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.

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$^{dHHEX\text{-}V15721}$, Dcr-2 larvae are hyperglycemic.

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

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

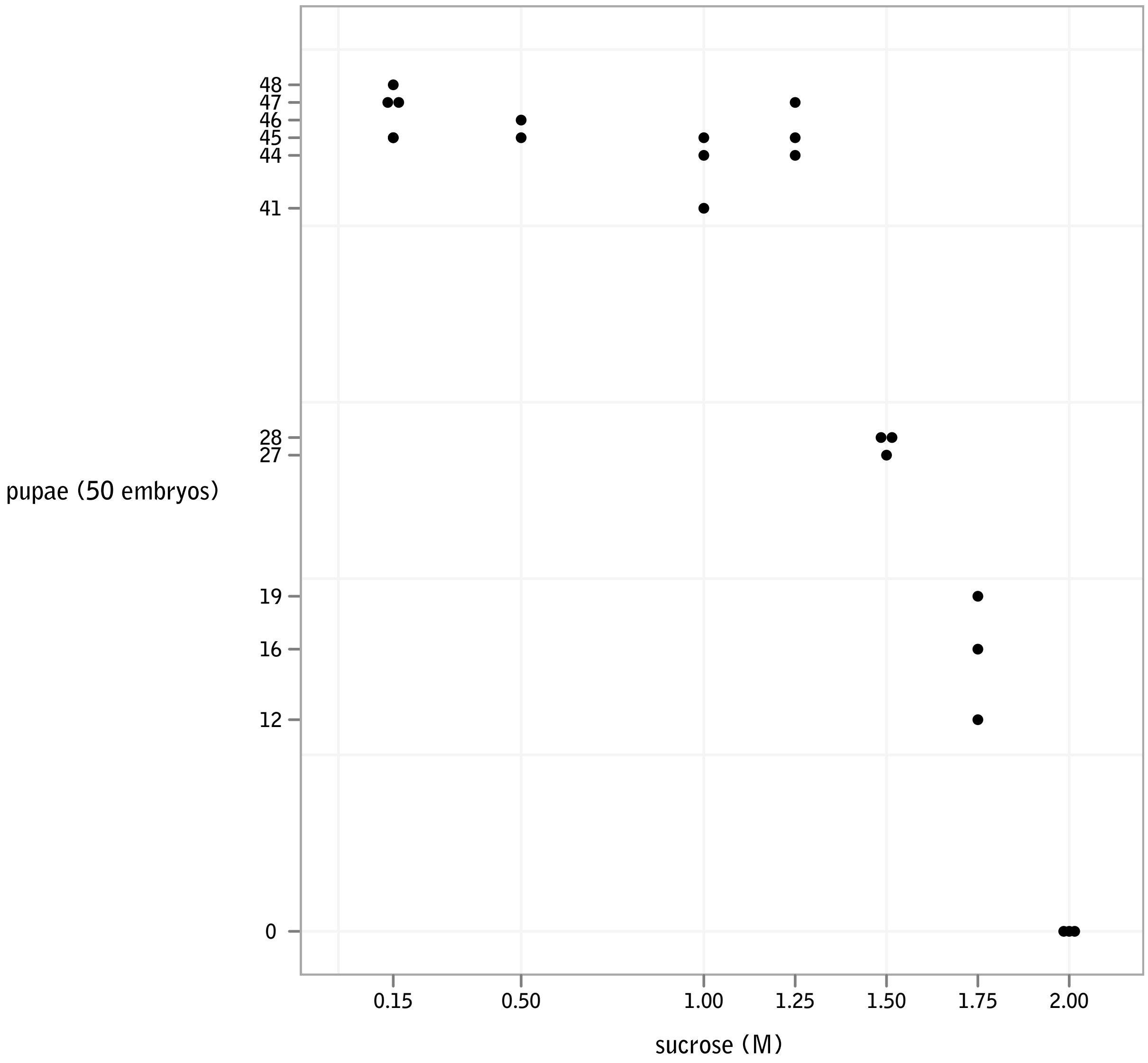

Figure S1. Wild type flies tolerate up to 1.25 M dietary sucrose. Survival to pupariation of w^{1118} flies reared with different levels of dietary sucrose, starting from 50 embryos per trial. Survival is comparable on 0.15 M, 1.0 M, and 1.25 M sucrose, but it decreases in a dose-dependent manner on 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)

