Supplementary Figures

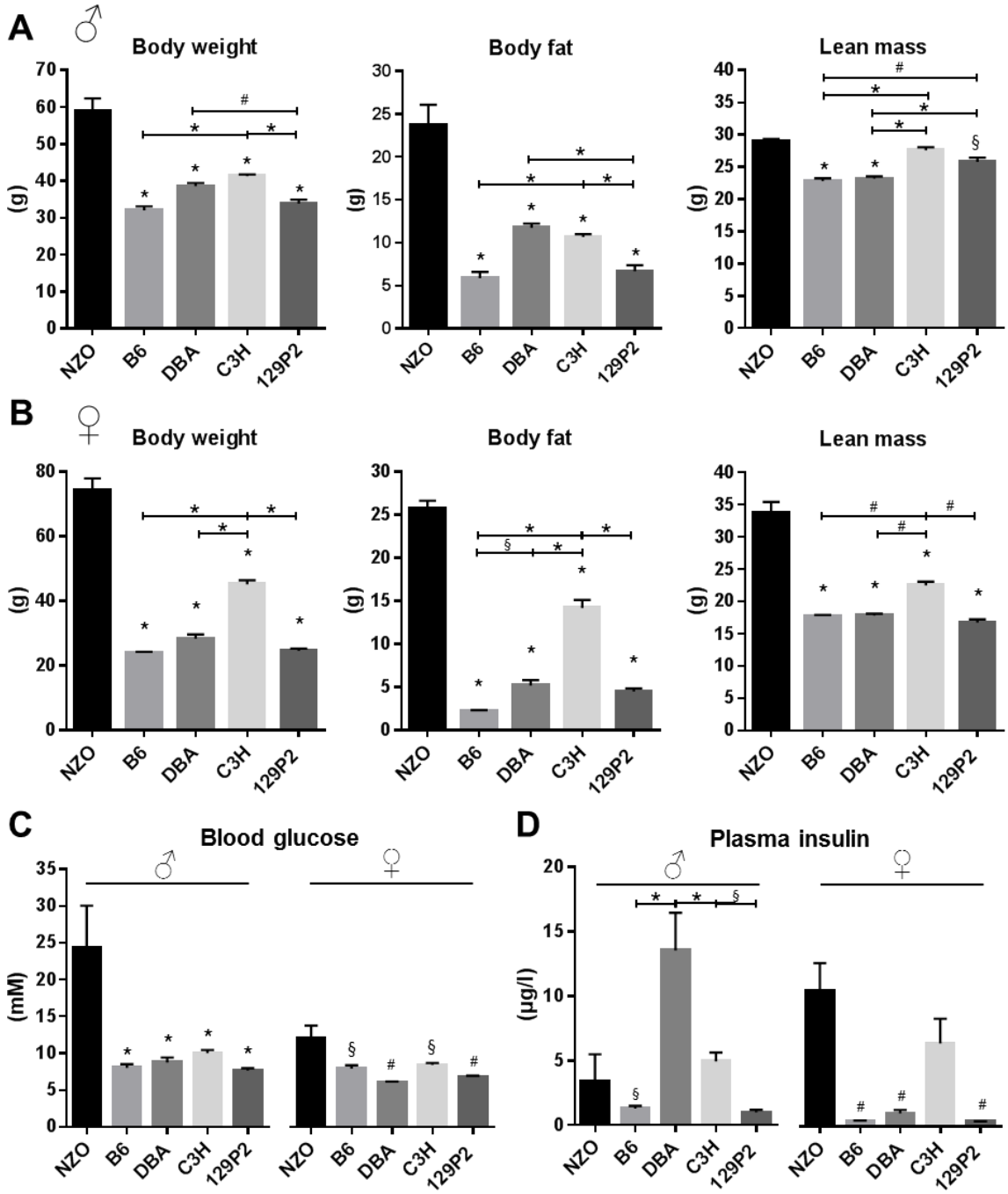

Figure S1. Phenotypical characterization of parental mice of the DZD collaborative diabetes cross project. Phenotypical parameters characterizing the state of obesity in male (A) and female (B) parental mice at 16 (male) and 22 (female) weeks of age. (C) Blood glucose and (D) plasma insulin levels in parental mice at 16 (male) and 22 (female) weeks of age. Data represent mean ± SEM (n=5-18). Differences between groups were calculated with one-way ANOVA followed by post hoc Bonferroni test. $^{\S}p<0.05$; $^{\#}p<0.01$; $^{*}p<0.001$ by comparison to NZO unless otherwise stated.

