

Supplementary material for

Pendse J, Ramachandran PV, Na J, Narisu N, Fink JL, Cagan RL, Collins FS, and Baranski TJ:

A *Drosophila* functional evaluation of candidates from human genome-wide association studies of type 2 diabetes and related metabolic traits identifies tissue-specific roles for dHHEX. [BMC Genomics 2013 14:136](#). PMID 23445342.

Figure S1. Wild type flies tolerate up to 1.25 M dietary sucrose.

Table S1. RNAi screen for sucrose sensitivity: knockdowns.

Table S2. RNAi screen for sucrose sensitivity: controls.

Table S3. Diet survey. Ubiquitous dHHEX knockdown results in intolerance to sugar and salt but not other stressors.

Table S4. Driver survey, part 1. Knockdown of dHHEX in the tubP or esg domains results in sucrose intolerance.

Table S5. Driver survey, part 2. Knockdown of dHHEX in the Dot domain results in sucrose intolerance.

Table S6. Cg>RNAi^{dHHEX-V15721}, Dcr-2 larvae are hyperglycemic.

Table S7. Cg>RNAi^{dHHEX-V15721}, Dcr-2 flies have reduced body mass.

Table S8. Cg>RNAi^{dHHEX-V15721}, Dcr-2 flies have reduced triglyceride levels.

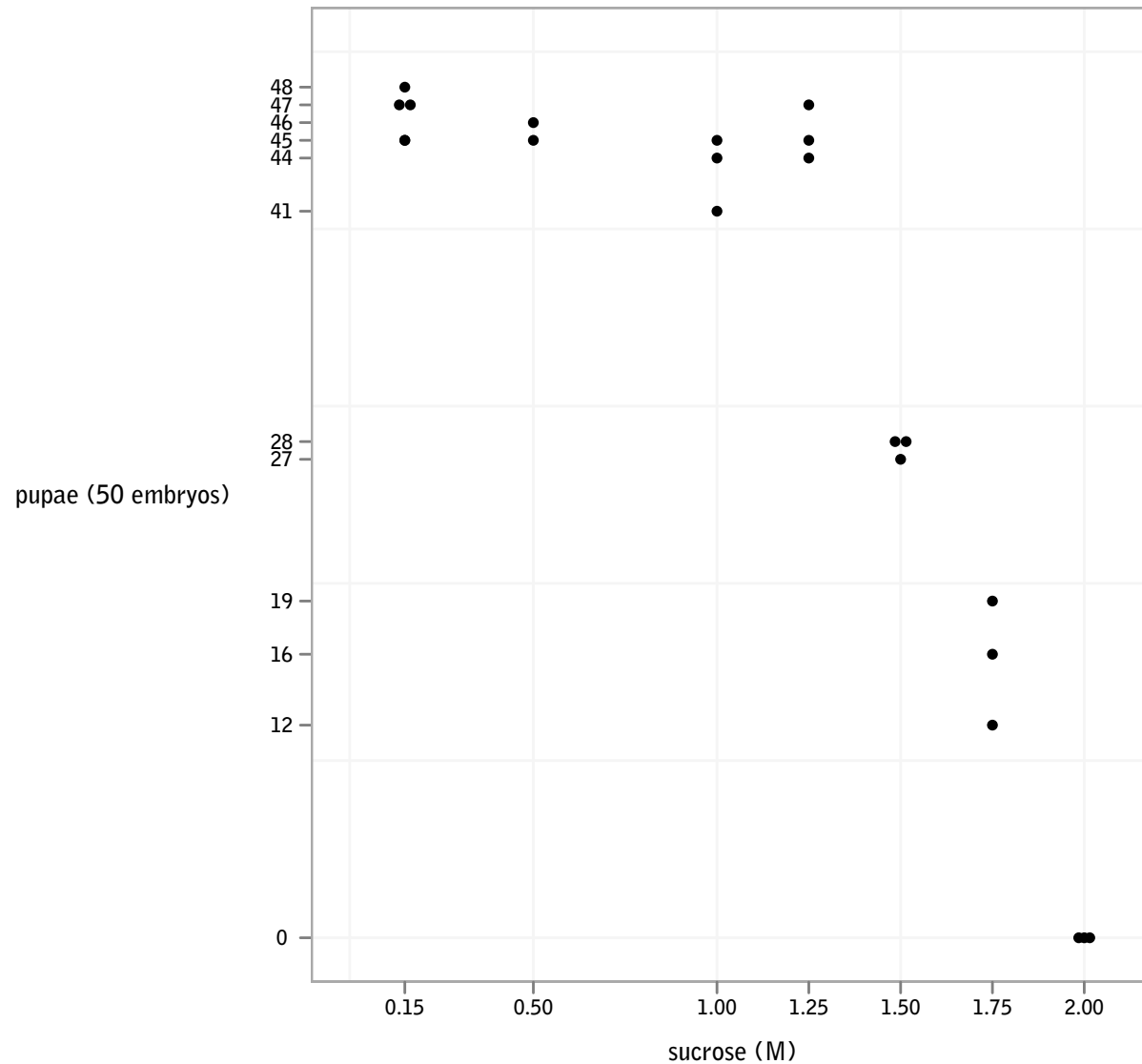


Figure S1. Wild type flies tolerate up to 1.25 M dietary sucrose. Survival to pupariation of w^{1118} flies reared with different levels of dietary sucrose, starting from 50 embryos per trial. Survival is comparable on 0.15 M, 1.0 M, and 1.25 M sucrose, but it decreases in a dose-dependent manner on 1.5 M and 1.75 M sucrose, and no pupae are seen on 2.0 M sucrose.

Table S1 – RNAi screen
(data associated with Figures 1–2)

Locus	Human Gene	Fly Gene	Insertion	scoring: $tub_P > RNAi$				ln(OR)	confidence interval bounds				p-value
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
				RNAi	control	RNAi	control		lower	upper	lower	upper	
1p32.3 low-density lipoprotein Willer: rs11206510 Kathiresan: rs11591147	TMEM61 (no ortholog)												
	BSND (no ortholog)												
	PCSK9 (no ortholog)												
	USP24 (no ortholog)												
1p31.3 triglyceride Willer: rs1748195 Kathiresan: rs12130333	ANGPTL3 (many-to-one ortholog)	CG9593	V24164	108	110	112	104	−0.0922	−0.4866	0.3016	−0.7862	0.5999	6.3276E−01
				28	21	25	23						
				72	80	50	41						
				8	9	37	40	−0.3634	−0.6298	−0.0984	−0.8360	0.1040	6.2409E−03
				29	48	48	47						
				82	119	103	103						
				43	61	159	169	−0.2434	−0.4577	−0.0295	−0.6235	0.1355	2.2373E−02
				400	490	301	289						
				144	187	66	65						
				78	125	103	96	0.3075	−0.0218	0.6367	−0.2737	0.8880	6.1945E−02
				178	178	132	128						
DOCK7 (no ortholog)													
ATG4C (many-to-one ortholog)	CG6194	V22293	109	130	175	284	−0.7501	−0.9808	−0.5216	−1.1610	−0.3473	3.2261E−11	
			26	21	41	57							
			51	59	68	114							
			32	50	66	113	−0.7501	−0.9808	−0.5216	−1.1610	−0.3473	3.2261E−11	
			167	315	557	496							
			74	141	79	95							
			48	71	161	125	−0.7501	−0.9808	−0.5216	−1.1610	−0.3473	3.2261E−11	
			45	103	317	276							
1p13.3 low-density lipoprotein Willer: rs599839 Kathiresan: rs646776	KIAA1324 (no ortholog)												
	SARS (one-to-one ortholog)	CG17259	no RNAi										