				scoring: tub$_P$ > RNAi					confidence interval bounds				
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
Locus	**Human Gene**	**Fly Gene**	**Insertion**	RNAi	control	RNAi	control	**ln(OR)**	lower	upper	lower	upper	**p-value**
1p32.3 low-density lipoprotein Willer: rs11206510 Kathiresan: rs11591147	**TMEM61** (no ortholog)												
	BSND (no ortholog)												
	PCSK9 (no ortholog)												
	USP24 (no ortholog)												
1p31.3	**ANGPTL3**	**CG9593**	**V24164**	**108**	**110**	**112**	**104**	**–0.0922**	–0.4866	0.3016	–0.7862	0.5999	**6.3276E–01**
triglyceride	(many-to-one ortholog)			28	21	25	23						
Willer: rs1748195				72	80	50	41						
Kathiresan: rs12130333				8	9	37	40						
			V24165	**154**	**228**	**310**	**319**	**–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						
			V105528	**400**	**490**	**301**	**289**	**–0.2434**	–0.4577	–0.0295	–0.6235	0.1355	**2.2373E–02**
				144	187	66	65						
				78	125	103	96						
				178	178	132	128						
	DOCK7 (no ortholog)												
	ATG4C	**CG6194**	**V22293**	**109**	**130**	**175**	**284**	**0.3075**	–0.0218	0.6367	–0.2737	0.8880	**6.1945E–02**
	(many-to-one ortholog)			26	21	41	57						
				51	59	68	114						
				32	50	66	113						
			V22294	**167**	**315**	**557**	**496**	**–0.7501**	–0.9808	–0.5216	–1.1610	–0.3473	**3.2261E–11**
				74	141	79	95						
				48	71	161	125						
				45	103	317	276						
1p13.3 low-density lipoprotein Willer: rs599839	**KIAA1324** (no ortholog)												
Kathiresan: rs646776	**SARS** (one-to-one ortholog)	**CG17259**	no RNAi										

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Table S1 — continued from previous page

				scoring: $\text{tub}_P > \text{RNAi}$					confidence interval bounds				
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
Locus	**Human Gene**	**Fly Gene**	**Insertion**	RNAi	control	RNAi	control	**ln(OR)**	lower	upper	lower	upper	**p-value**
	CELSR2	**CG11895**	**V1665**	**83**	**66**	**145**	**163**	**0.3454**	–0.0657	0.7593	–0.3751	1.0757	**9.0359E–02**
	(many-to-one ortholog)	starry night		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)												
1p12	**ADAM30**												
type 2 diabetes	(no ortholog)												
Zeggini: rs10923931													
	NOTCH2	**CG3936**	**V100002**	**0**	**291**	**1**	**211**	**toxic knockdown**					
	(many-to-one ortholog)	Notch		0	139	0	62						
				0	68	1	90						
				0	84	0	59						
1q42.13	**GALNT2**	**CG3254**	**V26162**	**105**	**106**	**162**	**165**	**0.0089**	–0.3523	0.3700	–0.6273	0.6450	**1.0000E+00**
triglyceride,	(one-to-one ortholog)	polypeptide GalNAc		30	46	76	82						
high-density lipoprotein		transferase 2		75	60	86	83						
Willer: rs2144300													
Kathiresan: rs4846914			**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						

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Table S1 — continued from previous page

				scoring: tub_P > RNAi					confidence interval bounds				
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
Locus	**Human Gene**	**Fly Gene**	**Insertion**	RNAi	control	RNAi	control	**ln(OR)**	lower	upper	lower	upper	**p-value**
2p24.1	**APOB**												
low-density lipoprotein	(no ortholog)												
Willer, Kathiresan: rs693													
2p23.3	**NRBP1**	**CG1098**	**V27346**	**135**	**285**	**316**	**344**	**–0.6617**	–0.9267	–0.3993	–1.1331	–0.2000	**2.8896E–07**
triglyceride	(many-to-one ortholog)	Madm		66	128	55	59						
Kathiresan: rs780094				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	$-\infty$	–1.0679	**8.0921E–10**
				0	80	7	54						
				0	77	23	111						
				1	103	0	35						
	KRTCAP3												
	(no ortholog)												
	IFT172	**CG13809**	**V24793**	**73**	**80**	**175**	**167**	**–0.1381**	–0.5385	0.2613	–0.8436	0.5636	**4.9701E–01**
	(one-to-one ortholog)	osm-1		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)												
2p21	**THADA**	**CG15618**	**V40006**	**0**	**134**	**57**	**212**	$-\infty$	$-\infty$	–2.2206	$-\infty$	–1.3286	**1.2392E–11**
type 2 diabetes	(one-to-one ortholog)			0	65	23	83						
Scott: rs7578597				0	69	34	129						
	PLEKHH2	**CG43867**	not tested										
	(many-to-one ortholog)												

