CORRELATED RESPONSES IN BODY COMPOSITION
BASED ON SELECTION FOR DIFFERENT
INDICATOR TRAITS IN MICE

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ABSTRACT

Correlated responses in whole-body composition were determined in 12-wk-old male mice from replicate lines selected for 12 generations for high (HF) or low (LF) epididymal fat pad weight as a percentage of body weight (EPID) and high (HL) or low (LL) hind carcass weight as a percentage of body weight. The HF and LF lines diverged (P < .01) in body fat percentage (FAT) and subcutaneous depot fat by 93 and 71%, respectively, of the control line (RC) mean. EPID increased (P < .01) proportionately more than FAT in the HF line; EPID decreased (P < .01) proportionately less than FAT in LF. Protein, fat and water as a percentage of empty body weight showed negative correlated responses (P < .01) due to selection for EPID, but lean body mass, body weight and body length had positive correlated responses (P < .01). Correlated responses of fat-free protein and ash percentage were minor. Correlated responses in HL and LL were the mirror images of those in HF and LF, but they generally were of smaller magnitude. The results indicate that, although there are high positive genetic correlations between fat depots in mice, local control of lipogenesis and/or lipolysis exists at different sites of fat deposition. Further, the lack of correlated responses in fat-free percentage of protein (and percentage of ash) suggests that additive genetic variances are low for these traits and/or the genetic correlations of these traits with the selection criteria are low.

(Key Words: Correlated Responses, Body Composition, Selection, Mice.)


Introduction

The livestock industry is making strides toward reducing carcass fat in response to marketing and consumer demands (Topel and Kauffman, 1988). Methods of reducing fat content include nutrition, restricted feeding, delivery of partitioning agents, immunization against specific hormones and genetic selection (Speer, 1988; Eisen, 1989). Of these, only selection has a permanent effect on a population.

The mouse has proven useful as a model system to study direct and correlated responses to selection for body composition traits (see review by Eisen, 1989). Obtaining a suitable predictor of body composition is important in a research program designed to modify or monitor fat and lean tissue percentage (Topel and Kauffman, 1988). In the mouse, several selection studies have been based on indicator traits of whole-body composition in order to reduce the cost and time involved in doing complete chemical analysis of the carcass (McLellan and Frahm, 1973; Sharp et al., 1984; Eisen, 1987a). The objective of the present study was to determine the outcome of selection for two different indicator traits on body composition in mice.

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Materials and Methods

Mice used in this study were from the following replicate lines: HF1, HF2 and LF1, LF2 selected respectively for high and low right epididymal fat pad weight as a percentage of body weight (EPID); HL1, HL2 and LL1, LL2 selected respectively for high and low hind carcass weight as a percentage of body weight (HC); and RC1, RC2 selected randomly. Omission of the replicate number will indicate pooling of replicates. Selection was conducted on 12-wk-old male mice.

EPID was used as an indicator of body fat percentage. Advantages of EPID are a high positive phenotypic correlation with total fat content (Rogers and Webb, 1980; Eisen and Leatherwood, 1976) and ease of dissection on a large number of mice (Eisen and Roberts, 1981). HC was used as an indirect measure of lean tissue content (Bhuvanakumar et al., 1985). Further details of the selection experiment are given elsewhere (Eisen, 1987a,b).

In generation 12 of selection, 20 males were chosen randomly from each replicate selection treatment. The males were weaned at 3 wk of age, housed four to a cage, and given ad libitum access to Purina Laboratory Chow 50014. When the mice reached 12 wk of age, body weight and length were recorded, and mice were killed by cervical dislocation. The right epididymal and right hindlimb subcutaneous fat pads were excised, weighed and placed in the body cavity. Empty body weight was determined after flushing the gut contents. Mice were stored at -18°C until they were lyophilized for 48 h and dry body weight was recorded. Water, fat, protein and ash were calculated as a percentage of empty body weight. Protein and ash also were calculated on a fat-free basis. Other measurements were as follows: lean body mass defined as empty body weight minus total body fat weight, protein to ash ratio, subcutaneous fat pad weight as a percentage of body fat, and the epididymal fat pad weight to total body weight ratio.

