Animal Welfare Legislation (approval no. G0152/04).

**Glucose Level**

Glucose concentrations were measured using the glucose analyzer Ascensia Elite (Bayer HealthCare, Leverkusen, Germany). Blood
samples were collected by puncturing the tail of nonfasted animals at 8, 10, 12, 14, 17, and 20 wk.

**Statistical Analyses**

To compare the BFMI lines with B6, analyses were made to compare the four mouse lines (BFMI856, BFMI860, BFMI861, B6) fed the SBD with adjustment for sex. For the analysis of diet-specific effects among the BFMI lines, comparisons were made between the two diets (SBD, HFD) in mice of the same line and adjusted for sex. To find sex effects within each BFMI line, the two sexes of the same line and the same diet were analyzed.

To compare time courses, the longitudinal data were subjected to a permutation test, specifically developed for this purpose (16, 26). The calculations were performed using the R statistical software package (26). The data of the distinct fat pads, quadriceps and carcass weights, inner organ weights, and food consumption were analyzed using the following general linear model

\[ Y_{ijklm} = \mu + L_i + F_j + D_k + S_l + (L \times D)_{ik} + (D \times S)_{kl} + \beta W + e_{ijklm} \]

where \( Y_{ijklm} \) denotes the measurement of the \( m \)-th animal of line \( i \) in family \( j \) at diet \( k \) and of sex \( l \); \( \mu \) is the average of the variable of interest for all animals. The index \( i \) represents the family effect within line \( i \), \( L \), \( F \), and \( D \) are the factors introduced by the family line, diet, and sex, respectively, with \( F \) being a subordinate factor of \( L \). \( L \times D \) and \( D \times S \) are the interaction terms between family line and diet on the one hand and diet and sex on the other. The body weight \( W \) is introduced as a covariate with the coefficient \( \beta \), and \( e_{ijklm} \) is the residual error of the measurements. Following a significant result, Tukey’s protected \( t \)-test and Student’s \( t \)-test were used as post hoc tests for multiple and two-group comparisons, respectively, to determine which groups differ significantly. These calculations were performed using the SAS 9.1 statistical software package (SAS Institute, Cary, NC). \( P \) values <0.05 were considered statistically significant.

**RESULTS**

**Phenotypic Characterization of BFMI Lines on SBD**

**BFMI lines compared with B6.** Initially, mice of the genetically related BFMI lines were compared with B6 mice to demonstrate the extreme obese phenotype of the BFMI lines on SBD. Subsequently, line-specific effects among BFMI856, BFMI860, and BFMI861 were analyzed.

Figure 1 shows the growth curves for body weight, body fat mass, and body lean mass, and body fat percentage in all lines on SBD during the developmental phase between 3 and 20 wk. Already at the age of 3 wk, mice of all BFMI lines were on average 2.8 g heavier than B6 mice.

The comparison of the curves representing the development of the different traits between 3 and 20 wk by a permutation test revealed that animals of BFMI lines were significantly heavier, accumulated more body fat mass, and had a higher body fat percentage than B6 mice over the entire experimental period. Although animals of BFMI lines also had higher body lean mass than B6 animals, these differences were negligible compared with the huge increase of body fat mass in the selected lines. The \( P \) values of the permutation test comparing the growth curves among different animal groups are summarized in Supplemental Table 2 (supplemental data are available in the online version of this article).

Data on the body weight and body composition characteristics at 20 wk, when animals were dissected, as well as data on feed consumption and glucose concentrations, are presented in Supplemental Table 3. In Table 3 (see also Supplemental Table 3), the ANOVA \( P \) values of the variance analysis for the influence of different factors on different traits are given for all four investigated lines.

At the age of 20 wk, mice of the selected inbred lines were 1.5–1.8 times as heavy as B6 animals. Males of the BFMI lines weighed 44–47 g and females 34–41 g. According to the QMR measurements, mice of the BFMI lines had 5.3–11.8 times higher body fat mass but only 1.1–1.3 times higher body lean mass than B6 animals. Mice of the selected inbred lines had a body fat percentage of 22–30% in males and 28–37% in females, respectively, vs. 6% in both sexes of B6.