continued on next page

continued on next page

Table S1 — continued from previous page

Locus	Human Gene	Fly Gene	Insertion	scoring: <i>tubP</i> > RNAi				ln(OR)	confidence interval bounds				p-value
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
				RNAi	control	RNAi	control		lower	upper	lower	upper	
1p12 type 2 diabetes Zeggini: rs10923931	CELSR2 (many-to-one ortholog)	CG11895 starry night	V1665	83	66	145	163	0.3454	−0.0657	0.7593	−0.3751	1.0757	9.0359E−02
				32	20	59	66						
				32	28	53	58						
				19	18	33	39						
	V51379	153	221	118	95	−0.5835	−0.9390	−0.2303	−1.2119	0.0367	7.8596E−04		
		34	55	19	18								
		37	70	53	20								
		82	96	46	57								
	V51382	234	308	146	181	−0.0598	−0.3457	0.2265	−0.5645	0.4466	6.7268E−01		
		50	62	37	45								
		58	79	35	42								
		126	167	74	94								
	V107993	62	358	116	236	−1.0418	−1.4102	−0.6803	−1.6981	−0.4109	2.4612E−09		
		21	66	22	52								
		21	126	42	102								
		20	166	52	82								
	PSRC1 (no ortholog)												
	MYBPHL (no ortholog)												
	SORT1 (no ortholog)												
	ADAM30 (no ortholog)												
NOTCH2 (many-to-one ortholog)	CG3936 Notch	V100002	0	291	1	211	toxic knockdown						
			0	139	0	62							
			0	68	1	90							
			0	84	0	59							
1q42.13 triglyceride, high-density lipoprotein Willer: rs2144300 Kathiresan: rs4846914	GALNT2 (one-to-one ortholog)	CG3254 polypeptide GalNAc transferase 2	V26162	105	106	162	165	0.0089	−0.3523	0.3700	−0.6273	0.6450	1.0000E+00
				30	46	76	82						
				75	60	86	83						
V26163	115	104	218	168	−0.1597	−0.5065	0.1872	−0.7709	0.4518	3.5103E−01			
	63	42	106	86									
	52	62	112	82									

continued on next page

continued on next page

Table S1 — continued from previous page

Locus	Human Gene	Fly Gene	Insertion	scoring: $tub_P > RNAi$				ln(OR)	confidence interval bounds				p-value												
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni														
				RNAi	control	RNAi	control		lower	upper	lower	upper													
2p24.1 low-density lipoprotein Willer, Kathiresan: rs693	APOB (no ortholog)																								
2p23.3 triglyceride Kathiresan: rs780094	NRBP1 (many-to-one ortholog)	CG1098 Madm	V27346	135	285	316	344	-0.6617	-0.9267	-0.3993	-1.1331	-0.2000	2.8896E-07												
				66	128	55	59																		
				14	28	76	98																		
				55	129	185	187																		
			V27347	361	378	587	520	-0.1671	-0.3580	0.0236	-0.5061	0.1712	7.8999E-02												
				130	145	115	109																		
				168	160	105	134																		
				63	73	367	277																		
			V101758	1	260	30	200	-3.6591	-7.3682	-1.8468	-∞	-1.0679	8.0921E-10												
				0	80	7	54																		
				0	77	23	111																		
				1	103	0	35																		
KRTCAP3 (no ortholog)	IFT172 (one-to-one ortholog)	CG13809 osm-1	V24793	73	80	175	167	-0.1381	-0.5385	0.2613	-0.8436	0.5636	4.9701E-01												
				50	64	13	17																		
				23	16	82	69																		
						80	81																		
			V24795	110	88	210	194	0.1437	-0.2118	0.5007	-0.4813	0.7744	4.3453E-01												
				74	63	12	18																		
				36	25	80	80																		
						118	96																		
			FNDC4 (no ortholog)	GCKR (no ortholog)	C2orf16 (no ortholog)	ZNF512 (no ortholog)	THADA (one-to-one ortholog)	CG15618	V40006	0	134	57	212	-∞	-∞	-2.2206	-∞	-1.3286	1.2392E-11						
										0	65	23	83												
										0	69	34	129												
										PLEKHH2 (many-to-one ortholog)	CG43867	not tested													

continued on next page

continued on next page

Table S1 — continued from previous page

Locus	Human Gene	Fly Gene	Insertion	scoring: $tub_P > RNAi$				ln(OR)	confidence interval bounds				p-value	
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni			
				RNAi	control	RNAi	control		lower	upper	lower	upper		
2q24.3 fasting glucose Chen: rs563694	NOSTRIN (one-to-one ortholog)	CG42388	V26372*	206	172	112	142	0.4170	0.0851	0.7506	−0.1667	1.0069	1.1872E−02	
				129	104	44	55							
				46	47	68	87							
				31	21									
		V40328	9	117	23	163	−0.6049	−1.5406	0.2467	−2.3273	0.8290	1.8269E−01		
			5	59	7	50								
			4	58	16	113								
		V48694	0	125	0	312	toxic knockdown							
			0	63	0	136								
			0	62	0	176								
	V48695	0	138	0	280	toxic knockdown								
		0	79	0	115									
		0	59	0	165									
	SPC25 (no ortholog)	G6PC2 (many-to-one ortholog)	CG15400	V7261	51	72	32	26	−0.5494	−1.2318	0.1247	−1.7471	0.6194	1.0972E−01
					23	34	26	14						
					28	38	6	12						
ABC811 (many-to-many ortholog)		CG3879 Multi drug resistance 49	V42513	494	418	377	409	0.2484	0.0527	0.4443	−0.0985	0.5963	1.1368E−02	
				246	173	86	94							
				105	111	145	168							
				143	134	146	147							
			V42514	502	462	375	373	0.0776	−0.1180	0.2734	−0.2694	0.4250	4.3571E−01	
				197	164	99	85							
				178	165	138	138							
				127	133	138	150							
CG8523 Multi drug resistance 50	V51165	0	416	0	420	toxic knockdown								
		0	101	0	68									
		0	227	0	175									
		0	88	0	177									
ABC811 (many-to-many ortholog)	CG3879 Multi drug resistance 49	V51166	256	119	729	587	0.5491	0.3003	0.8017	0.1121	1.0003	8.0946E−06		
			37	26	167	176								
			112	55	182	193								
			107	38	380	218								
		CG10181 Multiple drug resistance 65	V9019	177	234	233	240	−0.2493	−0.5243	0.0250	−0.7361	0.2348	6.8223E−02	
				20	30	37	35							
				45	50	84	105							
				112	154	112	100							
CG10226	V108196	502	716	531	542	−0.3344	−0.5034	−0.1657	−0.6349	−0.0350	7.6364E−05			
		92	152	105	99									
		201	252	230	220									
		209	312	196	223									