The statistical analysis was based on the model \[ Y_{ijk} = \mu + R_i + L_j + (RL)_{ij} + e_{ijk} \] where \( Y_{ijk} \) is an observation on the \( k \)th mouse in the \( i \)th line and \( j \)th replicate, \( \mu \) is the overall mean, \( R_i \) is the \( i \)th replicate effect (random), \( L_j \) is the \( j \)th selection treatment effect (fixed), \((RL)_{ij}\) is the \( ij \)th interaction effect and \( e_{ijk} \) is the random residual effect. The interaction mean square was used as an error term to test for selection treatment differences.

Selection treatment effects were compared using four linear contrasts: HF - LF and HF + LF - 2(RC) tested significance of divergence and asymmetry, respectively, in the lines selected for EPID; HL - LL and HL + LL - 2(RC) provided analogous tests of significance in the lines selected for HC.

Results

Least squares means of measurements on 12-wk-old male mice in generation 12 of selection are in Table 1 by selection treatment pooled across replicates; linear contrasts are given in Table 2.

Divergent Selection for EPID. The HF and LF lines diverged substantially \((P < .01)\) in EPID, the trait undergoing selection, as well as in correlated measurements of adiposity, i.e., subcutaneous fat pad as percentage of body weight (SUBC) and percent body fat (FAT). Selection for EPID resulted in the epididymal fat pad accounting for a greater \((P < .01)\) percentage of body fat (EPID/FAT) in HF mice than in controls and vice versa for LF mice. Percentage of water (WAT) mirrored the divergence in the measures of fat, as did percentage of protein (PROT) and percentage of ash (ASH), to a lesser degree. The ratio of protein to ash (PROT/ASH) did not show significant divergence \((P > .05)\). On a fat-free basis, percentage of protein (PROT-FF) was larger \((P < .05)\) in HF than in LF, whereas percentage of ash (ASH-FF) did not differ between the lines. Body weight and body length of HF mice were greater \((P < .01)\) than that of LF mice. HF mice also had a larger
TABLE 1. LEAST SQUARES MEANS AND STANDARD ERRORS (SE) BY SELECTION TREATMENT*

<table>
<thead>
<tr>
<th>Trait</th>
<th>HF</th>
<th>LF</th>
<th>HL</th>
<th>LL</th>
<th>RC</th>
<th>SE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body length, cm</td>
<td>11.5</td>
<td>11.0</td>
<td>11.0</td>
<td>11.4</td>
<td>11.0</td>
<td>.045</td>
</tr>
<tr>
<td>Full body weight, g</td>
<td>43.3</td>
<td>35.5</td>
<td>35.1</td>
<td>41.1</td>
<td>37.9</td>
<td>.89</td>
</tr>
<tr>
<td>Empty body weight, g</td>
<td>39.4</td>
<td>32.1</td>
<td>31.8</td>
<td>37.5</td>
<td>34.3</td>
<td>.80</td>
</tr>
<tr>
<td>EPID, %</td>
<td>2.05</td>
<td>.43</td>
<td>.58</td>
<td>1.23</td>
<td>.99</td>
<td>.123</td>
</tr>
<tr>
<td>SUBC, %</td>
<td>.73</td>
<td>.37</td>
<td>.39</td>
<td>.59</td>
<td>.51</td>
<td>.034</td>
</tr>
<tr>
<td>FAT, %</td>
<td>18.2</td>
<td>7.2</td>
<td>7.9</td>
<td>13.5</td>
<td>11.8</td>
<td>1.10</td>
</tr>
<tr>
<td>PROT, %</td>
<td>18.7</td>
<td>20.7</td>
<td>20.6</td>
<td>19.5</td>
<td>20.0</td>
<td>.24</td>
</tr>
<tr>
<td>ASH, %</td>
<td>3.1</td>
<td>3.5</td>
<td>3.6</td>
<td>3.4</td>
<td>3.5</td>
<td>.05</td>
</tr>
<tr>
<td>WAT, %</td>
<td>60.0</td>
<td>68.6</td>
<td>68.0</td>
<td>63.7</td>
<td>64.9</td>
<td>.85</td>
</tr>
<tr>
<td>PROT-FF, %</td>
<td>22.8</td>
<td>22.3</td>
<td>22.3</td>
<td>22.5</td>
<td>22.6</td>
<td>.10</td>
</tr>
<tr>
<td>ASH-FF, %</td>
<td>3.8</td>
<td>3.8</td>
<td>3.9</td>
<td>3.9</td>
<td>4.0</td>
<td>.05</td>
</tr>
<tr>
<td>PROT/ASH</td>
<td>12.5</td>
<td>6.5</td>
<td>8.0</td>
<td>10.1</td>
<td>9.4</td>
<td>.45</td>
</tr>
<tr>
<td>Lean body mass, g</td>
<td>32.1</td>
<td>29.7</td>
<td>29.3</td>
<td>32.3</td>
<td>30.2</td>
<td>.64</td>
</tr>
</tbody>
</table>