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Table S1 — continued from previous page

				scoring: tub_{P} > RNAi					confidence interval bounds				
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
Locus	**Human Gene**	**Fly Gene**	**Insertion**	RNAi	control	RNAi	control	**ln(OR)**	lower	upper	lower	upper	**p-value**
2q24.3	**NOSTRIN**	**CG42388**	**V26372***	**206**	**172**	**112**	**142**	**0.4170**	0.0851	0.7506	–0.1667	1.0069	**1.1872E–02**
fasting glucose	(one-to-one ortholog)			129	104	44	55						
Chen: rs563694				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	**CG15400**	**V7261**	**51**	**72**	**32**	**26**	**–0.5494**	–1.2318	0.1247	–1.7471	0.6194	**1.0972E–01**
	(many-to-one ortholog)			23	34	26	14						
				28	38	6	12						
	ABCB11	**CG3879**	**V42513**	**494**	**418**	**377**	**409**	**0.2484**	0.0527	0.4443	–0.0985	0.5963	**1.1368E–02**
	(many-to-many ortholog)	Multi drug resistance 49		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	**V51165**	**0**	**416**	**0**	**420**	**toxic knockdown**					
		Multi drug resistance 50		0	101	0	68						
				0	227	0	175						
				0	88	0	177						
			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	**V9019**	**177**	**234**	**233**	**240**	**–0.2493**	–0.5243	0.0250	–0.7361	0.2348	**6.8223E–02**
		Multiple drug resistance 65		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						

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				scoring: tub_{P} > RNAi					**confidence interval bounds**				
				1.0 M sucrose		**0.15 M sucrose**			**95%**		**Bonferroni**		
Locus	**Human Gene**	**Fly Gene**	**Insertion**	RNAi	control	RNAi	control	**ln(OR)**	lower	upper	lower	upper	**p-value**
3p25.2	**PPARG**	**CG18023**	**V10396**	**197**	**351**	**487**	**482**	**–0.5875**	–0.8094	–0.3672	–0.9823	–0.1986	**7.4639E–08**
type 2 diabetes	(many-to-one ortholog)	Ecdysone-induced protein 78C		85	157	105	114						
Scott: rs1801282				60	112	156	136						
				52	82	226	232						
3p14.1	**ADAMTS9**	**CG14869**	**V33346**	**183**	**350**	**231**	**315**	**–0.3380**	–0.5927	–0.0841	–0.7896	0.1103	**7.1741E–03**
type 2 diabetes	(many-to-one ortholog)			57	102	38	64						
Zeggini: rs4607103				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	**IGF2BP2**	**CG1691**	**V20321**	**340**	**256**	**338**	**337**	**0.2806**	0.0531	0.5086	–0.1218	0.6850	**1.3260E–02**
type 2 diabetes	(many-to-one ortholog)	IGF-II mRNA-binding protein		107	80	124	112						
Scott: rs4402960				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						
	C3orf65												
	(no ortholog)												
5q13.3	**HMGCR**	**CG10367**	**V108617**	**0**	**131**	**0**	**563**	**toxic knockdown**					
low-density lipoprotein	(one-to-one ortholog)	HMG Coenzyme A reductase		0	39	0	36						
Kathiresan: rs12654264				0	92	0	450						
						0	77						
	COL4A3BP	**CG7207**	**V27914**	**48**	**38**	**52**	**50**	**0.1934**	–0.4214	0.8114	–0.8764	1.2745	**5.5851E–01**
	(one-to-one ortholog)	ceramide transfer protein		14	15	35	38						
				34	23	17	12						
6p22.3	**CDKAL1**	**CG6550**	**V4947**	**111**	**101**	**143**	**146**	**0.1149**	–0.2552	0.4857	–0.5360	0.7683	**5.2831E–01**
type 2 diabetes	(one-to-one ortholog)			69	63	10	14						
Scott: rs7754840				42	38	65	70						
						68	62						
6p21.32	**HLA-DPA1**												
low-density lipoprotein	(no ortholog)												
Willer: rs2254287													
	COL11A2												
	(no ortholog)												
	RXRB	**CG4380**	**V16893**	**97**	**190**	**299**	**332**	**–0.5670**	–0.8699	–0.2680	–1.1058	–0.0424	**1.3486E–04**
	(many-to-one ortholog)	ultraspiracle		40	72	66	63						
				33	63	115	113						
				24	55	118	156						
	SLC39A7	**CG10449**	**V7183***	**0**	**89**	**0**	**184**	**toxic knockdown**					
	(one-to-one ortholog)	Catecholamines up		0	50	0	29						
				0	19	0	82						
				0	20	0	73						

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Table S1 — continued from previous page