continued on next page

continued on next page

Table S1 — continued from previous page

Locus	Human Gene	Fly Gene	Insertion	scoring: $tub_P > RNAi$				ln(OR)	confidence interval bounds				p-value
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
				RNAi	control	RNAi	control		lower	upper	lower	upper	
3p25.2 type 2 diabetes Scott: rs1801282	PPARG (many-to-one ortholog)	CG18023 Ecdysone-induced protein 78C	V10396	197	351	487	482	-0.5875	-0.8094	-0.3672	-0.9823	-0.1986	7.4639E-08
				85	157	105	114						
				60	112	156	136						
				52	82	226	232						
3p14.1 type 2 diabetes Zeggini: rs4607103	ADAMTS9 (many-to-one ortholog)	CG14869	V33346	183	350	231	315	-0.3380	-0.5927	-0.0841	-0.7896	0.1103	7.1741E-03
				57	102	38	64						
				66	164	106	153						
				60	84	87	98						
	V33347	70	314	43	240	0.2182	-0.2150	0.6599	-0.5367	1.0040	3.4741E-01		
		22	105	15	58								
		19	133	17	129								
		29	76	11	53								
3q27.3 type 2 diabetes Scott: rs4402960	IGF2BP2 (many-to-one ortholog)	CG1691 IGF-II mRNA-binding protein	V20321	340	256	338	337	0.2806	0.0531	0.5086	-0.1218	0.6850	1.3260E-02
				107	80	124	112						
				99	75	106	109						
				134	101	108	116						
	V20322	329	310	512	457	-0.0541	-0.2591	0.1509	-0.4177	0.3095	6.1013E-01		
		125	120	216	191								
		135	110	138	137								
		69	80	158	129								
5q13.3 low-density lipoprotein Kathiresan: rs12654264	C3orf65 (no ortholog)												
	HMGCR (one-to-one ortholog)	CG10367 HMG Coenzyme A reductase	V108617	0	131	0	563	toxic knockdown					
				0	39	0	36						
				0	92	0	450						
	COL4A3BP (one-to-one ortholog)	CG7207 ceramide transfer protein	V27914	48	38	52	50	0.1934	-0.4214	0.8114	-0.8764	1.2745	5.5851E-01
				14	15	35	38						
				34	23	17	12						
	6p22.3 type 2 diabetes Scott: rs7754840	CDKAL1 (one-to-one ortholog)	CG6550	V4947	111	101	143	146	0.1149	-0.2552	0.4857	-0.5360	0.7683
69					63	10	14						
42					38	65	70						
						68	62						
6p21.32 low-density lipoprotein Willer: rs2254287	HLA-DPA1 (no ortholog)												
	COL11A2 (no ortholog)												
	RXRB (many-to-one ortholog)	CG4380 ultraspiracle	V16893	97	190	299	332	-0.5670	-0.8699	-0.2680	-1.1058	-0.0424	1.3486E-04
				40	72	66	63						
				33	63	115	113						
				24	55	118	156						
	SLC39A7 (one-to-one ortholog)	CG10449 Catecholamines up	V7183*	0	89	0	184	toxic knockdown					
				0	50	0	29						
0				19	0	82							
0				20	0	73							

continued on next page

continued on next page

Table S1 — continued from previous page

Locus	Human Gene	Fly Gene	Insertion	scoring: $tub_P > RNAi$				ln(OR)	confidence interval bounds				p-value
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
				RNAi	control	RNAi	control		lower	upper	lower	upper	
	HSD17B8 (one-to-one ortholog)	CG3603	V51662*	48 13 18 17	24 8 10 6	44 15 7 22	34 13 7 14	0.4324	-0.2793	1.1547	-0.7977	1.6992	2.4075E-01
	MIR219-1 (no ortholog)												
	RING1 (many-to-one ortholog)	CG5595 Sex combs extra	V27465	29 9 5 4 0 6 2 3	451 43 96 59 57 36 101	342 45 23 48 39 52 66 69	568 61 115 94 74 58 93 73	-2.2355	-2.6711	-1.8321	-3.0367	-1.5530	1.1701E-42
			V106328	0 0 0 0	520 189 148 183	0 0 0 0	484 111 173 200	toxic knockdown					
	VPS52 (one-to-one ortholog)	CG7371	V27985	64 30 34	58 31 27	56 44 12	63 40 23	0.2153	-0.3207	0.7535	-0.7204	1.1586	4.4048E-01
			V48711	145 79 66	162 84 78	258 105 153	322 151 171	0.1106	-0.1768	0.3978	-0.3974	0.6178	4.3665E-01
	RPS18 (many-to-one ortholog)	CG8900 Ribosomal protein S18	V23083	285 88 40 157	293 85 40 168	298 53 30 215	274 51 41 182	-0.1116	-0.3497	0.1264	-0.5335	0.3096	3.4608E-01
	7p15.2 type 2 diabetes Zeggini: rs864745	JAZF1 (one-to-one ortholog)	CG12054	125 55 70	138 69 69	229 79 150	247 86 161	-0.0232	-0.3364	0.2895	-0.5764	0.5284	9.3871E-01
			V45986	174 63 111	153 51 102	289 104 185	257 78 179	0.0113	-0.2727	0.2956	-0.4903	0.5141	9.4426E-01
	7p13 fasting glucose Dupuis: rs4607517	AEBP1 (no ortholog)											
	MIR4649 (no ortholog)												
	POLD2 (one-to-one ortholog)	CG12018 BcDNA:HL03874	not tested										
	MYL7 (many-to-one ortholog)	CG2184	not tested										

continued on next page

continued on next page

Table S1 — continued from previous page

Locus	Human Gene	Fly Gene	Insertion	scoring: $tub_P > RNAi$				ln(OR)	confidence interval bounds				p-value
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
				RNAi	control	RNAi	control		lower	upper	lower	upper	
7q11.23 triglyceride Willer: rs17145738 Kooner: rs3812316	GCK (many-to-many ortholog)	CG3001 Hexokinase A	V21054	0	420	315	349	-∞	-∞	-4.6121	-∞	-3.7697	7.9623E-85
				0	88	51	61						
				0	137	128	114						
				0	195	136	174						
		V104680	280	333	405	474	-0.0160	-0.2285	0.1963	-0.3930	0.3602	9.1591E-01	
			89	42	137	150							
			109	109	148	202							
			82	182	120	122							
		CG8094 Hexokinase C	V35337	208	368	344	445	-0.3129	-0.5403	-0.0865	-0.7168	0.0872	6.1959E-03
				102	186	196	229						
				76	100	55	65						
				30	82	93	151						
		V35338	12	561	161	466	-2.7803	-3.4739	-2.1786	-4.0913	-1.7942	4.6097E-36	
			1	222	92	259							
			9	221	37	107							
			2	118	32	100							
		CG32849 Hex-t2	V47331	355	431	336	379	-0.0735	-0.2820	0.1349	-0.4432	0.2960	5.0040E-01
				63	76	93	81						
				229	288	53	51						
				63	67	190	247						
		V100218	120	212	220	168	-0.8376	-1.1511	-0.5269	-1.3937	-0.2921	4.1872E-08	
			58	108	38	27							
			54	96	96	98							
			8	8	86	43							
	CG33102 Hex-t1	V46573	220	246	285	321	0.0072	-0.2421	0.2565	-0.4341	0.4482	1.0000E+00	
			59	52	73	96							
			119	129	73	74							
			42	65	139	151							
	V46574	323	344	687	756	0.0327	-0.1553	0.2206	-0.3012	0.3662	7.4297E-01		
		159	177	195	213								
		102	87	266	260								
		62	80	226	283								
YKT6 (one-to-one ortholog)	CG1515	not tested											
CAMK2B (no ortholog)													
7q11.23 triglyceride Willer: rs17145738 Kooner: rs3812316	BAZ1B (one-to-many ortholog)	CG4254 twinstar	no RNAi										
		CG6873	V22454	0	28	1	226	toxic knockdown					
				75	121	0	23						
				0	28	0	24						
						0	11						
			1	83									
			0	85									