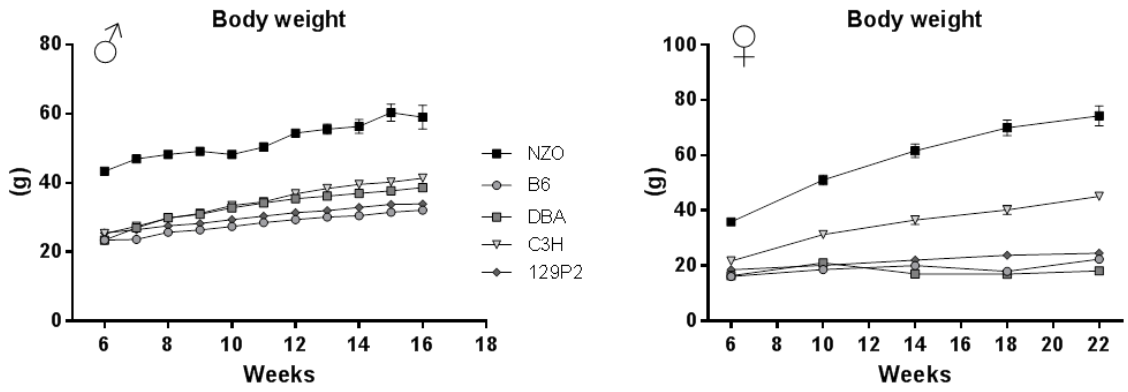

Figure S2. Development of obesity in parental mice of the DZD cross. Male (left panel) and female (right panel) mice were characterized on a 45% HFD and body weight was measured on a weekly or monthly basis for males and females, respectively. n=12-18