				scoring: $\text{tub}_\text{P} >$ RNAi					confidence interval bounds				
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
Locus	**Human Gene**	**Fly Gene**	**Insertion**	RNAi	control	RNAi	control	**ln(OR)**	lower	upper	lower	upper	**p-value**
	HSD17B8	**CG3603**	**V51662***	**48**	**24**	**44**	**34**	**0.4324**	–0.2793	1.1547	–0.7977	1.6992	**2.4075E–01**
	(one-to-one ortholog)			13	8	15	13						
				18	10	7	7						
				17	6	22	14						
	MIR219-1												
	(no ortholog)												
	RING1	**CG5595**	**V27465**	**29**	**451**	**342**	**568**	**–2.2355**	–2.6711	–1.8321	–3.0367	–1.5530	**1.1701E–42**
	(many-to-one ortholog)	Sex combs extra		9	43	45	61						
				5	96	23	115						
				4	59	48	94						
				0	59	39	74						
				6	57	52	58						
				2	36	66	93						
				3	101	69	73						
			V106328	**0**	**520**	**0**	**484**	**toxic knockdown**					
				0	189	0	111						
				0	148	0	173						
				0	183	0	200						
	VPS52	**CG7371**	**V27985**	**64**	**58**	**56**	**63**	**0.2153**	–0.3207	0.7535	–0.7204	1.1586	**4.4048E–01**
	(one-to-one ortholog)			30	31	44	40						
				34	27	12	23						
			V48711	**145**	**162**	**258**	**322**	**0.1106**	–0.1768	0.3978	–0.3974	0.6178	**4.3665E–01**
				79	84	105	151						
				66	78	153	171						
	RPS18	**CG8900**	**V23083**	**285**	**293**	**298**	**274**	**–0.1116**	–0.3497	0.1264	–0.5335	0.3096	**3.4608E–01**
	(many-to-one ortholog)	Ribosomal protein S18		88	85	53	51						
				40	40	30	41						
				157	168	215	182						
7p15.2	**JAZF1**	**CG12054**	**V45983**	**125**	**138**	**229**	**247**	**–0.0232**	–0.3364	0.2895	–0.5764	0.5284	**9.3871E–01**
type 2 diabetes	(one-to-one ortholog)			55	69	79	86						
Zeggini: rs864745				70	69	150	161						
			V45986	**174**	**153**	**289**	**257**	**0.0113**	–0.2727	0.2956	–0.4903	0.5141	**9.4426E–01**
				63	51	104	78						
				111	102	185	179						
7p13	**AEBP1**												
fasting glucose	(no ortholog)												
Dupuis: rs4607517													
	MIR4649												
	(no ortholog)												
	POLD2	**CG12018**	not tested										
	(one-to-one ortholog)	BcDNA:HL03874											
	MYL7	**CG2184**	not tested										
	(many-to-one ortholog)												

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				scoring: $\text{tub}_P > \text{RNAi}$					confidence interval bounds				
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
Locus	**Human Gene**	**Fly Gene**	**Insertion**	RNAi	control	RNAi	control	**ln(OR)**	lower	upper	lower	upper	**p-value**
	GCK	**CG3001**	**V21054**	**0**	**420**	**315**	**349**	**–∞**	–∞	–4.6121	–∞	–3.7697	**7.9623E–85**
	(many-to-many ortholog)	Hexokinase A		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	**V35337**	**208**	**368**	**344**	**445**	**–0.3129**	–0.5403	–0.0865	–0.7168	0.0872	**6.1959E–03**
		Hexokinase C		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	**V47331**	**355**	**431**	**336**	**379**	**–0.0735**	–0.2820	0.1349	–0.4432	0.2960	**5.0040E–01**
		Hex-t2		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	**V46573**	**220**	**246**	**285**	**321**	**0.0072**	–0.2421	0.2565	–0.4341	0.4482	**1.0000E+00**
		Hex-t1		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	**CG1515**	not tested										
	(one-to-one ortholog)												
	CAMK2B												
	(no ortholog)												
7q11.23	**BAZ1B**	**CG4254**	no RNAi										
triglyceride	(one-to-many ortholog)	twinstar											
Willer: rs17145738													
Kooner: rs3812316		**CG6873**	**V22454**	**0**	**28**	**1**	**226**	**toxic knockdown**					
				~~75~~	~~121~~	0	23						
				0	28	0	24						
						0	11						
						1	83						
						0	85						

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Table S1 — continued from previous page

				scoring: tub$_P$ > RNAi					confidence interval bounds				
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
Locus	**Human Gene**	**Fly Gene**	**Insertion**	RNAi	control	RNAi	control	**ln(OR)**	lower	upper	lower	upper	**p-value**
	BCL7B	**CG17252**	**V20410**	**303**	**309**	**225**	**217**	**–0.0557**	–0.3081	0.1965	–0.5025	0.3905	**6.6260E–01**
	(many-to-one ortholog)	BCL7-like		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	**CG18362**	**V52606**	**128**	**230**	**264**	**263**	**–0.5892**	–0.8754	–0.3053	–1.0972	–0.0898	**2.5790E–05**
	(many-to-one ortholog)	Mio		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	**CG1115**	not tested										
	(many-to-one ortholog)												
	DNAJC30	**CG11035**	**V8478**	**126**	**106**	**140**	**180**	**0.4234**	0.0699	0.7786	–0.1977	1.0507	**1.5748E–02**
	(one-to-one ortholog)			48	48	14	13						
				78	58	58	59						
						68	108						
	WBSCR22	**CG10903**	**V27334**	**0**	**164**	**0**	**321**	**toxic knockdown**					
	(one-to-one ortholog)			0	72	0	92						
				0	92	0	229						
	STX1A												
	(no ortholog)												
8p21.3	**LPL**	**CG5966**	**V13163**	**45**	**61**	**35**	**35**	**–0.3025**	–0.9551	0.3473	–1.4428	0.8281	**3.5573E–01**
triglyceride,	(many-to-many ortholog)	(shared: LIPC (15q21.3)		2	8	35	35						
high-density lipoprotein		and LIPG (18q21.1))		20	18								
Willer: rs10503669				23	35								
Kathiresan: rs328													
			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	**V22451**	**0**	**87**	**21**	**72**	**$-\infty$**	$-\infty$	–1.7861	$-\infty$	–0.8024	**3.3388E–07**
		(shared: LIPC (15q21.3)		0	29	6	25						
		and LIPG (18q21.1))		0	21	5	13						
				0	37	10	34						