continued on next page

continued on next page

Table S1 — continued from previous page

Locus	Human Gene	Fly Gene	Insertion	scoring: $tub_P > RNAi$				ln(OR)	confidence interval bounds				p-value
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
				RNAi	control	RNAi	control		lower	upper	lower	upper	
8p21.3 triglyceride, high-density lipoprotein Willer: rs10503669 Kathiresan: rs328	BCL7B (many-to-one ortholog)	CG17252 BCL7-like	V20410	303	309	225	217	-0.0557	-0.3081	0.1965	-0.5025	0.3905	6.6260E-01
				108	108	78	53						
				112	115	89	110						
				83	86	58	54						
	V106828	333	419	278	309	-0.1239	-0.3466	0.0987	-0.5186	0.2704	2.6919E-01		
		117	154	71	71								
		96	129	81	98								
		120	136	126	140								
	TBL2 (no ortholog)												
	MLXIPL (many-to-one ortholog)	CG18362 Mio	V52606	128	230	264	263	-0.5892	-0.8754	-0.3053	-1.0972	-0.0898	2.5790E-05
				54	112	104	99						
				50	86	105	105						
				24	32	55	59						
	V52607	166	288	390	400	-0.5252	-0.7697	-0.2825	-0.9598	-0.0972	1.4864E-05		
		59	87	121	125								
		100	183	133	163								
		7	18	136	112								
VPS37D (many-to-one ortholog)													
DNAJC30 (one-to-one ortholog)	CG11035	V8478	126	106	140	180	0.4234	0.0699	0.7786	-0.1977	1.0507	1.5748E-02	
			48	48	14	13							
			78	58	58	59							
					68	108							
WBSCR22 (one-to-one ortholog)	CG10903	V27334	0	164	0	321	toxic knockdown						
			0	72	0	92							
			0	92	0	229							
STX1A (no ortholog)													
8p21.3 triglyceride, high-density lipoprotein Willer: rs10503669 Kathiresan: rs328	LPL (many-to-many ortholog)	CG5966 (shared: LIPC (15q21.3) and LIPG (18q21.1))	V13163	45	61	35	35	-0.3025	-0.9551	0.3473	-1.4428	0.8281	3.5573E-01
				2	8	35	35						
				20	18								
				23	35								
	V13164	181	203	211	213	-0.1051	-0.3913	0.1807	-0.6110	0.3995	4.8116E-01		
		55	64	53	59								
		40	30	35	33								
		86	109	123	121								
	CG6847 (shared: LIPC (15q21.3) and LIPG (18q21.1))	V22451	0	87	21	72	-∞	-∞	-1.7861	-∞	-0.8024	3.3388E-07	
			0	29	6	25							
			0	21	5	13							
			0	37	10	34							

continued on next page

continued on next page

Table S1 — continued from previous page

Locus	Human Gene	Fly Gene	Insertion	scoring: $tub_p > RNAi$				ln(OR)	confidence interval bounds				p-value
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
				RNAi	control	RNAi	control		lower	upper	lower	upper	
8q24.11 type 2 diabetes Scott: rs13266634	SLC30A8 (many-to-many ortholog)	CG3994 ZnT35C	V3836	76	74	56	80	0.3820	−0.1113	0.8788	−0.4790	1.2555	1.2304E−01
				22	21	18	23						
				27	24	11	9						
				27	29	27	48						
			V103263	691	636	509	570	0.1960	0.0320	0.3603	−0.0954	0.4881	1.7454E−02
				182	165	101	99						
				292	296	216	203						
				217	175	192	268						
		CG31860	V7688	0	375	0	403	toxic knockdown					
				0	36	0	61						
				0	112	0	179						
				0	227	0	163						
		V103398	422	772	417	570	−0.2913	−0.4685	−0.1143	−0.6062	0.0229	1.0656E−03	
			104	137	59	68							
			146	244	150	166							
			172	391	208	336							
8q24.13 triglyceride Willer: rs17321515	TRIB1 (many-to-one ortholog)	CG5408 tribbles	V22113	280	347	598	626	−0.1687	−0.3670	0.0291	−0.5209	0.1818	9.4502E−02
				108	134	160	182						
				115	141	173	182						
				57	72	265	262						
			V22114	210	291	458	521	−0.1972	−0.4210	0.0258	−0.5947	0.1971	7.7562E−02
				118	152	87	85						
				61	88	174	220						
				31	51	197	216						
			V106774	461	582	498	475	−0.2802	−0.4596	−0.1012	−0.5990	0.0375	1.7888E−03
				149	185	79	60						
				115	152	124	85						
				181	169	166	178						
9p21.3 type 2 diabetes Scott: rs10811661	MTAP (one-to-many ortholog)	CG4802	not tested	16	76	129	152						
		CG31115	not tested										
		CDKN2A (no ortholog)											
		CDKN2B (no ortholog)											
		9q31.1 high-density lipoprotein Willer: rs4149268 Kathiresan: rs3890182	ABCA1 (no ortholog)										
		10p13 type 2 diabetes Zeggini: rs12779790	NUDT5 (no ortholog)										
	CDC123 (no ortholog)												
	CAMK1D (no ortholog)												

continued on next page

Table S1 — continued from previous page

Locus	Human Gene	Fly Gene	Insertion	scoring: $tub_P > RNAi$				ln(OR)	confidence interval bounds				p-value
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
				RNAi	control	RNAi	control		lower	upper	lower	upper	
10q23.33 type 2 diabetes Scott: rs1111875	IDE (one-to-one ortholog)	CG5517 Insulin degrading metalloproteinase	V15957	55	178	66	216	0.0112	−0.4204	0.4403	−0.7504	0.7639	1.0000E+00
				38	98	6	17						
				17	80	17	101						
						43	98						
			V15958	71	174	252	411	−0.4068	−0.7404	−0.0797	−1.0023	0.1644	1.2433E−02
				29	54	9	12						
				3	39	26	54						
				20	21	72	85						
			V101317	9	16	45	71	0.1055	−0.1956	0.4069	−0.4258	0.6380	5.0496E−01
				10	44	62	94						
						38	95						
	KIF11 (one-to-one ortholog)	CG9191 Kinesin-like protein at 61F	V52548	191	185	170	183	−0.2057	−0.4642	0.0518	−0.6639	0.2489	1.1241E−01
				82	92	120	126						
				38	43	23	24						
				71	50	27	33						
			V52549	166	223	332	363	0.4925	0.1606	0.8262	−0.0914	1.0830	2.6050E−03
				62	80	112	84						
				46	94	129	153						
				32	14	14	15						
			V109280	13	14	27	32	−0.2054	−0.5034	0.0919	−0.7322	0.3191	1.6503E−01
				13	21	50	79						
				113	94	243	331						
				76	57	112	143						
	HHEX (one-to-one ortholog)	CG7056	V15719	28	28	121	170	−∞	−∞	−2.2184	−∞	−1.2822	2.2235E−10
				9	9	10	18						
				163	217	179	194						
				61	97	131	133						
			V15721	49	42	18	32	−3.2599	−4.0624	−2.5923	−4.8014	−2.1858	2.1611E−52
				53	78	30	29						
				0	59	46	72						
				0	14	4	9						
			V100292	0	16	6	23	−∞	−∞	−1.3184	−∞	−0.2890	3.2854E−05
				0	4	36	40						
				0	9								
				0	20								
	V100292	9	263	647	725	−∞	−∞	−1.3184	−∞	−0.2890	3.2854E−05		
		7	106	19	12								
		1	70	53	84								
		1	87	108	103								
	V100292	68	90	356	383	−∞	−∞	−1.3184	−∞	−0.2890	3.2854E−05		
		43	53										
		0	354	13	285								
		0	184	2	142								
V100292	0	77	4	70	−∞	−∞	−1.3184	−∞	−0.2890	3.2854E−05			
	0	93	7	73									

continued on next page

continued on next page

Table S1 — continued from previous page

Locus	Human Gene	Fly Gene	Insertion	scoring: $tub_P > RNAi$				ln(OR)	confidence interval bounds				p-value	
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni			
				RNAi	control	RNAi	control		lower	upper	lower	upper		
10q25.2 type 2 diabetes Sladek: rs7903146	TCF7L2 (many-to-one ortholog)	CG34403 pangolin	V3014	7	32	82	77	-1.5754	-2.6214	-0.6662	-3.5391	-0.0785	1.3333E-04	
				7	32	71	53							11
11p15.1 type 2 diabetes Scott: rs5219	NUCB2 (many-to-one ortholog)	CG32190 NUCB1	V5319	224	212	543	546	0.0605	-0.1679	0.2891	-0.3440	0.4658	6.1022E-01	
				101	88	105	95							92
			V100688	230	330	290	289	-0.3641	-0.6057	-0.1233	-0.7926	0.0615	2.4160E-03	
				74	133	80	73							79
	NCR3LG1 (no ortholog)													
	KCNJ11 (many-to-many ortholog)	CG4370 Inwardly rectifying potassium channel 2	V4341	84	260	21	226	1.2442	0.7187	1.8075	0.3522	2.2708	3.6149E-07	
				33	138	9	84							9
			V108140	0	72	0	304	toxic knockdown						
				0	14	0	103		0	35	0	117	0	23
		CG6747 Inwardly rectifying potassium channel	V28430	0	338	0	482	toxic knockdown						
				0	135	0	219		0	73	0	123	0	130
			V28431	0	482	0	484	toxic knockdown						
				0	55	0	254		0	165	0	79	0	262
			V107389	81	115	195	193	-0.3602	-0.7238	0.0007	-1.0035	0.2729	4.3830E-02	
				18	24	82	68							30
		CG10369 Inwardly rectifying potassium channel 3	V3886	232	216	187	222	0.2427	-0.0347	0.5208	-0.2470	0.7349	8.7180E-02	
				131	94	45	52							43
			V101174	103	282	288	387	-0.7111	-0.9950	-0.4314	-1.2174	-0.2207	2.2441E-07	
				56	160	49	54							21
	ABCC8 (many-to-one ortholog)	CG7806	V2804	265	216	626	639	0.2249	0.0087	0.4416	-0.1576	0.6099	3.6819E-02	
				123	101	175	201							82

