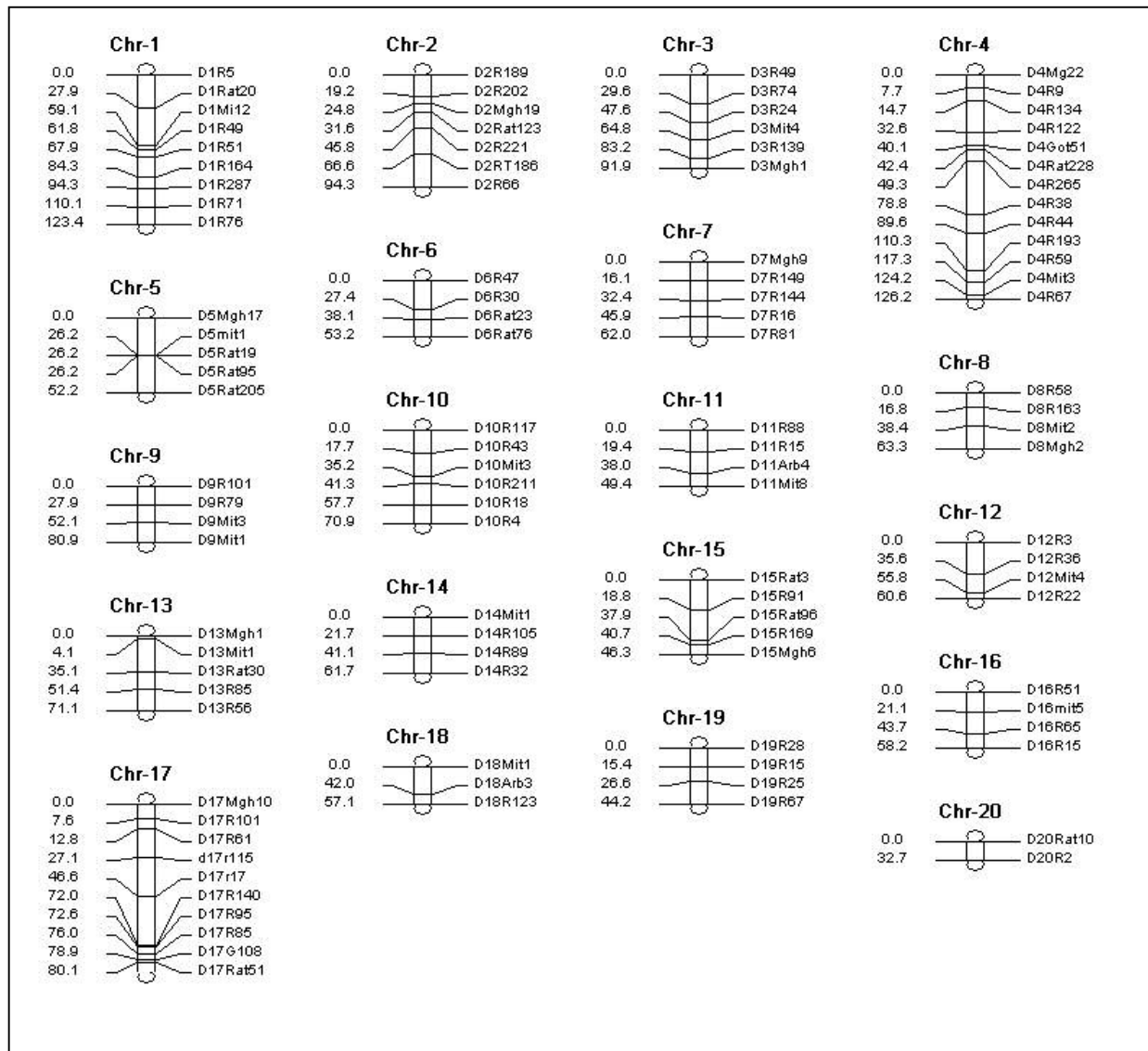


APPENDIX

Appendix: Figure 3



Legend to Figure 3: Polymorphic markers used in this study. DNA samples and microsatellite markers. Genomic DNA was prepared using one of two protocols. Snap-frozen livers were ground on dry ice and the dispersed tissue was treated with Proteinase K in the presence of 10% sarkosyl and 0.5M EDTA (pH 8.0). DNA was purified from these digests by phenol-chloroform extraction and dialysis against Tris EDTA (0.01M Tris/0.001M EDTA, pH 7.4). Alternatively, genomic DNA was extracted from rat tail snips using the QIAamp Tissue kit (Qiagen, Stanford,