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				scoring: $\text{tub}_P > \text{RNAi}$					confidence interval bounds				
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
Locus	**Human Gene**	**Fly Gene**	**Insertion**	RNAi	control	RNAi	control	**ln(OR)**	lower	upper	lower	upper	**p-value**
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						
				16	76	129	152						
9p21.3 type 2 diabetes Scott: rs10811661	**MTAP** (one-to-many ortholog)	**CG4802**	not tested										
		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)												

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Table S1 — continued from previous page

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

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Table S1 — continued from previous page

				scoring: tub_P > RNAi					confidence interval bounds				
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
Locus	**Human Gene**	**Fly Gene**	**Insertion**	RNAi	control	RNAi	control	**ln(OR)**	lower	upper	lower	upper	**p-value**
10q25.2	**TCF7L2**	**CG34403**	**V3014**	**7**	**32**	**82**	**77**	**–1.5754**	–2.6214	–0.6662	–3.5391	–0.0785	**1.3333E–04**
type 2 diabetes	(many-to-one ortholog)	pangolin		7	32	71	53						
Sladek: rs7903146						11	24						
11p15.1	**NUCB2**	**CG32190**	**V5319**	**224**	**212**	**543**	**546**	**0.0605**	–0.1679	0.2891	–0.3440	0.4658	**6.1022E–01**
type 2 diabetes	(many-to-one ortholog)	NUCB1		101	88	105	95						
Scott: rs5219				92	101	194	215						
				31	23	244	236						
			V100688	**230**	**330**	**290**	**289**	**–0.3641**	–0.6057	–0.1233	–0.7926	0.0615	**2.4160E–03**
				74	133	80	73						
				79	91	139	145						
				77	106	71	71						
	NCR3LG1												
	(no ortholog)												
	KCNJ11	**CG4370**	**V4341**	**84**	**260**	**21**	**226**	**1.2442**	0.7187	1.8075	0.3522	2.2708	**3.6149E–07**
	(many-to-many ortholog)	Inwardly rectifying potassium channel 2		33	138	9	84						
				9	34	12	101						
				42	88	0	41						
			V108140	**0**	**72**	**0**	**304**	**toxic knockdown**					
				0	14	0	103						
				0	35	0	117						
				0	23	0	84						
		CG6747	**V28430**	**0**	**338**	**0**	**482**	**toxic knockdown**					
		Inwardly rectifying potassium channel		0	135	0	219						
				0	73	0	123						
				0	130	0	140						
			V28431	**0**	**482**	**0**	**484**	**toxic knockdown**					
				0	55	0	254						
				0	165	0	79						
				0	262	0	151						
			V107389	**81**	**115**	**195**	**193**	**–0.3602**	–0.7238	0.0007	–1.0035	0.2729	**4.3830E–02**
				18	24	82	68						
				30	46	57	64						
				33	45	56	61						
		CG10369	**V3886**	**232**	**216**	**187**	**222**	**0.2427**	–0.0347	0.5208	–0.2470	0.7349	**8.7180E–02**
		Inwardly rectifying potassium channel 3		131	94	45	52						
				43	56	102	118						
				58	66	40	52						
			V101174	**103**	**282**	**288**	**387**	**–0.7111**	–0.9950	–0.4314	–1.2174	–0.2207	**2.2441E–07**
				56	160	49	54						
				21	48	167	250						
				26	74	72	83						
	ABCC8	**CG7806**	**V2804**	**265**	**216**	**626**	**639**	**0.2249**	0.0087	0.4416	–0.1576	0.6099	**3.6819E–02**
	(many-to-one ortholog)			123	101	175	201						
				82	76	252	241						
				60	39	199	197						

