QUANTITATIVE TRAIT LOCUS ANALYSIS FOR OBESITY REVEALS A COMPLEX NETWORK OF INTERACTING LOCI.

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We have identified an interacting network of genetic loci affecting different aspects of obesity in an SM x NZB intercross. Different but overlapping sets of QTL affect total body weight, individual fat pad weights and the relative weight of different fat deposits throughout the body. Several main effect QTL were identified in the three different analyses with the strongest QTL on chromosome 19 (52 cM) found for bodyweight (LOD 7.1) and fat pad weight (LOD 9.9). This locus and a locus on chromosome 6 are in the center of the network (Figure 1). The hormones insulin and ghrelin, both controlling food intake, are attractive candidates for these loci. As the genes underlying interacting QTL must interact biologically in some way (e.g. receptor-ligand, transcription factor-expression, heterodimer) or be in the same pathway, the great value of constructing networks like the one described here is that it allows formulating hypotheses for candidate genes and their interactions. This network of interactive genetic effects on body size QTL reflects the inherent complexity of body size and composition and has implications for human studies of obesity.

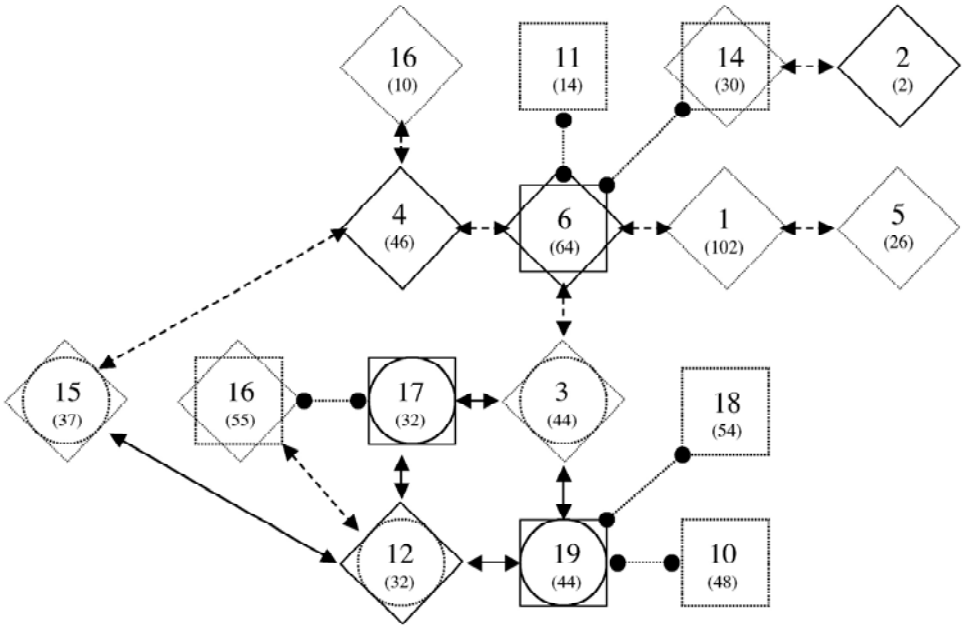

Figure 1. Graphical representation of the main effect QTL of the three different analyses, total body weight (circles), individual fat pad weights (squares) and the relative distribution of fat deposits through the body (diamonds) and the interactions between the QTL. For each locus the chromosome number and the position of the peak marker (in cM) is given. Solid lines represent main effect QTL while dotted lines represent loci detected only as interacting QTL.