*Pooled over replicates; each line mean is based on a total of 40 male mice (20 per replicate) at 12 wk of age.

Asymmetric responses were found for body length, ASH, ASH-FF and PROT/ASH. Although the increases in EPID and FAT in the HF line were about twice as large as the decreases for these traits in the LF line, asymmetry was not significant (P > .05). Previous reports have shown significant asymmetry for EPID in these lines (Eisen, 1987a; Prasetyo and Eisen, 1989).

Divergent Selection for HC. High versus low divergence in the lines selected for HC was opposite in direction for all traits compared with the divergence in lines selected for EPID. The divergence was smaller for compositional traits, but it was of similar magnitude for body size traits. Lean body mass was similar for the HF and LL lines and for the LF and HL lines. Only body length had an asymmetric (P < .05) correlated response in the HL and LL lines.

Phenotypic Correlations. Pooled within replicate x selection treatment, phenotypic correlations (df = 190) of FAT with EPID, SUBC and WAT were .81, .87 and -.95, respectively.

TABLE 2. LINEAR CONTRASTS AND STANDARD ERRORS (SE)*

<table>
<thead>
<tr>
<th>Trait</th>
<th>HF - LF</th>
<th>HF + LF - 2(RC)</th>
<th>HL - LL</th>
<th>HL + LL - 2(RC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body length, cm</td>
<td>.5 ± .07**</td>
<td>.3 ± .11*</td>
<td>-.4 ± .07**</td>
<td>.3 ± .11*</td>
</tr>
<tr>
<td>Body weight, g</td>
<td>7.8 ± 1.25**</td>
<td>2.9 ± 2.17</td>
<td>-.6 ± 1.25**</td>
<td>.4 ± 2.17</td>
</tr>
<tr>
<td>EPID, %</td>
<td>1.62 ± .17**</td>
<td>.48 ± .30</td>
<td>-.65 ± .17*</td>
<td>-.17 ± .30</td>
</tr>
<tr>
<td>SUBC, %</td>
<td>3.6 ± .05**</td>
<td>10.0 ± .09</td>
<td>-.20 ± .05*</td>
<td>.94 ± .09</td>
</tr>
<tr>
<td>FAT, %</td>
<td>11.0 ± 1.55**</td>
<td>1.9 ± 2.69</td>
<td>-.56 ± 1.55*</td>
<td>-.22 ± 2.69</td>
</tr>
<tr>
<td>PROT, %</td>
<td>-.20 ± .33**</td>
<td>-.5 ± .58</td>
<td>1.1 ± .33*</td>
<td>.1 ± .58</td>
</tr>
<tr>
<td>ASH, %</td>
<td>-.4 ± .07**</td>
<td>-.4 ± .12*</td>
<td>.2 ± .07*</td>
<td>-.1 ± .12</td>
</tr>
<tr>
<td>WAT, %</td>
<td>-.8 ± 1.20**</td>
<td>-.12 ± 2.07</td>
<td>.43 ± 1.20*</td>
<td>1.9 ± 2.07</td>
</tr>
<tr>
<td>PROT-FF, %</td>
<td>.5 ± .14*</td>
<td>-.1 ± .25</td>
<td>-.2 ± .14</td>
<td>-.4 ± .25</td>
</tr>
<tr>
<td>ASH-FF, %</td>
<td>0.0 ± .07</td>
<td>-.4 ± .11*</td>
<td>-.1 ± .07</td>
<td>-.2 ± .11</td>
</tr>
<tr>
<td>EPID/FAT, %</td>
<td>5.7 ± .64**</td>
<td>0.0 ± 1.10</td>
<td>-.21 ± .64*</td>
<td>-.8 ± 1.10</td>
</tr>
<tr>
<td>PROT/ASH</td>
<td>.14 ± .11</td>
<td>.60 ± .20*</td>
<td>.00 ± .11</td>
<td>.18 ± .20</td>
</tr>
<tr>
<td>Lean body mass, g</td>
<td>2.4 ± .9*</td>
<td>1.4 ± 1.6</td>
<td>-.30 ± .9*</td>
<td>1.2 ± 1.6</td>