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				scoring: $tub_P > RNAi$					confidence interval bounds				
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
Locus	**Human Gene**	**Fly Gene**	**Insertion**	RNAi	control	RNAi	control	**ln(OR)**	lower	upper	lower	upper	**p-value**
11p11.2	**EXT2**	**CG8433**	**V4902**	**139**	**153**	**175**	**173**	**–0.1073**	–0.4310	0.2159	–0.6786	0.4624	**5.2576E–01**
type 2 diabetes	(one-to-one ortholog)	Ext2		94	103	14	14						
Sladek: rs1113132				45	50	80	83						
rs11037909						81	76						
rs3740878													
			V4903	**50**	**43**	**215**	**196**	**0.0582**	–0.4175	0.5370	–0.7755	0.9028	**8.1903E–01**
				22	21	5	16						
				28	22	81	71						
						129	109						
			V49808*	**4**	**63**	**3**	**101**	**toxic knockdown**					
				3	46	3	66						
				0	8	0	35						
				1	9								
			V49809	**85**	**86**	**254**	**234**	**–0.0936**	–0.4575	0.2702	–0.7352	0.5473	**6.5675E–01**
				34	31	143	113						
				51	55	111	121						
	ALX4												
	(no ortholog)												
11q23.3	**BUD13**	**CG13625**	not tested										
triglyceride	(one-to-one ortholog)												
Willer: rs12286037													
Kathiresan: rs28927680	**ZNF259**	**CG9060**	**V12665***	**0**	**93**	**1**	**191**	**toxic knockdown**					
	(one-to-one ortholog)	Zpr1		0	32	1	47						
				0	37	0	86						
				0	24	0	58						
	APOA5												
	(no ortholog)												
	APOA4												
	(no ortholog)												
	APOC3												
	(no ortholog)												
	APOA1												
	(no ortholog)												
	SIK3	**CG42856**	not tested										
	(one-to-one ortholog)	Salt-inducible kinase 3											
12q15	**TSPAN8**	**CG6120**	**V3422**	**179**	**169**	**163**	**195**	**0.2364**	–0.0700	0.5435	–0.3037	0.7791	**1.3196E–01**
type 2 diabetes	(many-to-one ortholog)	Tetraspanin 96F		49	52	33	42						
Zeggini: rs7961581				42	27	111	122						
				88	90	19	31						
			V3423	**190**	**200**	**155**	**155**	**–0.0512**	–0.3608	0.2582	–0.5977	0.4948	**7.6107E–01**
				33	21	47	42						
				44	43	69	72						
				113	136	39	41						
			V101411	**208**	**264**	**179**	**227**	**–0.0008**	–0.2770	0.2755	–0.4888	0.4877	**1.0000E+00**
				72	105	52	69						
				76	93	81	100						
				60	66	46	58						
	LGR5												
	(no ortholog)												

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				scoring: $\mathrm{tub}_P >$ RNAi					confidence interval bounds				
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
Locus	**Human Gene**	**Fly Gene**	**Insertion**	RNAi	control	RNAi	control	**ln(OR)**	lower	upper	lower	upper	**p-value**
12q23.3 high-density lipoprotein Willer: rs2338104	**MYO1H** (no ortholog)												
	KCTD10 (many-to-one ortholog)	**CG10465**	**V107131**	**198**	**313**	**244**	**255**	**–0.4134**	–0.6718	–0.1560	–0.8713	0.0410	**1.2206E–03**
				75	103	46	34						
				54	99	145	170						
				69	111	53	51						
	UBE3B (one-to-one ortholog)	**CG5087**	not tested										
	MMAB (no ortholog)												
	MVK (one-to-one ortholog)	**CG33671**	**V49772***	**10**	**65**	**34**	**39**	**–1.7222**	–2.6514	–0.8691	–3.4127	–0.2930	**1.1478E–05**
				2	21	20	26						
				6	23	14	13						
				2	21								
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**	**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: LPL (8p21.3) and LIPG (18q21.1))	**V22451**	**0**	**87**	**21**	**72**	$-\infty$	$-\infty$	–1.7861	$-\infty$	–0.8024	**3.3388E–07**
				0	29	6	25						
				0	21	5	13						
				0	37	10	34						
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)												

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				scoring: tub$_P$ > RNAi					confidence interval bounds				
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
Locus	**Human Gene**	**Fly Gene**	**Insertion**	RNAi	control	RNAi	control	**ln(OR)**	lower	upper	lower	upper	**p-value**
	SLC12A3	**CG4357**	**V30000**	**473**	**445**	**269**	**381**	**0.4088**	0.2012	0.6172	0.0414	0.7790	**7.7131E–05**
	(many-to-many ortholog)	sodium chloride		214	203	42	58						
		cotransporter 69		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	**CG14536**	**V11724**	**198**	**167**	**614**	**539**	**0.0400**	–0.2030	0.2837	–0.3897	0.4722	**7.6354E–01**
	(many-to-one ortholog)	Homocysteine-induced		94	64	110	98						
		endoplasmic reticulum protein		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						
	MIR138-2												
	(no ortholog)												
18q21.1	**LIPG**	**CG5966**	**V13163**	**45**	**61**	**35**	**35**	**–0.3025**	–0.9551	0.3473	–1.4428	0.8281	**3.5573E–01**
high-density lipoprotein	(many-to-many ortholog)	(shared: LPL (8p21.3)		2	8	35	35						
Willer: rs2156552		and LIPC (15q21.3))		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	**V22451**	**0**	**87**	**21**	**72**	**–∞**	–∞	–1.7861	–∞	–0.8024	**3.3388E–07**
		(shared: LPL (8p21.3)		0	29	6	25						
		and LIPC (15q21.3))		0	21	5	13						
				0	37	10	34						
	ACAA2	**CG4600**	**V26562**	**92**	**62**	**216**	**191**	**0.2712**	–0.1209	0.6675	–0.4153	0.9730	**1.8314E–01**
	(one-to-one ortholog)	yippee interacting protein 2		25	18	103	102						
				67	44	113	89						

