

CHARACTERIZATION OF OBESITY PHENOTYPES IN CHROMOSOME 2 CONGENIC STRAINS

Farber CR¹, Chiu S², Warden CH² and Medrano JF¹

¹Department of Animal Science, ²Rowe Program in Genetics, University of California, Davis, CA 95616-8521, USA

Mouse chromosome (chr.) 2 likely contains multiple mouse homologs of human obesity genes as several studies have identified linkage of either mouse chr. 2 or the corresponding human chromosome to obesity or related traits. In this study, we describe the development and characterization of four congenic strains derived from three different donor and background strains with overlapping donor regions containing approximately 66% of chr. 2. One congenic was developed to fine map a body fat quantitative trait locus (QTL) identified proximal to the agouti locus in a backcross of (C57BL/6J x *Mus spretus*) F₁ x C57BL/6J (BSB). The congenic was developed by introgressing SPRET/Ei donor alleles onto a C57BL/6J-*Lipic*^{-/-} background (B6.SPRET). The donor region extends from 142.3 to 166.4 Mbp and is associated with a significant decrease in adiposity index (AI, total fat pad weight/body weight), body mass index (BMI) and lower weights for femoral (FFP), gonadal (GFP), mesenteric (MFP) and retroperitoneal (RFP) fat pads in males of an F₂ intercross (Diament et al, Mammalian Genome, In Press). Another congenic, B10.UW- *H3b we Pax1*^{um} *a/Sn* (B10.UW), has UW donor alleles spanning from approximately 117.2 to 157.5 Mbp. Through a congenic strain survey, the B10.UW congenic was identified as having significantly lower AI and weights of FFP, GFP, MFP, and RFP in both males and females as compared to the C57BL/10SnJ background strain and was confirmed in an F₂ intercross (Warden et al, Mammalian Genome, In Press). Two congenics, B6.CAST-2*PMhg/hg* (2PM) and B6.CAST-2*Mhg/hg* (2M), were developed to fine map QTL for growth-related traits identified on chr. 2 segregating in an F₂ intercross between CAST/EiJ and C57BL/6J-*hg/hg*. The C57BL/6J-*hg/hg* strain is a congenic with the *high growth* (*hg*) mutation introgressed onto a C57BL/6J background. The minimal donor regions extend from 43.7 to 93.4 Mbp and 77.7 to 136.6 Mbp, for the 2PM and 2M strains, respectively. We characterized male and female homozygous congenic mice and background C57BL/6J-*hg/hg* control mice for obesity traits. When compared to background, 2PM mice displayed significantly lower weights for GFP, FFP, MFP and RFP and lower values for AI and BMI. Additionally, 2M mice showed a significant strain by sex interaction for RFP, FFP, AI and BMI in which 2M females were leaner and 2M males were fatter than background. Together, these four congenics demonstrate the complex role of chr. 2 in obesity and the presence of multiple genes influencing adiposity, since there is no common overlap including all four donor regions. This collection of congenics provides a novel resource to fine map regions influencing obesity. The production of subcongenic strains from these four congenics will aid in the identification of genes underlying obesity traits on mouse chr. 2 and homologous human chromosomes.