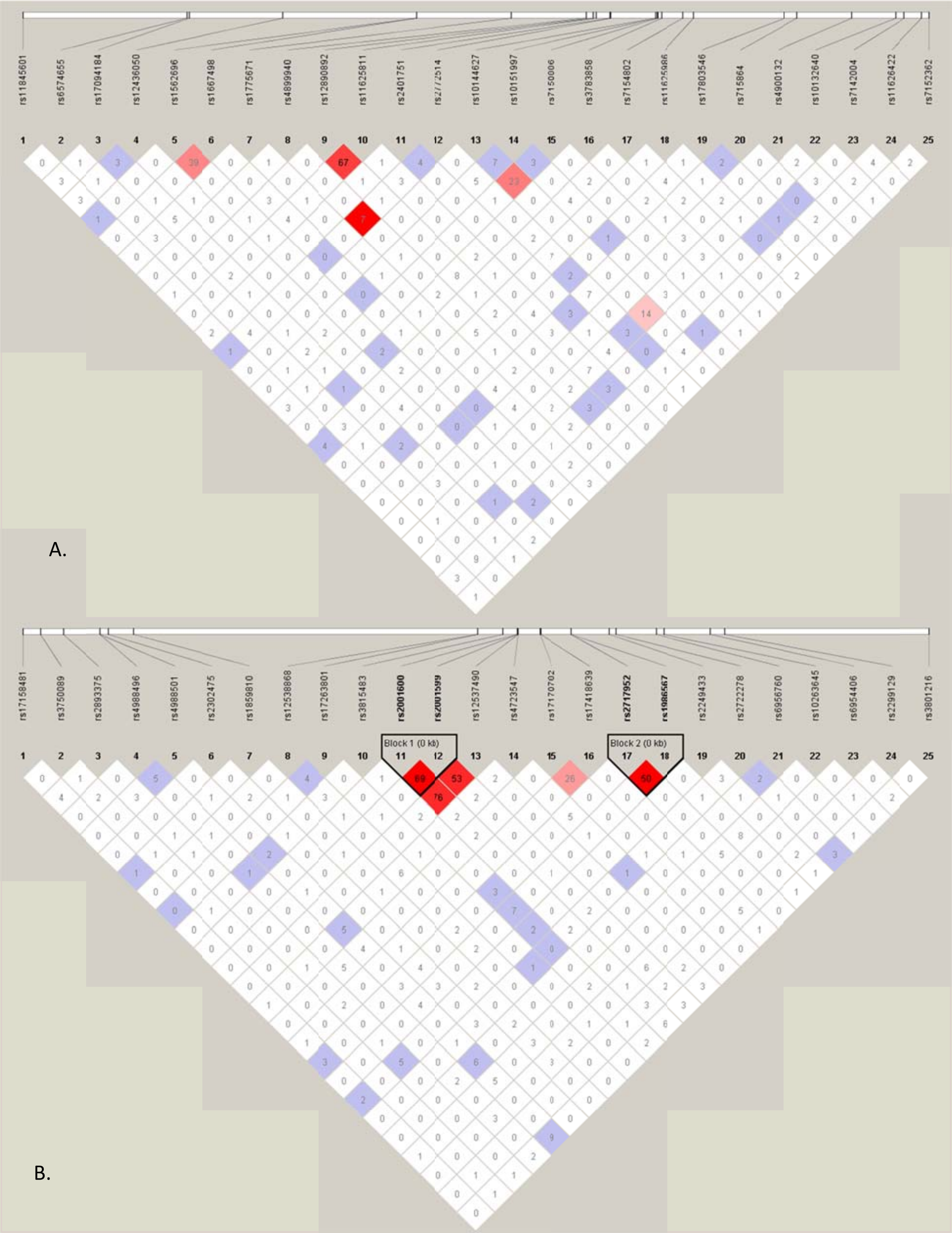
Supplementary Figure: Linkage disequilibrium between the 50 SNPs further evaluated in the validation cohort



Supplementary figure legend:

We prioritized 50 SNPs (25 SNPs under each QTL) for validation in the NOMAS DR subcohort. Pairwise r^2 between these SNPs was estimated in the probands of the 100 DR families and is displayed by gray-shaded square with the hundredths of r^2 value inside. The shades of gray are proportional to the r^2 values, with the darkest gray being the highest r2 value. A). Chromosome 7 SNPs; B) Chromosome 14 SNPs.

Supplementary Table 1.