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				scoring: $\text{tub}_\text{P} >$ RNAi					confidence interval bounds				
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
Locus	**Human Gene**	**Fly Gene**	**Insertion**	RNAi	control	RNAi	control	**ln(OR)**	lower	upper	lower	upper	**p-value**
19p13.2	**SMARCA4**	**CG5942**	**V37720**	**0**	**197**	**0**	**189**	**toxic knockdown**					
low-density lipoprotein	(many-to-one ortholog)	brahma		0	62	0	36						
Willer: rs6511720				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)												
	SPC24												
	(no ortholog)												
	KANK2												
	(no ortholog)												
19p13.11	**GATAD2A**	**CG32067**	**V13066**	**281**	**500**	**271**	**539**	**0.1113**	–0.1006	0.3233	–0.2643	0.4873	**2.9266E–01**
triglyceride,	(many-to-one ortholog)	simjang		71	174	52	107						
low-density lipoprotein				115	172	80	167						
Willer: rs16996148				95	154	139	265						
			V100285	**0**	**437**	**0**	**303**	**toxic knockdown**					
				0	67	0	64						
				0	108	0	112						
				0	262	0	127						
	TSSK6	**CG14305**	**V17477**	**388**	**356**	**485**	**512**	**0.1402**	–0.0544	0.3349	–0.2048	0.4859	**1.6002E–01**
	(many-to-one ortholog)			161	137	78	77						
				126	110	156	157						
				101	109	251	278						
	NDUFA13	**CG3446**	**V42696***	**1**	**120**	**174**	**174**	**–4.7813**	–8.4498	–3.0197	$-\infty$	–2.3002	**4.1032E–28**
	(one-to-one ortholog)			1	80	37	54						
				0	24	68	57						
				0	16	69	63						
	YJEFN3	**CG2974**	not tested										
	(many-to-one ortholog)												
	CILP2												
	(no ortholog)												

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Table S1 — continued from previous page

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

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Table S1 — continued from previous page

				scoring: tub_P > RNAi					confidence interval bounds				
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
Locus	**Human Gene**	**Fly Gene**	**Insertion**	RNAi	control	RNAi	control	**ln(OR)**	lower	upper	lower	upper	**p-value**
	PVRL2	**CG17716**	**V6561**	**271**	**297**	**362**	**395**	**–0.0044**	–0.2282	0.2194	–0.4012	0.3921	**1.0000E+00**
	(many-to-one ortholog)	faint sausage		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	**CG8330**	**V23763**	**0**	**98**	**1**	**38**	**toxic knockdown**					
	(many-to-many ortholog)	tomboy40		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						
				0	74	14	151						
			V105557	**1**	**427**	**4**	**615**	**toxic knockdown**					
				0	207	0	47						
				1	139	4	308						
				0	81	0	260						
		CG12157	**V13177**	**0**	**309**	**0**	**303**	**toxic knockdown**					
		Translocase of outer membrane 40		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						

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Table S1 — continued from previous page

				scoring: tub$_P$ > RNAi					confidence interval bounds				
				1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
Locus	**Human Gene**	**Fly Gene**	**Insertion**	RNAi	control	RNAi	control	**ln(OR)**	lower	upper	lower	upper	**p-value**
	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**	**559**	**293**	**303**	**–0.3788**	–0.5919	–0.1660	–0.7569	–0.0019	**3.8680E–04**
				96	130	53	52						
				91	196	35	52						
				111	152	87	75						
				72	81	118	124						
			V45998	**183**	**216**	**117**	**136**	**–0.0153**	–0.3436	0.3135	–0.5939	0.5651	**9.3589E–01**
				51	72	29	32						
				56	75	36	31						
				40	42	36	38						
				36	27	16	35						
			V105491	**19**	**640**	**566**	**784**	**–3.1901**	–3.7162	–2.7203	–4.1735	–2.4106	**8.1235E–92**
				1	140	31	56						
				0	102	52	78						
				2	150	14	73						
				4	56	141	132						
				3	52	85	100						
				9	58	121	127						
				0	82	122	218						