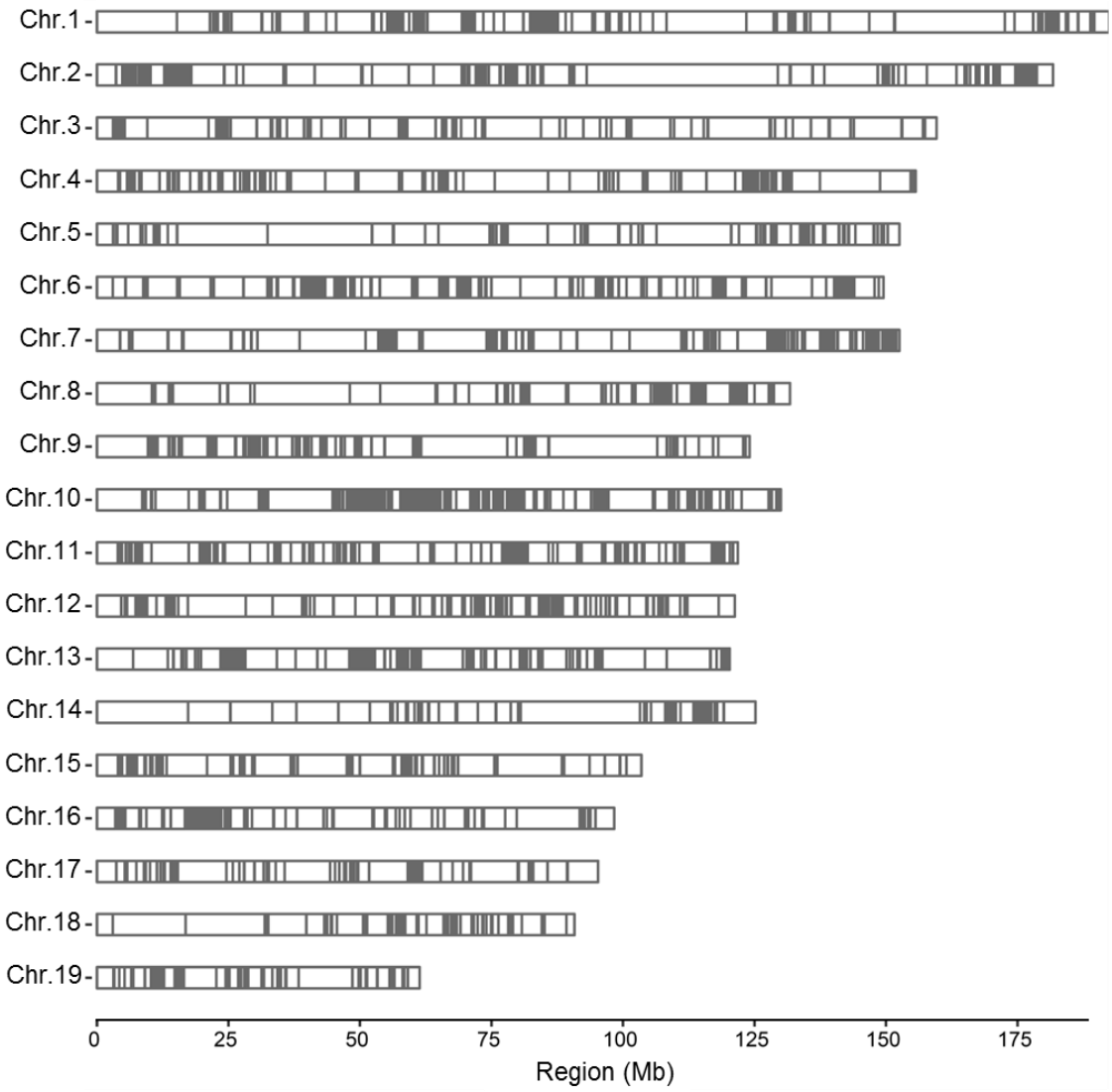

Figure S3. Genetic diversity of the different breeding partners. Regions of identity by descent (IBD) are indicated by grey lines among B6, DBA, C3H, 129P2, and NZO, representing regions of the genome in which all five strains are essentially identical. Analysis was performed with the Mouse Phylogeny Viewer (MPV) (1).

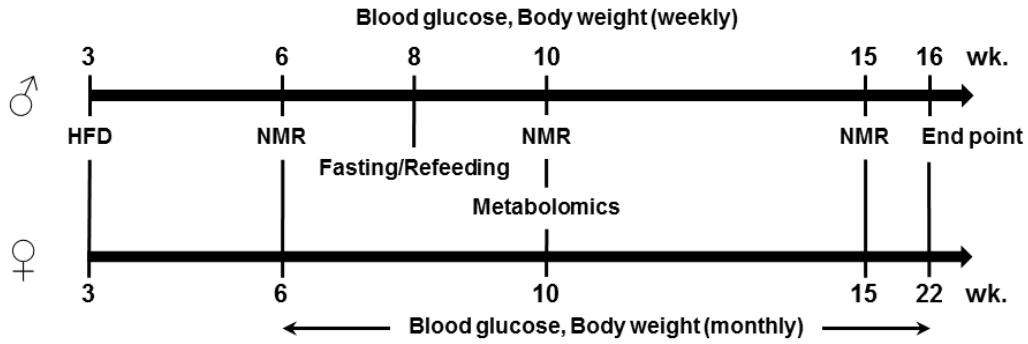

Figure S4. Phenotyping protocol of backcross mice kept on a 45% fat high-fat diet at the age of 3 weeks.