</tr>
</tbody>
</table>

*Replicate x selection treatment mean square (df = 4) was used as the error term.

**P < .05.

***P < .01.
Discussion

Indirect selection for total body fat percentage based on EPID as an indicator trait was successful. After 12 generations of divergent selection, the HF and LF lines differed in FAT by 93% of the control line mean. However, this figure is smaller than the difference in the direct response in EPID of 164%. Sharp et al. (1984) reported similar results on a relative basis after seven generations of divergent selection for epididymal fat as a proportion of body weight. Selection for EPID in HF and LF led to divergence as a proportion of the control line mean of 90 and 76%, respectively, in hind carcass fat and SUBC (Eisen, 1987b), the latter value being similar to the 71% in the present study. Despite these lower correlated responses as a percentage of the control, relative to the direct response in EPID, the realized genetic correlations between EPID and percentage of fat in the hind carcass (.90 ± .08) and between EPID and SUBC (1.04 ± .13) were not significantly different (P > .05) from one (Eisen, 1987b). Therefore, many of the loci that control lipogenesis and(or) lipolysis in EPID also control fat synthesis and degradation in other fat depots in the mouse.

The indicator trait, EPID, accounted for a larger proportion of FAT in the HF line relative to the control line, and it accounted for a smaller proportion in the LF line. A similar correlated response in EPID/FAT was found in other lines selected for EPID (Hastings and Hill, 1989). These results are consistent with comparisons made across several different fat depots in the HF and LF lines.

Prasetyo and Eisen (1989) compared correlated responses to selection for EPID in HF and LF for five fat depots across age and sex. The lines diverged with age and reached a maximum difference at 12 wk, the age of selection. The gonadal fat pad (epididymal in males and ovarian in females) made up the largest percentage of all the fat depots in the unselected control line. Divergent selection did not change the ranking of each fat pad as a percentage of total fat pad weight, but a redistribution of fat occurred, with a greater percentage being distributed to gonadal fat in the HF line and a lesser percentage in the LF line. Selection for EPID also changed the ratio of EPID to hind carcass fat; from data presented by Eisen (1987a,b), the ratios were calculated as 3.07, 2.23 and 1.75 in the HF, RC and LF lines, respectively. These results imply that whereas there are high positive genetic correlations between fat depots, in mice there is local control of lipogenesis and(or) lipolysis at different sites of fat deposition.