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)

	scoring: $\mathrm{tub_P} > \mathrm{RNAi}$					confidence interval bounds				
	1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
Fly Strain	RNAi	control	RNAi	control	**ln(OR)**	lower	upper	lower	upper	**p-value**
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 $\mathrm{tub_P}$-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)

	scoring					confidence interval bounds				
	> **RNAi**$^{\text{dHHEX-V15721}}$		**w**^{1118} **genetic background**			**95%**		**Bonferroni**		
Food	with tub$_{\text{P}}$ >	control	with tub$_{\text{P}}$ >	control	**ln(OR)**	lower	upper	lower	upper	**p-value**
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**	**$-\infty$**	$-\infty$	–2.6482	$-\infty$	–2.0831	**3.6364E–14**
	0	62	69	75						
0.15 M sucrose + 1.7 M fructose	**0**	**119**	**108**	**98**	**$-\infty$**	$-\infty$	–3.5113	$-\infty$	–2.9636	**2.2245E–28**
	0	119	108	98						
0.15 M sucrose + 0.1 M glucosamine	**0**	**100**	**27**	**55**	**$-\infty$**	$-\infty$	–2.4568	$-\infty$	–1.8684	**2.7095E–11**
	0	100	27	55						

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Table S3 — continued from previous page

	scoring					confidence interval bounds				
	> **RNAi$^{\mathrm{dHHEX\text{-}V15721}}$**		**w^{1118} genetic background**			**95%**		**Bonferroni**		
Food	with tub$_{\mathrm{P}}$>	control	with tub$_{\mathrm{P}}$>	control	**ln(OR)**	lower	upper	lower	upper	**p-value**
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**	**$-\infty$**	$-\infty$	–3.0785	$-\infty$	–2.5281	**5.6924E–21**
	0	34	23	25						
	0	31	26	39						
	0	58	28	47						
0.15 M sucrose + 10 mM H_2O_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$^{\mathrm{dHHEX\text{-}V15721}}$ and w^{1118} (genetic background control) males crossed to tub$_{\mathrm{P}}$-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)

			scoring					confidence interval bounds				
			1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
Driver	**crossed to**	**stage**	RNAi	control	RNAi	control	**ln(OR)**	lower	upper	lower	upper	**p-value**
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$^{dHHEX\text{-}V15721}$	(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						
					43	53						
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						
	UAS-RNAi$^{dHHEX\text{-}V15721}$	(eclosers)	**859**	**822**	**652**	**672**	**0.0742**	–0.0725	0.2210	–0.1370	0.2855	**3.2122E–01**
			155	150	116	145						
			410	370	266	294						
			294	302	270	233						
Sns$_{GCN}$-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$^{dHHEX\text{-}V15721}$	(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						

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Table S4 — continued from previous page

			scoring					confidence interval bounds				
			1.0 M sucrose		0.15 M sucrose			95%		Bonferroni		
Driver	**crossed to**	**stage**	RNAi	control	RNAi	control	**ln(OR)**	lower	upper	lower	upper	**p-value**
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$^{dHHEX\text{-}V15721}$	(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$^{dHHEX\text{-}V15721}$	(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$^{dHHEX\text{-}V15721}$	(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$_\mathrm{P}$ 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 w^{1118} (genetic background control) on 0.15 M and 1.0 M sucrose. Pupariation was scored for tub$_\mathrm{P}$-GAL4, sns$_\mathrm{GCN}$-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)

		scoring					confidence interval bounds				
		knockdown		background			95%		Bonferroni		
Driver	**Stage**	1.0 M sucrose	0.15 M sucrose	1.0 M sucrose	0.15 M sucrose	**ln(OR)**	lower	upper	lower	upper	**p-value**
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 w^{1118} (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$^{dHHEX\text{-}V15721}$, 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 1.45 1.47 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 1.42		1.39			
1.36 1.38 1.38 1.38 1.38 1.38 1.38 1.39 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$^{dHHEX\text{-}V15721}$, 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.

Table S8 – triglycerides

(data associated with Figure 4D–E)

triglycerides (µg/mg tissue)

(control)	**larvae**	(experimental)	(control)	**adults**	(experimental)
62.86	mean	51.11	53.24	mean	40.93
12.32	SD	11.47	14.53	SD	8.09
63.29	median	48.65	50.72	median	41.19
52.59-70.27	IQR	42.76-61.78	45.38-57.01	IQR	37.06-45.55
31.81-88.92	range	34.35-67.69	38.46-101.71	range	28.93-58.95
			101.71		
88.92					
81.31 81.93					
76.16 77.33 77.50 78.19					
74.01					
69.04 69.74 70.79					
64.74 64.78 65.85 66.80 66.95 67.40		64.55 65.93 67.69			
60.88 61.50 62.85 62.91 63.67			60.17		
59.06 59.44 59.68		59.00	56.14 56.97 57.06 58.35		58.95
53.96 55.06		55.20	52.81 53.39		
48.34 49.37 50.27 51.08 51.22		50.27	48.64		48.15 51.62 51.73
45.32 47.17 47.88		46.89 46.97 47.02	45.19 45.56 46.00 47.09		47.48
			40.33 43.96		40.91 41.46 41.50 42.47 42.99 43.61
		36.83 38.64	38.46		36.56 37.55 37.80 38.32 39.76
		34.35			
31.81					28.93 29.23 29.28 30.23

Table S8. Cg>RNAi$^{dHHEX\text{-}V15721}$, 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.