	Without SNP Covariates		With SNP Covariates		Chi-Square	Degree of Freedom	P value
SNP	**MLOD***	**Log-Likelihood**	**MLOD**	**Log-Likelihood**			
chromosom 7							
rs3815483	3.34	-418.10	2.35	-413.71	8.78	1	0.0061
rs2001600	3.34	-418.10	2.92	-414.03	8.15	1	0.0086
All SNPs	3.34	-418.10	1.89	-410.59	15.02	2	0.0002
chromosom 14							
rs7152362	2.18	-203.45	1.95	-202.59	1.71	1	0.3820
rs17803546	2.18	-203.45	1.90	-200.60	5.71	1	0.0337
rs10151430	2.17	-203.58	2.01	-202.32	2.52	1	0.2248
rs1667498	2.01	-202.26	1.93	-201.11	2.29	1	0.2604
rs10144627	2.18	-203.45	1.96	-201.37	4.15	1	0.0833
rs10151997	2.18	-203.45	1.96	-201.67	3.55	1	0.1191
All SNPs	2.00	-202.40	1.09	-193.81	17.17	6	0.0174

*MLOD=maximum of multipoint LOD score. To ensure a meaningful comparison of LOD score change before and after including the associated SNPs as covariates, we kept the same families used in the before and after analysis. As a result, the MLOD varied slightly in the analysis without inclusion of the associated SNP genotype as a covariate due to exclusion of different families that had| missing genotypes for the associated SNPs.

Supplementary Table 2.

						Family Date Set						NOMAS DR		
								P values						
Chr	SNP	BP	Allele*	Gene	Function	MAF**	β†	QTDT	MG	QLTD	FBAT	MAF**	β	P value
7	rs17158481	29927822	C	SCRN1	utr-3	0.064	-0.0324	0.008	0.497	0.055	0.062	0.083	-0.0020	0.844
7	rs3750089	30167123	C	C7orf41	utr-3	0.383	-0.0094	0.127	0.229	0.012	0.368	0.322	-0.0079	0.174
7	rs2893375	30477377	C	NOD1	intron	0.149	-0.0182	0.042	0.168	0.018	0.008	0.165	-0.0008	0.914
7	rs4988496	30975210	A	GHRHR	missense	0.149	0.0186	0.033	0.013	0.096	0.322	0.155	0.0060	0.425
7	rs4988501	30978009	G	GHRHR	intron	0.250	-0.0186	0.014	0.008	0.015	0.107	0.242	-0.0052	0.427
7	rs2302475	31088025	C	ADCYAP1R1	intron	0.484	0.0164	0.01	0.088	0.017	0.041	0.471	-0.0035	0.525
7	rs1859810	31428355	C			0.199	-0.0180	0.036	0.001	0.00035	0.294	0.192	-0.0091	0.191
7	rs12538868	36091051	T	PP13004	utr-3	0.332	-0.0125	0.051	0.152	0.109	0.042	0.389	0.0031	0.584
7	rs17263801	36091368	A	PP13004	utr-3	0.087	-0.0340	0.006	0.282	0.044	0.081	0.080	0.0019	0.861
7	rs3815483	36427864	G	ANLN	intron	0.069	0.0477	0.00023	0.00026	0.002	0.039	0.067	0.0000	0.998
7	rs2001600	36620605	C	AOAH	intron	0.410	-0.0198	0.001	0.001	0.003	0.00008	0.410	0.0059	0.309
7	rs2001599	36620762	C	AOAH	intron	0.500	-0.0175	0.004	0.003	0.019	0.00048	0.470	0.0062	0.274
7	rs12537490	36626416	T	AOAH	intron	0.398	-0.0190	0.002	0.005	0.016	0.00015	0.385	0.0020	0.73
7	rs4723547	36633473	A	AOAH	intron	0.133	-0.0216	0.006	0.062	0.001	0.065	0.135	-0.0018	0.828
7	rs17170782	36923066	A	ELMO1	intron	0.282	-0.0217	0.004	0.506	0.011	0.038	0.251	0.0053	0.415
7	rs17418639	36937132	G	ELMO1	intron	0.197	-0.0204	0.008	0.419	0.01	0.096	0.196	0.0039	0.587
7	rs2717952	37352622	C	ELMO1	intron	0.319	-0.0176	0.007	0.004	0.00046	0.023	0.317	-0.0051	0.433
7	rs1986567	37353174	G	ELMO1	intron	0.484	-0.0155	0.011	0.007	0.007	0.01	0.449	-0.0098	0.089
7	rs2249433	37867712	T	TXNDC3	intron	0.245	-0.0235	0.002	0.032	0.00015	0.269	0.177	0.0064	0.362
7	rs2722278	37957441	A	EPDR1	utr-3	0.106	-0.0094	0.361	0.041	0.036	0.33	0.125	0.0047	0.579
7	rs6956760	38504422	G	AMPH	intron	0.154	0.0255	0.002	0.874	0.39	0.003	0.182	-0.0072	0.316
7	rs10263645	38603415	C	AMPH	intron	0.282	-0.0142	0.035	0.727	0.01	0.003	0.293	0.0063	0.299
7	rs6954406	39243640	G	POU6F2	intron	0.495	-0.0131	0.034	0.005	0.006	0.032	0.492	0.0062	0.261
7	rs2299129	39433829	C	LOC100134410	intron	0.303	-0.0138	0.065	0.033	0.007	0.05	0.316	0.0078	0.187
7	rs3801216	42199807	A	GLI3	intron	0.226	0.0237	0.001	0.033	0.046	0.001	0.292	-0.0146	**0.02**
14	rs11845601	78260765	C	NRXN3	intron	0.133	-0.0175	0.009	0.02	0.028	0.11	0.149	-0.0007	0.922
14	rs6574655	80978357	A	LOC3882	intron	0.255	-0.0168	0.004	0.023	0.007	0.055	0.281	0.0093	0.067
14	rs17094184	81012569	C	SEL1L	utr-3	0.074	0.0173	0.096	0.025	0.13	0.079	0.061	0.0098	0.314