continued on next page

Table S1 — continued from previous page

Locus	Human Gene	Fly Gene	Insertion	scoring: $tub_P > RNAi$				ln(OR)	confidence interval bounds				p-value	
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni			
				RNAi	control	RNAi	control		lower	upper	lower	upper		
11p11.2 type 2 diabetes Sladek: rs1113132 rs11037909 rs3740878	EXT2 (one-to-one ortholog)	CG8433 Ext2	V4902	139 94 45	153 103 50	175 14 80 81	173 14 83 76	-0.1073	-0.4310	0.2159	-0.6786	0.4624	5.2576E-01	
			V4903	50 22 28	43 21 22	215 5 81 129	196 16 71 109	0.0582	-0.4175	0.5370	-0.7755	0.9028	8.1903E-01	
			V49808*	4 3 0 1	63 46 8 9	3 3 0	101 66 35	toxic knockdown						
			V49809	85 34 51	86 31 55	254 143 111	234 113 121	-0.0936	-0.4575	0.2702	-0.7352	0.5473	6.5675E-01	
	ALX4 (no ortholog)													
	11q23.3 triglyceride Willer: rs12286037 Kathiresan: rs28927680	BUD13 (one-to-one ortholog)	CG13625	not tested										
				V12665*	0 0 0 0	93 32 37 24	1 1 0 0	191 47 86 58	toxic knockdown					
				AP0A5 (no ortholog)										
				AP0A4 (no ortholog)										
	AP0C3 (no ortholog)													
	AP0A1 (no ortholog)													
	SIK3 (one-to-one ortholog)	CG42856 Salt-inducible kinase 3	not tested											
	12q15 type 2 diabetes Zeggini: rs7961581	TSPAN8 (many-to-one ortholog)	CG6120 Tetraspanin 96F	V3422	179 49 42 88	169 52 27 90	163 33 111 19	195 42 122 31	0.2364	-0.0700	0.5435	-0.3037	0.7791	1.3196E-01
				V3423	190 33 44 113	200 21 43 136	155 47 69 39	155 42 72 41	-0.0512	-0.3608	0.2582	-0.5977	0.4948	7.6107E-01
				V101411	208 72 76 60	264 105 93 66	179 52 81 46	227 69 100 58	-0.0008	-0.2770	0.2755	-0.4888	0.4877	1.0000E+00
		LGR5 (no ortholog)												

continued on next page

Table S1 — continued from previous page

Locus	Human Gene	Fly Gene	Insertion	scoring: $tub_P > RNAi$				ln(OR)	confidence interval bounds				p-value
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
				RNAi	control	RNAi	control		lower	upper	lower	upper	
12q23.3 high-density lipoprotein Willer: rs2338104	MY01H (no ortholog)												
	KCTD10 (many-to-one ortholog)	CG10465	V107131	198 75 54 69	313 103 99 111	244 46 145 53	255 34 170 51	-0.4134	-0.6718	-0.1560	-0.8713	0.0410	1.2206E-03
	UBE3B (one-to-one ortholog)	CG5087	not tested										
	MMAB (no ortholog)												
	MVK (one-to-one ortholog)	CG33671	V49772*	10 2 6 2	65 21 23 21	34 20 14	39 26 13	-1.7222	-2.6514	-0.8691	-3.4127	-0.2930	1.1478E-05
15q21.3 high-density lipoprotein Willer: rs4775041 Kathiresan: rs1800588	LIPC (many-to-many ortholog)	CG5966 (shared: LPL (8p21.3) and LIPG (18q21.1))	V13163	45 2 20 23	61 8 18 35	35 35	35	-0.3025	-0.9551	0.3473	-1.4428	0.8281	3.5573E-01
			V13164	181 55 40 86	203 64 30 109	211 53 35 123	213 59 33 121	-0.1051	-0.3913	0.1807	-0.6110	0.3995	4.8116E-01
		CG6847 (shared: LPL (8p21.3) and LIPG (18q21.1))	V22451	0 0 0 0	87 29 21 37	21 6 5 10	72 25 13 34	-∞	-∞	-1.7861	-∞	-0.8024	3.3388E-07
	16q12.1 type 2 diabetes Scott: rs8050136	RPGRIP1L (no ortholog)											
		FTO (no ortholog)											
16q12.2 high-density lipoprotein Willer: rs9989419 rs3764261 rs1864163 Kathiresan: rs1800775	CETP (no ortholog)												
	NLRC5 (no ortholog)												

continued on next page

continued on next page

Table S1 — continued from previous page

Locus	Human Gene	Fly Gene	Insertion	scoring: $tub_P > RNAi$				ln(OR)	confidence interval bounds				p-value
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
				RNAi	control	RNAi	control		lower	upper	lower	upper	
18q21.1 high-density lipoprotein Willer: rs2156552	SLC12A3 (many-to-many ortholog)	CG4357 sodium chloride cotransporter 69	V30000	473	445	269	381	0.4088	0.2012	0.6172	0.0414	0.7790	7.7131E-05
				214	203	42	58						
				138	136	100	92						
				121	106	127	231						
			V30001	232	244	539	547	-0.0357	-0.2572	0.1857	-0.4284	0.3566	7.8344E-01
				75	59	190	198						
				2	1	151	143						
				155	184	198	206						
			V106499	465	535	363	376	-0.1050	-0.3000	0.0900	-0.4511	0.2408	2.8562E-01
				131	168	82	84						
				182	183	198	182						
				152	184	83	110						
	CG31547	V8551	337	420	273	299	-0.1291	-0.3530	0.0948	-0.5259	0.2674	2.6624E-01	
			44	54	74	64							
			113	135	100	101							
			180	231	99	134							
		V8552	96	118	83	72	-0.3475	-0.7850	0.0877	-1.1176	0.4147	1.1362E-01	
			24	42	18	19							
			6	20	5	8							
			66	56	60	45							
		V105911	426	511	441	426	-0.2164	-0.4060	-0.0271	-0.5531	0.1194	2.3589E-02	
			121	148	64	63							
			148	187	212	223							
			157	176	165	140							
HERPUD1 (many-to-one ortholog)	CG14536 Homocysteine-induced endoplasmic reticulum protein	V11724	198	167	614	539	0.0400	-0.2030	0.2837	-0.3897	0.4722	7.6354E-01	
			94	64	110	98							
			56	45	299	252							
			48	58	205	189							
		V11725	56	51	147	152	0.1267	-0.3391	0.5940	-0.6900	0.9490	6.5239E-01	
			11	8	13	14							
			8	11	49	50							
			37	32	85	88							
	LIPG (many-to-many ortholog)	CG5966 (shared: LPL (8p21.3) and LIPC (15q21.3))	V13163	45	61	35	35	-0.3025	-0.9551	0.3473	-1.4428	0.8281	3.5573E-01
				2	8	35	35						
				20	18								
				23	35								
			V13164	181	203	211	213	-0.1051	-0.3913	0.1807	-0.6110	0.3995	4.8116E-01
				55	64	53	59						
				40	30	35	33						
				86	109	123	121						
			V22451	0	87	21	72	-∞	-∞	-1.7861	-∞	-0.8024	3.3388E-07
				0	29	6	25						
				0	21	5	13						
				0	37	10	34						
ACAA2 (one-to-one ortholog)	CG4600 yippee interacting protein 2	V26562	92	62	216	191	0.2712	-0.1209	0.6675	-0.4153	0.9730	1.8314E-01	
			25	18	103	102							
			67	44	113	89							

