Comment

To the Editor: Drs. Panhuysen et al. [1] report their findings of a genome-wide scan for quantitative traits in persons without diabetes. They observed several susceptibility loci notably on chromosomes 11 and 17 relating to fasting plasma insulin, and on chromosomes 9 and 19 for 2-h plasma insulin concentrations. Their analysis included adjustments for BMI, which is rather difficult because the relationship between BMI and insulin resistance is non-linear [2].

They conclude that these loci are suggestive regions for quantitative pre-diabetic insulin traits. However, plasma insulin is known to be strongly related to obesity especially and it may well be that one or more of these loci are actually relating to obesity. We have recently carried out a genome wide scan in Type 2 diabetic subjects [3]. In a subsequent quantitative trait analysis for obesity (BMI) in subjects with Type 2 diabetes, we found suggestive evidence for linkage of a locus between markers D11S940 and D11S2000 (11q14-q24) with a variance component LOD-score of 1.9. This locus seems to be at the similar location as the chromosome 11 locus found by Drs. Panhuysen et al. for fasting insulin and HOMA-IR. Interestingly, their evidence for suggestive linkage drops substantially for both traits after adjusting for BMI. Their results corroborate with our results and imply that obesity is primarily related to this locus, rather than plasma insulin concentrations. It would

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Authors' reply

To the Editor: We appreciate Dr. van Tilburg and colleagues' interest in our report. In our data there is essentially a linear relationship between body mass index and serum concentrations of fasting insulin [1]. Recently, other Framingham Heart Study investigators published a genome scan showing linkage to BMI (measured at least 6 times over 28 years of observation) on 11q14, with a maximum multipoint LOD score of 3.27, in a region replicating other reports, apparently including that of Dr. van Tilburg et al. [2]. Thus, although we agree that linkage to measures of insulin resistance in this genomic region may be accounted for by concomitant correlations with obesity, present data has not determined whether the observed relationships are explained by epistatic loci for both insulin resistance and obesity, or whether obesity is merely in the physiological causal pathway for insulin resistance (or vice versa).

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be interesting to know whether Drs. Panhuysen et al. have the possibility to perform a quantitative trait analysis for obesity in this interesting cohort with a low risk for diabetes, to confirm the presence of an obesity locus.

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