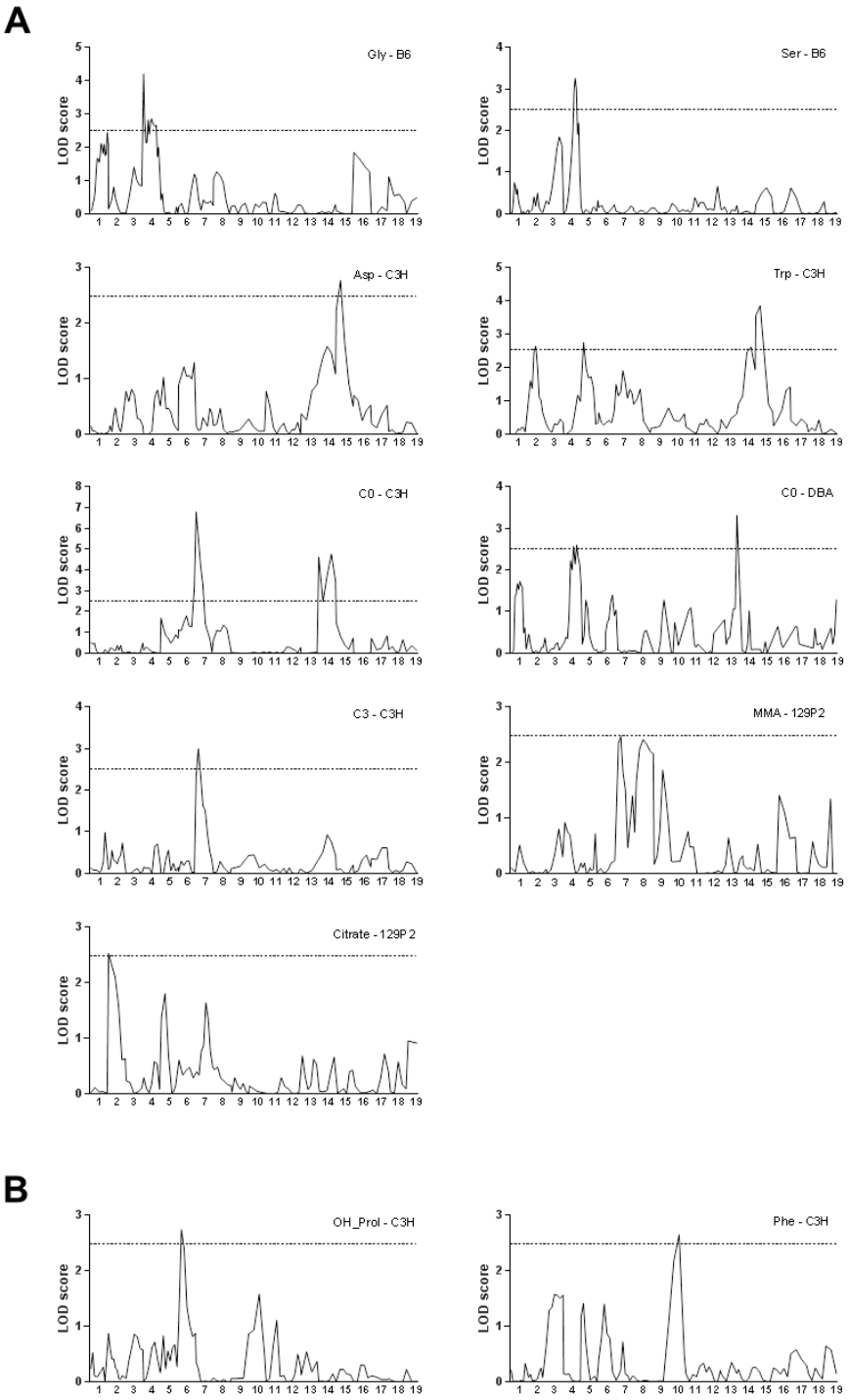

Figure S5. Genome-wide linkage analysis of the different NZO backcross populations for blood metabolites. Genome-wide logarithm of the odds (LOD) score distribution for blood metabolites with overlapping positions to QTL for obesity- and glucose-related traits in (A) male and (B) female backcross mice. The horizontal lines indicate the threshold of significance ($p<0.05$) calculated with 1,000 permutations. Genome-wide linkage analysis of N2 mice including genetic map, genotyping errors, and single QTL scans for individual traits were assessed with R/qtl and QTL intervals exceeding a genome-wide 5% significance threshold are shown. C0: free carnitine; C3: propionylcarnitine; MMA: Methylmalonyl-carnitine