Kempster and Evans (1979) found that leaner strains of pigs had a lower subcutaneous to intermuscular fat ratio at constant total fat weight. The change in this ratio may be the result of greater selection pressure against subcutaneous fat, generally the only measurement of overall fatness taken in selected strains. Jones et al. (1980) and Rook et al. (1987) also found genetic effects on the partitioning of fat in pigs. In contrast, Wood et al. (1983) found no evidence that selection in pigs for an index that included low backfat thickness caused relocation of body fat from subcutaneous to other sites in the body, but only a small reduction in total fat was achieved by selection. Selection for high and low abdominal fat in chickens produced a greater response in abdominal triglycerides than in total triglycerides, suggesting local control of fat deposition at different sites in chickens (Leclercq et al., 1989).

The mechanism of local control of fat synthesis, suggested by the results of selection for high or low fat content in mice and pigs, remains to be determined. In a fat line of chickens, in vitro sensitivity to lipolytic activity of glucagon is lower in abdominal adipocytes than in subcutaneous adipocytes, suggesting that the higher abdominal fat proportion is due partly to reduced lipolysis (Leclercq et al., 1988).

Lean body mass was greater in HF than LF; this result was a consequence of the positive correlated response in growth rate. In contrast, in another selection experiment for high and low EPID, no changes were found in lean body mass (Bishop and Hill, 1985; Hastings and Hill, 1989). The two studies conducted selection at different ages, 10 vs 12 wk, but this difference does not seem to be an adequate explanation for the difference in correlated response. Percentage of protein and ash were larger in LF than in HF, but this difference was caused largely by change in total fat percent-
age. On a fat-free basis, percentage of ash was not different, and percentage of protein was significantly higher in HF than in LF; the difference was relatively small. A small difference might be expected in that HF might have reached a later stage of lean growth relative to bone growth. In addition, selection for high or low hind carcass weight as a percentage of body weight, a measure of lean percentage, failed to modify fat-free percentage of protein and percentage of ash. Selection for growth in mice (Fowler, 1958; Timon et al., 1970) and feed efficiency in rats (Palmer et al., 1946) also failed to change percentage of protein on a fat-free basis. Thus, it is very difficult to change fat-free percentage of protein and percentage of ash of the body by the selection criteria cited, suggesting that additive genetic variances may be relatively low for these traits and(or) that the genetic correlations of these traits with the selection criteria are low.

Correlated responses in the HL and LL lines were the mirror images of those observed in HF and LF, except that they generally were of a lower magnitude. This finding is not surprising because of the high negative genetic correlation between EPID and HC (Eisen, 1987a; Eisen and Prasetyo, 1988).

The phenotypic correlation between FAT and WAT exceeded that between FAT and EPID or between FAT and SUBC. Hastings and Hill (1989) also obtained a high correlation between total body fat and percentage of dry body weight, the complement of percentage of water, and concluded that percentage of dry weight would be superior to EPID as an indicator trait for fat. This procedure would avoid the problem of selecting for a fraction of total fat and possibly causing a redistribution of fat. An alternative approach would be to select using a noninvasive method of determining total body fat such as total body electrical conductivity (Bracco et al., 1983) or bioelectrical impedance analysis (Lukaski et al., 1986).

Implications

Fat content can be changed readily by selection for indicator traits. However, it is difficult to change fat-free protein and ash percentages by selection for fat or lean tissue percentage. If the indicator trait is based on a fraction of total fat, then total body fat should be evaluated periodically to be certain that indirect selection remains efficient in later cycles of selection. Many of the genetic loci that control lipogenesis and(or) lipolysis operate across all fat depots. However, in mice there also is local control of lipogenesis and(or) lipolysis at the different sites of fat deposition.

Literature Cited