CA) according to the manufacturer's instructions. Most microsatellite primers used in this study are available from Research Genetics, Inc. (Huntsville, AL). The general map location of these microsatellites was taken from our own segregating backcrosses, and from maps published by the Rat Genome Database (<http://www.rgd.mcw.edu>) and by Dr. R. Wilder and Dr. E. Remmers (www.nih.gov/niams/scientific/ratgbase/index.htm). Additional primer pairs were developed from unique sequences flanking short sequence repeats discovered by inspection of repeat regions in the *Iddm4* and *ART2* intervals (UCSC genome database). Primers found to be polymorphic between parental strains were used. The position of markers on the genetic map was established by inspection of the data set and conventional calculation methods to establish meiotic map distances, which are expressed in megabases (Mb) according to the rat genome sequence, June 2003 build (<http://genome.ucsu.edu>). Chr: chromosome.

Appendix Table 3**TABLE 3****FREQUENCY OF DIABETES AS A FUNCTION OF *Iddm4* AND *Iddm20* GENOTYPE**

<i>Iddm4</i> →	d	h	w	d	h	w
<i>Iddm20</i> ↓	<i>sick</i>	<i>sick</i>	<i>sick</i>	<i>well</i>	<i>well</i>	<i>well</i>
d	5	13	1	4	9	6
h	16	19	0	16	32	24
w	2	3	0	6	24	10

Table 3: As documented by the low frequency of diabetes in the shaded cells, diabetes susceptibility in KRV-infected rats requires *Iddm20*, *Iddm4*, or both. “d” homozygous for the BBDR-origin allele; “w” homozygous for the WF-origin alleles; “h” heterozygous.

Appendix Table 4

TABLE 4

CANDIDATE GENES IN THE *Iddm20* INTERVAL

Rat Chr	Rat Chr Start (bp)	Description	Mouse Chr	Mouse Chr Start (bp)	Mouse <i>Idd14</i> region	Rat <i>Iddm20</i>
17	29713540	PAK/PLC-interacting protein 1	13	40443433	idd14-NON	
17	28451133	Zinc finger protein 40 (Alpha A-crystallin-binding 1)	13	41502581	idd14-NON	
17	28306727	Endothelin-1 precursor (ET-1).	13	41748723	idd14-NON	
17	27138814	NAD-dependent deacetylase sirtuin 5	13	42822790	idd14-NON	<i>Iddm20</i>
17	27046741	RAN BP9; B cell antigen receptor Ig beta associated p1	13	42855480	idd14-NON	<i>Iddm20</i>
17	26709913	CD83 antigen.	13	43237577	idd14-NON	<i>Iddm20</i>
17		Jumonji protein	13	44287373	idd14-NON	<i>Iddm20</i>
17		Adenylyl cyclase-associated protein 2 (CAP 2).	13	46018959	idd14-NON	<i>Iddm20</i>
17	23821596	Kinesin-like protein KIF13A.	13	46244160	idd14-NON	<i>Iddm20</i>
17	23728906	Malin	13	46507913	idd14-NON	<i>Iddm20</i>
17	23701239	Thiopurine S-methyltransferase	13	46519516	idd14-NON	<i>Iddm20</i>
17	23634062	DEK oncogene (DNA binding).	13	46579123	idd14-NON	<i>Iddm20</i>
17		RNP particle component (Fragment).	13	47794113	idd14-NON	<i>Iddm20</i>
17	21994289	Homeobox protein BarH-like 1.	13	48158986	idd14-NON	<i>Iddm20</i>
17	21806043	PHD finger protein 2 (GRC5).	13	48298466	idd14B6	<i>Iddm20</i>