The mass of total white fat tissues of dissected animals at 20 wk was 5.5–13.6 times higher in BFMI animals than in B6 animals (Supplemental Table 3). The percentage of total white fat tissues relative to body weight was ~16% (BFMI856 and BFMI860) and 11% (BFMI861) in males and ~17% (BFMI856 and BFMI861) and 23% (BFMI860) in females. B6 mice had ~3% total white fat tissue in both sexes. In all BFMI lines, the reproductive fat pad was the largest fat tissue, which likely serves as a main fat depot. The brown adipose tissues were also heavier in the selected animals compared with B6.

The weekly feed intake of animals within a line did not vary much between the age of 8 and 20 wk. Within this period, animals of the BFMI lines consumed significantly more food and correspondingly more energy than B6 mice (Supplemental Table 3). Weekly records of body fat mass permitted the calculation of the ratio of body fat gain per energy intake over time. This ratio showed that the efficiency in fat deposition was \(-1.0–1.8 \text{ mg/kJ}\) in the mice of the selected inbred lines; this was 5.1–18 times higher than in B6 mice. The average feed efficiency, which refers to body weight gain per kilojoule consumed, was ~1.1–2.0 times higher in mice of BFMI lines than in B6 mice.

The control of the blood glucose concentration as a hint on glucose metabolism and glucose homeostasis showed that BFMI lines and B6 were inconspicuous until the age of 17 wk. However, males of line BFMI861 had an increased glucose concentration at 20 wk, which might be an indication of glucose imbalance in conjunction with the development of diabetes.

**Differences among BFMI lines.** Among the BFMI lines, significant differences were found for the development of body fat mass and body fat percentage between 3 and 20 wk (Supplemental Table 2) as well as for the weights of dissected fat pads and inner organs and glucose concentrations at 20 wk (Table 3 and Supplemental Table 3). On SBD, the BFMI lines did not differ in body weight, body length, weights of brown adipose tissue, quadriceps, and carcasses as well as feed consumption traits. Table 3 (see also Supplemental Table 3) gives the ANOVA \( P \) values for the influence of different factors on the phenotypes in the BFMI lines.

Mice of line BFMI860 had the highest body fat percentage among BFMI lines and differed significantly in the mass of total white fat tissues from the other lines. This was particularly due to the significantly heaviest subcutaneous fat depots but also to heavier reproductive fat depots, which were significantly different from line BFMI861. In line BFMI860, the obese phenotype was more pronounced in females, but sex-specific differences were found only for carcass weight, which was heaviest in males.
Mice of line BFMI861 had the lowest amount of total white fat tissue among BFMI lines mainly because of the significantly smallest reproductive fat depots. Males were significantly leaner than females. The liver weight was notably high and differed significantly not only from liver weights of BFMI860, the fattest mouse line, but also from those of line BFMI856. Mice of the line BFMI861 had higher spleen weights than other lines and significantly higher spleen weights than line BFMI856. The blood glucose concentrations were generally highest in BFMI861, differing significantly from animals in line BFMI856. At 20 wk, males of this line showed hyperglycemia (242 mg glucose/ml serum).

Mice of line BFMI856 did not differ much from those of line BFMI861, but in line BFMI856 the greatest differences between sexes were found. At 20 wk, the body weights differed by 13 g (Supplemental Table 3). During the whole experimental period, males gained more body weight and were longer than females. Males had higher carcass and organ weights and tended also to have more total white fat tissue mass than females. This effect is likely the result of the significantly higher energy uptake in males compared with females. Glucose concentrations were similar in both sexes.

