OBESITY AND INFERTILITY IN THE LETHAL YELLOW MOUSE MODEL — DOES THE MUTANT GENE DIRECTLY AFFECT FERTILITY?

Maureen Diggins, Michelle Cederburg and Travis Dierke
Department of Biology
Augustana College
Sioux Falls, SD  57197

Nels H. Granholm
Department of Biology and Microbiology
South Dakota State University
Brookings, SD 57007

ABSTRACT

The lethal yellow mouse has a genetic mutation at the agouti locus on chromosome two. Mice homozygous for the lethal yellow gene (Ay/Ay) die during development. Heterozygous mice survive but exhibit a collection of characteristics known as the lethal yellow syndrome. Some of the characteristics of the syndrome are increasing obesity in adulthood, progressive infertility, and a yellow coat color. The working hypothesis was that dietary restriction in the lethal yellow mouse would reduce obesity and prolong fertility. Therefore, any effects of the mutation on fertility would result from increased adiposity.

Black mice (a/a) without the mutation were used as controls for the experiment. Mice were selected in their prime reproductive time and studied at three different ages (120, 150 and 180 days of age). Ten yellow females and ten black control females in each age category had been raised on a low fat (4%) diet. An equal number of mice in each age category had been raised on a high fat (10%) diet. Females in each group were mated with black males. Fertility was assessed by observation of first pregnancy. This was determined by observation of body weight, by assaying for progesterone with EIA (Enzyme ImmunoAssay) at five and twelve days after mating, and by the eventual observation of litters.

Dietary restriction appeared to diminish the degree of obesity and prolong fertility in the yellow mouse. In mice raised on low fat diets, day 5 progesterone levels were significantly lower in yellow mice compared to black mice at 150 and 180 days of age. Pregnancy in the yellow mice raised on low fat diets was delayed when compared to controls, but not prevented. In the mice raised on a high fat diet, pregnancy did not occur in 6 out of 10 yellow mice at 150 days of age. At 180 days of age, only 1 of 10 yellow mice raised on high fat became pregnant. Progesterone levels were significantly reduced in both groups. Therefore, the increased adiposity in the Ay mouse appears to cause decreased fertility. This does not, however, rule out other more direct effects of the gene on the reproductive system.