continued on next page

Table S1 — continued from previous page

Locus	Human Gene	Fly Gene	Insertion	scoring: $tub_P > RNAi$				ln(OR)	confidence interval bounds				p-value										
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni												
				RNAi	control	RNAi	control		lower	upper	lower	upper											
19p13.2 low-density lipoprotein Willer: rs6511720	SMARCA4 (many-to-one ortholog)	CG5942 brahma	V37720	0	197	0	189	toxic knockdown	0.1113	-0.1006	0.3233	-0.2643	0.4873	2.9266E-01									
				0	62	0	36																
				0	70	0	76																
				0	25	0	46																
				0	40	0	31																
			V37721	0	266	1	315	toxic knockdown															
				0	77	0	64																
				0	62	0	64																
				0	100	0	65																
				0	27	1	122																
	LDLR (no ortholog)		V13066	281	500	271	539																
				71	174	52	107																
				115	172	80	167																
				95	154	139	265																
	SPC24 (no ortholog)		V100285	0	437	0	303	toxic knockdown															
				0	67	0	64																
				0	108	0	112																
				0	262	0	127																
	TSSK6 (many-to-one ortholog)	CG14305	V17477	388	356	485	512	0.1402						-0.0544	0.3349	-0.2048	0.4859	1.6002E-01					
				161	137	78	77																
				126	110	156	157																
				101	109	251	278																
	NDUFA13 (one-to-one ortholog)	CG3446	V42696*	1	120	174	174	-4.7813						-8.4498	-3.0197	-∞	-2.3002	4.1032E-28					
				1	80	37	54																
				0	24	68	57																
				0	16	69	63																
	YJEFN3 (many-to-one ortholog)		CG2974	not tested																			
	CILP2 (no ortholog)																						

continued on next page

continued on next page

Table S1 — continued from previous page

Locus	Human Gene	Fly Gene	Insertion	scoring: $tub_P > RNAi$				ln(OR)	confidence interval bounds				p-value							
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni									
				RNAi	control	RNAi	control		lower	upper	lower	upper								
19q13.33 low-density lipoprotein Willer: rs10402271 rs4420638	PBX4 (many-to-one ortholog)	CG8933 extradenticle	V7802	0	164	0	66	toxic knockdown	-0.0860	-0.9274	0.7963	-1.5376	1.5059	8.4274E-01						
				0	19	0	47													
				0	56	0	7													
				0	89	0	12													
			V7803	0	106	0	268	toxic knockdown												
				0	35	0	57													
				0	52	0	113													
				5 0	41 19	0	98													
			V100259	3	379	0	315	toxic knockdown												
				3	115	0	49													
				0	104	0	82													
				0	160	0	184													
			V100687	17	315	11	187													
				2	67	1	37													
				8	86	1	49													
				7	162	9	101													
	LPAR2 (no ortholog)																			
	GMIP (no ortholog)																			
	ATP13A1 (one-to-one ortholog)	CG6230	V8897	0	134	44	179	-∞							-∞	-2.1193	-∞	-1.2139	3.4181E-10	
				0	86	9	14													
				0	48	21	74													
						14	91													
19q13.33 low-density lipoprotein Willer: rs10402271 rs4420638	BCL3 (no ortholog)																			
	CBLC (no ortholog)																			
	BCAM (no ortholog)																			

continued on next page

continued on next page

Table S1 — continued from previous page

Locus	Human Gene	Fly Gene	Insertion	scoring: $tub_P > RNAi$				ln(OR)	confidence interval bounds				p-value						
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni								
				RNAi	control	RNAi	control		lower	upper	lower	upper							
PVRL2 (many-to-one ortholog)	CG17716 faint sausage	V6561	271	297	362	395	-0.0044	-0.2282	0.2194	-0.4012	0.3921	1.0000E+00							
			92	126	130	126													
			109	108	121	140													
			70	63	111	129													
			V6562	131	138	116							137	0.1141	-0.2444	0.4732	-0.5167	0.7470	5.3981E-01
				65	73	70							83						
				47	37	23							28						
				19	28	23							26						
			V24476	359	359	640							649	0.0140	-0.1728	0.2007	-0.3176	0.3455	8.8897E-01
				177	175	84							119						
				52	57	132							125						
				130	127	424							405						
		V42236	177	273	235	317	-0.1339	-0.3958	0.1273	-0.5978	0.3276	3.0269E-01							
			63	82	56	97													
			80	120	138	146													
			34	71	41	74													
		V42237	103	167	154	200	-0.2215	-0.5587	0.1139	-0.8176	0.3683	1.8956E-01							
			27	33	27	20													
			47	79	84	103													
			29	55	43	77													
		V102073	125	159	121	146	-0.0527	-0.4029	0.2975	-0.6699	0.5641	7.9717E-01							
			55	63	29	40													
			33	54	62	72													
			37	42	30	34													
TOMM40 (many-to-many ortholog)	CG8330 tomboy40	V23763	0	98	1	38	toxic knockdown												
			0	69	0	32													
			0	4	1	5													
			0	25	0	1													
		V23764	92	226	86	235	0.1063	-0.2546	0.4679	-0.5291	0.7442	5.9658E-01							
			45	91	14	50													
			8	31	44	118													
			39	104	28	67													
		V42439	2	626	35	882	-2.5185	-4.6722	-1.1531	-7.1161	-0.4745	1.5529E-06							
			2	182	4	98													
			0	22	1	175													
			0	176	12	294													
			0	95	1	61													
			0	77	3	103													
		V105557	0	74	14	151	toxic knockdown												
			1	427	4	615													
			0	207	0	47													
			1	139	4	308													
		CG12157 Translocase of outer membrane 40	V13177	0	309	0	303	toxic knockdown											
				0	130	0	42												
				0	113	0	108												
				0	66	0	153												
		V13178	135	318	156	366	-0.0040	-0.2890	0.2804	-0.5083	0.4980	1.0000E+00							
			59	172	76	207													
41	68		47	81															
35	78		33	78															

continued on next page

Table S1 — continued from previous page

Locus	Human Gene	Fly Gene	Insertion	scoring: $tub_P > RNAi$				ln(OR)	confidence interval bounds				p-value
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
				RNAi	control	RNAi	control		lower	upper	lower	upper	
	APOE (no ortholog)												
	APOC1 (no ortholog)												
	APOC4 (no ortholog)												
	APOC2 (no ortholog)												
	CLPTM1 (one-to-one ortholog)	CG3702	not tested										
	RELB (many-to-one ortholog)	CG6667 dorsal	V45996	370 96 91 111 72	559 130 196 152 81	293 53 35 87 118	303 52 52 75 124	-0.3788	-0.5919	-0.1660	-0.7569	-0.0019	3.8680E-04
			V45998	183 51 56 40 36	216 72 75 42 27	117 29 36 36 16	136 32 31 38 35	-0.0153	-0.3436	0.3135	-0.5939	0.5651	9.3589E-01
			V105491	19 1 0 2 4 3 9 0	640 140 102 150 56 52 58 82	566 31 52 14 141 85 121 122	784 56 78 73 132 100 127 218	-3.1901	-3.7162	-2.7203	-4.1735	-2.4106	8.1235E-92

Table S1. RNAi screen for sucrose sensitivity: knockdowns. Experimental data associated with Figures 1–2. Human genomic regions and SNPs, human genes within ~100 kb radius window and their Ensembl 43 fly orthologs, fly RNAi lines (as VDRC catalog numbers), and experimental results are shown, as well as p-values and confidence intervals for the null hypothesis that the odds of knockdown vs. non-knockdown survival are the same on 1.0 M sucrose as on 0.15 M sucrose. Survival to pupariation was scored except for a small number of crosses, marked in the table with asterisks, where survival to eclosion was scored for technical reasons. In the “scoring” columns, bold numbers are total counts, and counts for individual trials are listed immediately underneath them.

