The FASEB Journal. 2007;21:737.22)

737.22

The C57BL/6NCrl-lb Mouse: A New Model for Metabolic Syndrome

Dwight R. Owens[1], Richard G. Peterson[2], Wu-Kuang Yeh[2], Yiyun Wang[2], Kathleen R. Pritchett-Corning[1], Bruce Elder[1], Charles B. Clifford[1] and Joan Flanagan[1]

[1] Charles River Laboratories, 251 Ballardvale Street, Wilmington, MA, 01887,
[2] PreClinOmics, 7918 Zionsville Rd, Indianapolis, IN, 46268

ABSTRACT

A novel mutation, *lb* in the leptin receptor gene, has been identified in C57 BL/6NCrl mice from a barrier production colony at Charles River Laboratories. Animals heterozygous for the mutation exhibit a wild-type phenotype. The mutant *lb/lb* mice have been characterized by metabolic, genetic, and phenotypic methods. The *lb*/*lb* mutant mice display key features of the metabolic syndrome; they are markedly obese, and hyperinsulinemic by 8 weeks of age, with insulin levels exceeding 200 ng/ml by 18 weeks of age. When compared to other models of metabolic syndrome, mutant *lb* mice also had hyperglycemia greater than that of the B6.V-*Lep*^{ob}/J (*ob*) mouse, but less than the BKS.Cg-*m*+/+*Lepr*^{db}/J (*db*). Like *db* mice, the *lb* mice had increased leptin levels, higher in fact, than *db* mice at 17-18 weeks of age. Genetic complementation studies crossing mice heterozygous for the *lb* mutation with *Lepr*^{db} heterozygous mice produced 25% fat and 75% lean offspring, confirming that the mutations are in the same gene. DNA sequence analysis of the leptin receptor coding sequence in *lb* mice has not revealed any mutations. These mice have characteristics of the *ob* and the *db* mice. This distinct phenotype makes these mice an additional model for drug discovery studies of metabolic syndrome.