14	rs12436050	82572244	G			0.293	0.0130	0.025	0.024	0.012	0.005	0.282	-0.0087	0.081
14	rs1562696	84784436	T			0.101	-0.0243	0.005	0.27	0.028	0.012	0.123	-0.0094	0.179
14	rs1667498	84784618	A			0.081	-0.0313	0.00062	0.103	0.006	0.1	0.088	-0.0083	0.33
14	rs1775671	86373672	C			0.261	-0.0187	0.002	0.387	0.005	0.007	0.265	0.0033	0.542
14	rs4899940	87623620	A			0.473	0.0140	0.006	0.007	0.003	0.021	0.485	0.0089	0.062
14	rs12890892	87741400	A	KCNK1	intron	0.431	0.0167	0.002	0.012	0.003	0.074	0.446	0.0067	0.171
14	rs11625811	87792126	A	KCNK1	intron	0.452	0.0115	0.034	0.004	0.008	0.644	0.468	0.0033	0.5
14	rs2401751	88016374	A	PTPN21	missense	0.319	0.0115	0.032	0.204	0.098	0.192	0.305	0.0098	0.07
14	rs2772514	88023156	C	PTPN21	intron	0.080	-0.0145	0.135	0.019	0.008	0.015	0.073	-0.0076	0.401
14	rs10144627	88766285	T	FOXN3	intron	0.442	0.0198	0.00023	0.023	0.002	0.047	0.456	0.0023	0.624
14	rs10151997	88786186	T	FOXN3	intron	0.053	0.0394	0.001	0.032	0.047	0.452	0.069	-0.0020	0.835
14	rs7150886	88801851	C	FOXN3	intron	0.362	-0.0180	0.001	0.215	0.006	0.45	0.334	-0.0082	0.09
14	rs3783858	88863309	C	FOXN3	intron	0.176	-0.0186	0.012	0.15	0.039	0.014	0.127	0.0108	0.13
14	rs7154802	89222935	C			0.239	-0.0140	0.018	0.168	0.022	0.008	0.288	0.0001	0.98
14	rs11625986	89398930	G	C14orf143	intron	0.117	-0.0204	0.006	0.133	0.009	0.155	0.135	0.0057	0.4
14	rs17803546	90906477	A	CCDC88C	intron	0.218	0.0222	0.001	0.008	0.001	0.089	0.217	0.0037	0.517
14	rs715864	91116389	T	CATSPERB	near-gene-5	0.069	-0.0091	0.344	0.007	0.022	0.037	0.078	0.0025	0.784
14	rs4900132	92029990	G	SLC24A4	utr-3	0.192	-0.0077	0.234	0.314	0.033	0.89	0.201	-0.0002	0.967
14	rs10132640	92754566	C	C14orf13	intron	0.266	-0.0178	0.005	0.581	0.028	0.001	0.197	-0.0060	0.329
14	rs7142004	92905338	A	KIAA149	intron	0.043	-0.0346	0.005	0.131	0.017	0.02	0.066	0.0099	0.315
14	rs11626422	93191522	A	KIAA149	intron	0.170	-0.0199	0.003	0.042	0.003	0.02	0.163	0.0021	0.738
14	rs7152362	93310468	A	PRIMA1	intron	0.441	-0.0197	0.00007	0.095	0.002	0.003	0.413	-0.0098	**0.047**

*Allele is the minor allele and also the tested allele for both family-based and NOMAS DR association

**MAF: minor allele frequency for the family study was computed in probands only and in everyone for the NOMAS DR cohort

† regression coefficients for the within family components of the genotype scores, taken from SOLAR QTDT

We prioritized 50 SNPs (25 SNPs under each QTL) for validation in the NOMAS DR subcohort. P values from the QTDT QLTD, MG and FBAT tests in 100 DR families and the linear regression test in 553 NOMAS DR subjects are shown in the table. P values less than 0.05 in the linear regression test are in bold.