Table S2 – RNAi backgrounds
(data associated with Figure 1)

Fly Strain	scoring: $tub_P > RNAi$				ln(OR)	confidence interval bounds				p-value
	1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
	RNAi	control	RNAi	control		lower	upper	lower	upper	
GD control: w^{1118}	261	278	1497	1526	−0.0439	−0.2317	0.1437	−0.3776	0.2891	6.4045E−01
	39	39	295	318						
	71	64	382	396						
	41	49	76	74						
	9	13	78	80						
	12	14	71	69						
	70	76	105	73						
	19	23	95	110						
			194	159						
			109	119						
			92	128						
KK control: $y^- w^{1118}; P\{attP y^+ w^3\}VIE-260B$	234	239	419	403	−0.0600	−0.2928	0.1727	−0.4725	0.3521	6.0406E−01
	89	79	148	146						
	23	31	58	62						
	33	44	106	87						
	34	36	4	11						
	55	49	103	97						

Table S2. RNAi screen for sucrose sensitivity: controls. Control data associated with Figure 1. Survival to pupariation of progeny of w^{1118} and $y^- w^{1118}$; P{attP $y^+ w^3$ }VIE-260B males crossed to tub_P -GAL4/TM6B unmated females. In the “scoring” columns, bold numbers are total counts, and counts for individual trials are listed immediately underneath them. Similar survival indicates that the genetic backgrounds in the study are not themselves differentially sucrose-sensitive.

Table S3 – diet survey
(data associated with Figure 3A)

Food	scoring				ln(OR)	confidence interval bounds				
	> RNAi ^{dHHEX-V15721} with tub _P >		w ¹¹¹⁸ genetic background with tub _P >			95%		Bonferroni		p-value
	control		control			lower	upper	lower	upper	
0.15 M sucrose	647	725	1497	1526	-0.0946	-0.2245	0.0352	-0.2836	0.0941	1.5196E-01
	19	12	295	318						
	53	84	382	396						
	108	103	76	74						
	68	90	78	80						
	356	383	71	69						
	43	53	105	73						
			95	110						
			194	159						
			109	119						
			92	128						
0.5 M sucrose	42	83	83	78	-0.7407	-1.2567	-0.2332	-1.4862	-0.0151	2.6870E-03
	42	83	83	78						
0.75 M sucrose	3	10	24	21	-1.3152	-3.1725	0.2066	-4.1229	0.7668	6.5918E-02
	3	10	24	21						
1.0 M sucrose	9	263	261	278	-3.3087	-4.1234	-2.6238	-4.5385	-2.3728	3.7116E-46
	7	106	39	39						
	1	70	71	64						
	1	87	41	49						
			9	13						
			12	14						
			70	76						
			19	23						
0.15 M sucrose + 1.7 M glucose	0	62	69	75	-∞	-∞	-2.6482	-∞	-2.0831	3.6364E-14
	0	62	69	75						
0.15 M sucrose + 1.7 M fructose	0	119	108	98	-∞	-∞	-3.5113	-∞	-2.9636	2.2245E-28
	0	119	108	98						
0.15 M sucrose + 0.1 M glucosamine	0	100	27	55	-∞	-∞	-2.4568	-∞	-1.8684	2.7095E-11
	0	100	27	55						
continued on next page										

continued on next page

Table S3 — continued from previous page

Food	scoring				ln(OR)	confidence interval bounds				p-value
	> RNAi ^{dHHEX-V15721}		w ¹¹¹⁸ genetic background			95%		Bonferroni		
	with tub _P >	control	with tub _P >	control		lower	upper	lower	upper	
0.15 M sucrose + 140 mg/mL fat	226	235	360	416	0.1054	−0.1321	0.3430	−0.2387	0.4497	3.7758E−01
	100	107	115	131						
	56	66	123	146						
	70	62	122	139						
0.15 M sucrose + 0.5 M NaCl	0	123	77	111	−∞	−∞	−3.0785	−∞	−2.5281	5.6924E−21
	0	34	23	25						
	0	31	26	39						
	0	58	28	47						
0.15 M sucrose + 10 mM H ₂ O ₂	197	285	258	296	−0.2317	−0.4864	0.0224	−0.6009	0.1359	6.8937E−02
	35	64	57	54						
	79	102	57	52						
	83	119	144	190						
0.15 M sucrose + 600 μM AgNO ₃	30	89	46	63	−0.7695	−1.3759	−0.1744	−1.6444	0.0792	7.6202E−03
	4	24	9	11						
	6	21	22	30						
	20	44	15	22						
0.15 M sucrose, heat-shocked	48	69	65	75	−0.2189	−0.7468	0.3058	−0.9784	0.5334	4.4913E−01
	17	22	27	26						
	12	27	19	28						
	19	20	19	21						

Table S3. Diet survey. Ubiquitous dHHEX knockdown results in intolerance to sugar and salt but not other stressors. Data associated with Figure 3A: survival to pupariation of progeny of UAS-RNAi^{dHHEX-V15721} and w¹¹¹⁸ (genetic background control) males crossed to tub_P-GAL4/TM6B unmated females, reared on different diets. In the “scoring” columns, bold numbers are total counts, and counts for individual trials are listed immediately underneath them.

Table S4 – driver survey, part 1
(data associated with Figure 3B)

Driver	crossed to	stage	scoring				ln(OR)	confidence interval bounds					p-value
			1.0 M sucrose		0.15 M sucrose			95%		Bonferroni			
			RNAi	control	RNAi	control		lower	upper	lower	upper		
tub _P -GAL4	w ¹¹¹⁸	(pupae)	261	278	1497	1526	-0.0439	-0.2317	0.1437	-0.3140	0.2257	6.4045E-01	
			39	39	295	318							
			71	64	382	396							
			41	49	76	74							
			9	13	78	80							
			12	14	71	69							
			70	76	105	73							
			19	23	95	110							
					194	159							
					109	119							
			92	128									
	UAS-RNAi ^{dHHEX-V15721}	(pupae)	9	263	647	725	-3.2599	-4.0624	-2.5923	-4.4615	-2.3568	2.1611E-52	
			7	106	19	12							
			1	70	53	84							
			1	87	108	103							
					68	90							
					356	383							
	dilp2-GAL4	w ¹¹¹⁸	(eclosers)	649	645	823	765	-0.0669	-0.2165	0.0827	-0.2823	0.1485	3.8894E-01
				258	271	347	310						
219				203	260	267							
172				171	216	188							
Sn _{GCN} -GAL4	w ¹¹¹⁸	(pupae)	17	15	114	98	-0.0260	-0.8384	0.7954	-1.1773	1.1452	1.0000E+00	
			17	15	68	64							
					46	34							
UAS-RNAi ^{dHHEX-V15721}	(pupae)	44	24	215	171	0.3763	-0.1873	0.9598	-0.4189	1.2163	1.8523E-01		
		27	17	21	17								
		17	7	81	53								
				46	36								
				67	65								

continued on next page

Table S4 — continued from previous page

Driver	crossed to	stage	scoring				ln(OR)	confidence interval bounds				
			1.0 M sucrose		0.15 M sucrose			95%	Bonferroni		p-value	
			RNAi	control	RNAi	control			lower	upper		lower
byn-GAL4	w ¹¹¹⁸	(pupae)	88	95	99	109	0.0196	-0.3977	0.4369	-0.5759	0.6151	1.0000E+00
			88	95	99	109						
	UAS-RNAi ^{dHHEX-V15721}	(pupae)	99	91	110	95	-0.0622	-0.4772	0.3526	-0.6547	0.5296	7.6324E-01
			99	91	110	95						
MyoIA-GAL4	w ¹¹¹⁸	(eclosers)	1022	691	779	695	0.2772	0.1341	0.4204	0.0712	0.4835	1.2528E-04
			343	229	309	275						
			351	259	193	156						
			328	203	277	264						
	UAS-RNAi ^{dHHEX-V15721}	(eclosers)	360	374	368	507	0.2821	0.0799	0.4846	-0.0083	0.5732	5.6701E-03
			167	162	54	50						
			102	104	157	244						
			91	108	157	213						
esg-GAL4	w ¹¹¹⁸	(eclosers)	948	623	630	468	0.1225	-0.0373	0.2822	-0.1075	0.3523	1.2855E-01
			326	187	257	150						
			289	221	160	133						
			333	215	213	185						
	UAS-RNAi ^{dHHEX-V15721}	(eclosers)	8	192	150	224	-2.7734	-3.6572	-2.0346	-4.0945	-1.7726	4.7473E-24
			2	68	43	55						
			6	99	64	112						
			0	25	43	57						