**Line-Specific Responses to HFD**

During the developmental period between 3 and 20 wk, animals of different BFMI lines and B6 responded to the HFD in a different manner. In all lines, the energy uptake was significantly increased on HFD, but body weight gain and obesity developed differently in these lines. The diet-induced effects on body weight, body fat mass, and body lean mass in the different BFMI lines and B6 during 3 and 20 wk are illustrated in Fig. 2. In Supplemental Table 3, mean values of phenotypic traits at 20 wk are summarized, and in Table 3 P values for the influence of line, diet, sex, line by diet, and sex by diet are given for all four lines, including the analysis of the BFMI lines without B6.
In B6 animals, body weight remained almost constant on HFD, but body composition changed significantly. The weights of all fat depots were about twice as high on HFD than on SBD. Aside from higher energy uptake, these animals used the consumed energy more efficiently (Supplemental Table 3).

Animals of line BFMI860, which was the fattest line on SBD, responded most to HFD by diet-induced body weight gain. This was due to increased fat deposition (higher body fat mass) but also higher protein accretion (higher body lean mass) during the entire period of feeding HFD (Supplemental Table 2). The biggest difference in body fat percentage between animals on SBD and those on HFD was observed at ~12 wk. Afterward, the curves of the body fat percentage belonging to different diets converged toward the end of the experiment at 20 wk. The dissection of animals at 20 wk showed that the additional accumulated fat was mainly deposited in subcutaneous fat tissue. Concordant with higher lean mass, the carcass weights were increased. The weights of liver and spleen were also elevated. The diet-induced changes of body composition were more apparent in males than females. The HFD also had an effect on increased glucose concentration in this line (Supplemental Table 2).

Animals of line BFMI861 responded to the HFD by an increased body fat mass and body fat percentage during the high-fat feeding period but not with higher body weight. At 20 wk, the animals were significantly longer than on SBD. However, with regard to the feed uptake on HFD, the animals were conspicuous. Considering the sexes separately, three of four males in this line developed hyperphagia in conjunction with a lower feed efficiency; their body weight was not increasing on HFD. In the hyperphagic BFMI861 males, the glucose concentration rose above 200 mg/dl from the age of 17 wk on. However, the increase in only three of four males resulted from an incomplete inbreeding and accounted for a high standard deviation with no significant result.

During the HFD feeding period, animals of line BFMI856 became lighter because of a lower body lean mass compared with SBD. Concordant with the lean mass, the carcass weights were reduced at 20 wk. Liver and kidney weight was also reduced in this line. The effects were particularly significant for males, which had a reduced fat gain per consumed energy and a lowered feed efficiency. The responses of BFMI856 and BFMI861 males to HFD resulted in significant line-by-diet and sex-by-diet interaction effects for feed efficiency (Table 3 and Supplemental Table 3).

**DISCUSSION**

The inbred mouse lines BFMI856, BFMI860, and BFMI861 were derived from the line BFM, which had been selected for low protein content and subsequently for low body weight and high fatness. As a result of selection, the BFMI lines notably differ from B6, an unselected and widely used inbred mouse line. Despite long-term selection, inbreeding of the outbred line with randomly chosen founder sib-pairs resulted in genetically related inbred lines that differed from one another in traits characterizing adiposity by various subphenotypes. As such we have analyzed body weight, growth rate, body composition, and feed consumption traits in the different selected inbred lines in response to standard breeding and high-fat diets. Males and females of the different lines were analyzed between the ages of 3 and 20 wk.
Because of the selection response, the BFMI lines were disposed to higher body weight, body fat mass, and body lean mass than the B6 line, independent of age, sex, and diet. Likewise, the selected inbred lines differed dramatically from the control line B6 in each distinct depot-specific fat pad but also in liver and kidney weights at 20 wk. In each case, the BFMI lines had higher weights than B6. Within each BFMI line, the sexes differed in either body weight, body fat percentage, or their response to high-fat diet.