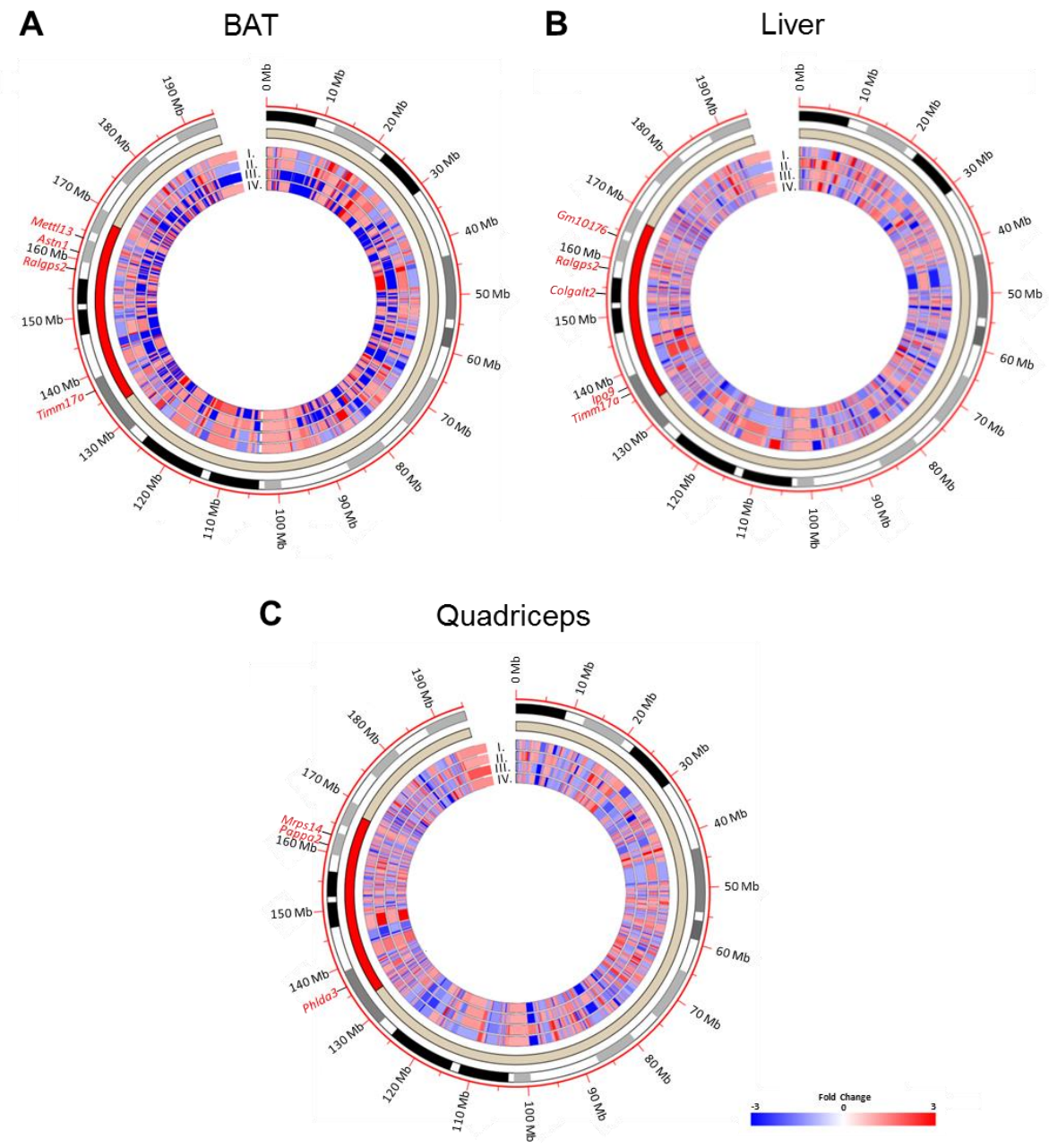

Figure S6. Transcriptome data of parental strains in different tissues. Circos plot showing mouse chromosome 1 with integration of transcriptome data from (A) brown adipose tissue (BAT), (B) liver, and (C) quadriceps of parental strains (I. DBA; II. 129P2; III. NZO; IV. C3H) compared to B6. The red bar within the outer circle indicates the critical region of the *Nob5* and genes with differential expression are highlighted. Expression data are presented as fold change relative to B6 of 3-4 samples/strain. The plot was generated with the RCircos package (2, 3).

Supplementary Table

Supplementary Table 1. List of bioinformatic packages.

Package	Version	Application	Reference
SNPtools	1.1 (edited by M.J.)	Haplotype plot	(4)
R.devices	2.15.1	Haplotype plot	(5)
ggplot2	2.2.1	IBD plot	(6)
scales	0.5.0	IBD plot	(7)
chromPlot	1.3.2 (edited by L.Z.)	chromPlot	(8)
shiny	1.0.5	QTL web application	(9)
shinyjs	1.0	QTL web application	(10)
biomaRt	2.34.1	Gene position	(11, 12)
R version	3.4.3		(13)
RStudio	1.1.423		https://www.rstudio.org
qtl	1.41-6	LOD Scores	(14)

Table S2. Sequence variants within the six candidate genes of the *Nob5* locus. Genomic sequence data were obtained from the Sanger Trust Institute and indicate variations of DBA, 129P2, NZO, and C3H compared to the C57BL/6J reference genome.

Gene	Strain	Total	Upstream	Splice	Missense	Stop variant	Frameshift
Atp2b4	129P2	155	26	-	-	-	-
	C3H	1	-	-	-	-	-
	DBA	155	26	-	-	-	-
	NZO	5	1	-	-	-	-
Lmod1	129P2	363	65	-	1	-	-
	C3H	365	66	-	1	-	-
	DBA	390	61	-	1	-	-
	NZO	354	39	1	1	-	-
Pla2g4a	129P2	134	3	1	-	-	-
	C3H	418	74	-	-	-	-
	DBA	665	36	2	-	-	-
	NZO	135	4	1	-	-	-
Cep350	129P2	77	8	1	-	-	-
	C3H	1030	178	-	6	-	-
	DBA	1035	178	-	6	-	-
	NZO	1032	178	-	6	-	-
Soat1	129P2	17	-	-	-	-	-
	C3H	411	-	3	2	-	-
	DBA	410	-	3	2	-	-
	NZO	16	-	-	-	-	-
Mrps14	129P2	5	1	-	-	-	-
	C3H	5	1	-	-	-	-
	DBA	32	2	-	-	-	-
	NZO	5	1	-	-	-	-

*Not a direct sum of columns, due to overlapping field criteria

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