Novel genes on rat chromosome 10 are linked to body fat mass, preadipocyte number and adipocyte size

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Background: The genetic architecture of obesity is multifactorial. We have previously identified a quantitative trait locus (QTL) on rat chromosome 10 in a F2 cross of Wistar Ottawa Karlsburg (WOKW) and Dark Agouti (DA) rats responsible for obesity. The QTL was confirmed in congenic DA.WOKW10 rats. To pinpoint the region carrying causal genes, we established two new sub-congenic lines, L1 and L2, with refined segments of chromosome 10.
Methods: All lines were extensively characterized under different diet conditions. We employed transcriptome analysis in visceral adipose tissue (AT) by RNA-Seq technology to identify potential underlying genes in the segregating regions. Three candidate genes were measured in human paired samples of visceral and subcutaneous (SC) AT (N=232) individuals with a wide range of body weight and glucose homeostasis.
Results: Under chow diet, body weight as well as fat mass measurements showed that male sub-congenic strains remained obese compared to parental strain whereas under high fat diet (HFD) conditions L1 rats were protected from diet induced obesity. Interestingly, adipocyte size distribution in subcutaneous and epigonadal (EPI) AT of L1 sub-congenic rats did not undergo typically ballooning under HFD and the number of preadipocytes in AT was significantly elevated in L2 compared to L1 and parental rats. Transcriptome analysis identified 3 candidate genes in visceral AT on rat chromosome 10. In humans, those candidate genes were differentially expressed between SC and visceral AT and one gene, head involution defective (HID1) mRNA was strongly correlated with parameters of obesity and glucose metabolism.
Conclusions: Our data provide novel candidate genes for obesity which map on rat chromosome 10 in an interval 102.2-104.7Mb strongly associated with body fat mass regulation, preadipocyte number and adipocyte size in rats. Our human mRNA results suggest that changes in AT HID1 expression are related to fat distribution and glucose homeostasis.