Table S4. Driver survey, part 1. Knockdown of dHHEX in the tub_P or esg domains results in sucrose intolerance. Data associated with Figure 3B: survival of progeny of various drivers crossed to UAS-RNAi^{dHHEX} or to w¹¹¹⁸ (genetic background control) on 0.15 M and 1.0 M sucrose. Pupariation was scored for tub_P-GAL4, sns_{GCN}-GAL4, and byn-GAL4; eclosion was scored for dilp2-GAL4, MyoIA-GAL4, and esg-GAL4. In the “scoring” columns, bold numbers are total counts, and counts for individual trials are listed immediately underneath them.

Table S5 – driver survey, part 2
(data associated with Figure 3C)

Driver	Stage	scoring				ln(OR)	confidence interval bounds					p-value
		knockdown		background			95%		Bonferroni			
		1.0 M sucrose	0.15 M sucrose	1.0 M sucrose	0.15 M sucrose		lower	upper	lower	upper		
Dot-GAL4	(pupae)	164	162	169	179	0.0697	−0.2439	0.3834	−0.3792	0.5190	6.9997E−01	
		45	45	42	43							
		42	43	39	47							
		38	39	43	47							
		39	35	45	42							
	(eclosers)	43	160	168	179	−1.2484	−1.6723	−0.8381	−1.8603	−0.6684	1.3922E−10	
		13	43	42	43							
		13	43	38	47							
		10	39	43	47							
		7	35	45	42							
Cg-GAL4	(pupae)	219	227	259	266	−0.0092	−0.2697	0.2513	−0.3829	0.3643	9.4874E−01	
		38	40	44	44							
		41	33	40	46							
		34	46	44	43							
		34	33	44	42							
		37	37	44	45							
		35	38	43	46							
srp.Hemo-GAL4	(pupae)	106	79	42	66	0.7434	0.2341	1.2606	0.0215	1.4832	2.5370E−03	
		31	15	11	21							
		27	31	20	21							
		48	33	11	24							
GMH5	(pupae)	102	124	129	119	−0.2754	−0.6539	0.1017	−0.8168	0.2628	1.4185E−01	
		34	38	46	43							
		35	36	46	47							
		33	50	37	29							

Table S5. Driver survey, part 2. Knockdown of dHHEX in the Dot domain results in sucrose intolerance. Data associated with Figure 3C: survival of progeny of various drivers crossed to UAS-RNAi^{dHHEX} or to w¹¹¹⁸ (genetic background control) on 0.15 M and 1.0 M sucrose. Pupariation (for 50 embryos per trial) was scored for Dot-GAL4, Cg-GAL4, srp.Hemo-GAL4, and GMH5. Eclosion was also scored for Dot-GAL4. In the “scoring” columns, bold numbers are total counts, and counts for individual trials are listed immediately underneath them.

Table S6 – circulating glucose
(data associated with Figure 4A)

hemolymph glucose (mg/dL)			
(control)		(experimental)	
63.0	mean	71.1	
10.3	SD	13.3	
62.8	median	71.7	
54.8-70.9	IQR	62.3-76.7	
45.7-82.5	range	50.9-97.6	
		97.6	
		96.4	
		91.6	93.0
		85.8	
82.5			
		77.9	
76.7		76.7	
73.2 73.4 73.4		74.0	
		71.7 71.7 72.1 72.9 73.0	
67.4 68.6			
65.1 66.2		65.8 66.0	
		63.9	
61.6 62.8		61.6 62.3 62.5 62.8	
59.3 60.2		59.0 60.4	
55.4			
53.5 54.2		54.0	
		52.9	
50.6		50.9	
45.7 46.9			

Table S6. Cg>RNAi^{dHHEX-V15721}, Dcr-2 larvae are hyperglycemic.
Data associated with Figure 4A. We measured hemolymph glucose of groups of 5–8 wandering third-instar females reared on 1.0 M sucrose food.

Table S7 – body mass
(data associated with Figure 4B–C)

per-animal mass (mg)						
(control)	larvae	(experimental)	(control)	adults	(experimental)	
1.42	mean	1.32	1.00	mean	0.85	
0.09	SD	0.05	0.09	SD	0.09	
1.42	median	1.31	0.98	median	0.83	
1.38-1.47	IQR	1.28-1.38	0.93-1.07	IQR	0.78-0.93	
1.13-1.80	range	1.23-1.39	0.81-1.22	range	0.65-1.03	
1.80						
1.54						
1.51 1.51 1.52 1.52 1.53						
1.48 1.48 1.48 1.49 1.50 1.50						
1.45 1.45 1.45 1.45 1.47 1.47 1.47						
1.43 1.43 1.43 1.43 1.43 1.43 1.44						
1.40 1.40 1.40 1.40 1.42 1.42 1.42 1.42		1.39				
1.36 1.38 1.38 1.38 1.38 1.38 1.39 1.39 1.39		1.38 1.38 1.38				
1.33 1.33 1.34 1.34		1.33 1.35				
1.30 1.30 1.30 1.30 1.32		1.30 1.31 1.32				
1.27 1.28		1.28 1.28 1.29				
1.26		1.27				
		1.23				
			1.22			
			1.19			
			1.16			
1.13			1.12 1.13 1.14			
			1.09 1.09 1.11			
			1.06 1.06 1.06 1.07 1.07 1.07 1.07 1.08 1.08			
			1.05 1.05		1.03	
			1.00 1.00 1.01 1.01 1.02		1.00 1.01	
			0.97 0.97 0.97 0.98 0.98 0.98 0.98 0.98		0.97 0.97 0.97 0.99 0.99	
			0.94 0.94 0.95 0.96 0.96 0.96		0.95 0.95 0.95 0.95 0.95	
			0.91 0.91 0.91 0.91 0.92 0.92 0.92 0.92 0.92 0.93 0.93		0.91 0.91 0.92 0.93 0.93	
			0.89 0.90		0.88 0.88 0.89 0.89	
					0.85 0.86 0.86	
					0.83 0.83 0.83 0.83	
			0.81 0.82		0.79 0.79 0.79 0.80 0.80 0.80 0.80 0.80 0.80 0.81 0.82	
					0.76 0.77 0.77 0.77 0.78 0.78 0.78 0.78 0.78	
					0.73	
					0.70	
					0.67 0.69	
					0.65	

Table S7. Cg>RNAi^{dHHEX-V15721}, Dcr-2 flies have reduced body mass. Data associated with Figure 4B–C. We measured mean per-animal mass of groups of 6–10 wandering third-instar and newly eclosed adult females reared on 1.0 M sucrose food.

[illegible]

Table S8. Cg>RNAi^{dHHEX-V15721}, Dcr-2 flies have reduced triglyceride levels. Data associated with Figure 4D–E. We measured mean whole-animal triglyceride levels (per mg tissue) for groups of 6–10 wandering third-instar and newly eclosed adult females reared on 1.0 M sucrose food.