So far, linkage analyses in various crossbred populations identified some QTLs with different effects on body weight in males and females (6, 7). Other sex-specific QTLs have been identified for adiposity and regulation of total fat deposition (28). The sex-related differences in obesity might be due to the effects of sex steroid hormones, which contribute to the regulation of the amount and distribution of fat in different adipose tissues (20). Sex-specific effects in obesity were also found in humans (for review see Refs. 20, 34). Our mouse lines demonstrated that sex also plays a crucial role in the development of obesity in mice with almost the same genetic background.

In general, obesity results from excess energy intake. This excess energy can be stored as fat or transferred to proteins (lean mass). The portion of excess energy stored as fat depends on resting energy consumption, food conversion efficiency, thermogenesis, and behavior. The experimental data of the BFMI lines demonstrated that there are different genetic effects contributing to energy distribution. The presented results indicate that our selected inbred lines may generally have lower resting energy consumption and/or higher food conversion efficiency than B6 animals. Food consumption (in terms of food intake in grams) does not vary much across the lines, sexes, and diets. Diet-induced obesity as result of higher energy intake on high-fat diet was evident in line BFMI860 and, to a lesser extent, in line BFMI861 but not in line BFMI856. When consumption was calculated as energy intake, it rose uniformly in the high-fat regime across the lines and sexes, with males of line BFMI861 developing hyperphagia. Despite hyperphagia in males of line BFMI861 fed the high-fat diet, obesity was only slightly increased, but the excess energy intake resulted in the development of hyperglycemia in adulthood in these mice. This feature could indicate the development of diabetes.

Across the different BFMI lines, the genetic differences in the ability to store fat are more important for the development of obesity than the increase in caloric uptake. Animals of the line BFMI860 and, less evidently, of the line BFMI861 became obese faster on high-fat diet conditions in the juvenile phase. However, in adult mice, the fat accretion slowed down so that the curves of body fat mass converged between animals of either diet. At 20 wk, differences in body fat accumulation between animals on standard breeding and high-fat diets were much smaller than before, when animals were in the growth phase; thus there seemed to be a plateau effect of dietary manipulations that promote obesity. We assume that many genes causing obesity as a result of selection are most likely different from those involved in the response to diet-induced obesity.

Although the BFMI lines do not exhibit an extreme degree of obesity, as do some monogenic models such as obese, agouti, tubby, and fat mouse lines, the selection for high fatness in the BFMI line and subsequent inbreeding to generate the BFMI lines created excellent polygenic models to study the genetics of obesity. The BFMI lines exhibited a similar fatness when compared with other polygenic models of obesity (9). Comparison with the F line, which has been selected for high fatness, showed that the BFMI lines have similar body weights but a lower body fat percentage (8). The NZO mouse, which has been selected for high body weight and obesity, is heavier than the BFMI lines, but the degree of obesity is similar. The line BFMI860 was most alike to the NZO line regarding fat percentage (29); however, it did not develop hyperglycemia until the age of 20 wk. Other polygenic models for obesity were mainly selected for growth-related traits such as high body weight in LG/J and DU6 or high weight gain in mouse line M16. Compared with these lines, the BFMI lines have less body weight but similar obesity (1, 9, 14).

Fig. 2. Weekly differences in body weight, body fat mass, and body lean mass between animals fed either standard breeding or high-fat diet for each line. Values are differences between means of the high-fat diet group and means of the standard breeding diet group. Means were adjusted for sex effects.
Assuming that BFMI mice and their obesity phenotypes are of polygenic nature, the BFMI lines are excellent models for the study of obesity in humans. Considering that animals of lines BFMI860 and BFMI861 showed the greatest differences in their body fat mass at the end of the juvenile phase, these lines could serve as models for humans who become obese near the end of their growth phase. In addition, the line BFMI861 could serve as a model for type 2 diabetes, as there is a tight connection between obesity and diabetes (23). Differences in obesity-related phenotypes among the three high-fatness selected inbred lines make it possible to map genes for obesity and hyperglycemia in LG/J and SM/J inbred mouse strains. Physiol Genomics 1: 33–39, 1999.