Rat Chr	Rat Chr Start (bp)	Description	Mouse Chr	Mouse Chr Start (bp)	Mouse <i>Idd14</i> region	Rat <i>Iddm20</i>
17	21410701	Ninjurin 1 (Nerve injury-induced protein 1).	13	48685927	idd14B6	<u><i>Iddm20</i></u>
17	21015178	Osteomodulin precursor (Osteoadherin) (OSAD)	13	49088364	idd14B6	<u><i>Iddm20</i></u>
17	19659967	Sphingosine 1-phosphate receptor Edg-3	13	50434260	idd14B6	<u><i>Iddm20</i></u>
17	19520647	SHC transforming protein 3 (SH2 domain protein C3)	13	50457472	idd14B6	<u><i>Iddm20</i></u>
17	19423770	Cyclin-dependent kinases regulatory subunit 2 (CKS-2).	13	50672083	idd14B6	<u><i>Iddm20</i></u>
17	19352632	Semaphorin 4D precursor	13	50728006	idd14B6	<u><i>Iddm20</i></u>
17	19230896	GADD45 gamma (Cytokine responsive protein)	13	50873436	idd14B6	<u><i>Iddm20</i></u>
17	18443785	Tyrosine-protein kinase SYK (Spleen)	13	51630629	idd14B6	<u><i>Iddm20</i></u>
17	18106038	nuclear factor, interleukin 3, regulated.	13	52003799	idd14B6	
17	17736908	Tyrosine-protein kinase ROR2 precursor 2.	13	52145865	idd14B6	
17	17243262	Homeobox protein MSX-2 (Hox-8.1).	13	52506491	idd14B6	
17	16655985	D(1A) dopamine receptor.	13	53096324	idd14B6	
17	16497967	Histamine H2 receptor (H2R)	13	53258774	idd14B6	
17	16094098	ADP-ribosylation factor-like 10A	13	53665747	idd14B6	
17	15595893	Retinoid X receptor interacting protein 110.	13	54118171	idd14B6	

Rat Chr	Rat Chr Start (bp)	Description	Mouse Chr	Mouse Chr Start (bp)	Mouse <i>Idd14</i> region	Rat <i>Iddm20</i>
17	15512144	Fibroblast growth factor receptor 4 precursor	13	54244110	idd14B6	
17	15353521	Ras-related protein Rab-24 (Rab-16).	13	54409106	idd14B6	
17	15350379	Px19-like protein.	13	54409802	idd14B6	
17	15346165	Max dimerization protein 3.	13	54414783	idd14B6	
17	15313303	Vesicular integral-membrane protein VIP36 precursor	13	54432976	idd14B6	
17	15222027	Regulator of G-protein signaling 14 (RGS14)	13	54459599	idd14B6	
17	15261698	Profilin III.	13	54504680	idd14B6	
17	15251796	coagulation factor XII (Hageman factor)	13	54507774	idd14B6	
17	15194740	Drebrin (Developmentally regulated brain protein).	13	54563349	idd14B6	
17	15147111	DEAD (Asp-Glu-Ala-Asp) box polypeptide 41	13	54627408	idd14B6	
17	15033873	Calcium-signal modulating cyclophilin ligand (CAML).	13	54719996	idd14B6	
17	14834123	Pituitary homeobox 1 (PtX1).	13	54922627	idd14B6	
17	14286947	Small inducible cytokine B14 precursor (CXCL14)	13	55389282	idd14B6	
17	14068757	Interleukin-9 precursor (IL-9) (T-cell growth factor P40)	13	55582311	idd14B6	
17	13995183	Leukocyte cell-derived chemotaxin 2 precursor	13	55645800	idd14B6	

Rat Chr	Rat Chr Start (bp)	Description	Mouse Chr	Mouse Chr Start (bp)	Mouse <i>idd14</i> region	Rat <i>Iddm20</i>
17	13905503	transforming growth factor, beta induced 68kd	13	55712518	idd14B6	
17	13814377	Mothers against decapentaplegic homolog 5 (SMAD5)	13	55808625	idd14B6	
17	13661202	Short transient receptor potential channel 7 (TrpC7)	13	55879544	idd14B6	

Table 4: Genes in the *Iddm20* interval. Abbreviations: *idd14*-NON is the interval determined in the NOD x NON cross (14) and *idd14B6* is the interval determined in the NOD x B6 crosses and congenic (15). The rat *Iddm20* supported interval ± 1 LOD is shown in gray shading. Chr: chromosome; bp: base pairs