

SUPPLEMENTAL MATERIAL

UKCVD

The **HIFMECH** study comprises Caucasian male survivors of a first MI aged <60 years (excluding patients with FH and insulin-dependent diabetes mellitus) and population-based individuals of the same age and region recruited from four centres in Europe: Stockholm, Sweden and London, England for the North and Marseille, France and San Giovanni Retondo, Italy representing the South [1]. In all, a total of 598 post infarction patients and 653 controls were included in the study. Patients and control subjects were examined in parallel in the early morning after an overnight fast. Post-infarction patients were investigated 3 to 6 months after the acute event. Blood samples were obtained from the antecubital vein after an overnight fast, collected into citrate (3.8% citrate, 0.129 mol/L) and centrifuged at 2500g for 30 minutes at 4°C.

The **Simon Broome** study is a cross-sectional study comprising 410 Caucasian patients with treated heterozygous FH aged 18 years recruited from 6 lipid clinics in the UK. Recruitment methods, inclusion and exclusion and diagnostic criteria were as defined [2, 3]. CAD was documented in 104 of the 211 men and in 55 of the 199 women with mean ages of onset of 43.1 and 46.5 years, respectively.

University College London Diabetes and Cardiovascular disease Study (UDACS): UDACS is a cross-sectional sample of diabetes patients designed to study the association between common genetic variants and biochemical risk factors implicated in coronary heart disease (CHD) in patients with diabetes. It comprises of 1014 subjects consecutively recruited from the diabetes clinic at UCL Hospitals in 2001–2. All patients had diabetes according to WHO criteria and analysis was restricted to subjects with T2D with telomere length measurement data (N=742). The full characteristics of patients have been reported previously [4].

The European Atherosclerosis Research Study (EARS) II was undertaken to compare postprandial responses (oral glucose tolerance test [OGTT] and oral fat tolerance test [OFTT]) of male case subjects (n=407) between 18 and 28 years old whose father had a proven myocardial infarction before the age of 55 years and male control subjects (n=415) who were age-matched and were recruited irrespective of family history. The subjects were recruited from 14 European university student populations from 11 European countries, which were divided into 4 regions: Baltic (Estonia and Finland); United Kingdom; Middle Europe (Belgium, Denmark, Germany, and Switzerland); and South Europe (Greece, Italy, Portugal and Spain). The study design has been described previously [5].

UKTWIN

The UKTWIN cohort consisted of a group of twins ascertained to study the heritability and genetics of age-related diseases (<http://www.twinsuk.ac.uk/>). These unselected twins were recruited from the general population through national media campaigns in the UK and shown to be comparable to age-matched population singletons in terms of disease related and lifestyle characteristics [6]

NHS

The NHS is a prospective cohort study of 121,700 female registered nurses in 11 states in the United States who were 30-55 years of age at enrollment. In 1976 and biennially thereafter, detailed information from participants was collected by self-administered questionnaires. Participants in this study were selected for a nested case-control study of telomere length and postmenopausal breast cancer risk from the subcohort of 32,826 women who donated a blood sample in 1989-90 [7]. Eligible cases consisted of postmenopausal women of European ancestry with pathologically confirmed incident invasive breast cancer diagnosed anytime after blood collection up to June 1, 2004 with no prior diagnosis of cancer. Controls were randomly selected postmenopausal women free of cancer and matched to cases according to age, blood collection, and ethnicity. Completion of the questionnaire and submission of the blood sample was considered to imply informed consent. No significant difference was observed for log relative telomere length between 1,122 cases and 1,147 controls and no significant association with postmenopausal breast cancer risk [9]; therefore, we included telomere length data from both breast cancer cases and controls for the current study [8].

PLCO

The PLCO Cancer Screening Trial is an ongoing randomized trial with 154,942 persons aged 55 to 74 enrolled between September 1993 and July 2001 from 10 screening centers nationwide [9]. Detailed questionnaire data was collected from all subjects at baseline. Participants provided blood and tissue samples for etiologic studies of cancer [10] and all participants provided written informed consent. Participants in this study were male subjects selected for a nested case-control study of telomere length, prostate cancer risk, and life-style variables [11]. Eligible cases and controls consisted of non-Hispanic white men aged 55 to 74 who had been screened for prostate cancer (PSA test) prior to October 1, 2003, completed a baseline questionnaire of cancer risk factors, provided a blood sample 1 month to 3 years prior to prostate cancer diagnosis for cases, and did not have a personal history of cancer prior to study entry. All cases had pathologically confirmed incident aggressive prostate cancer and a Gleason

score of ≥ 7 . No significant difference was observed for relative telomere length between 616 cases and 1,061 matched controls and no significant association with aggressive prostate cancer risk [11]; therefore, we included telomere length data from both prostate cancer cases and controls for the current study.

MDACC

MD Anderson Cancer Center study included controls recruited from 3 independent case-control studies in lung, bladder, and kidney cancer. Detailed information on study population has been described previously. Controls were healthy individuals without a prior history of cancer (except nonmelanoma skin cancer) recruited from Kelsey-Seybold Clinic (Houston, TX) for lung and bladder studies and via random digit dialing in Texas for kidney study. Trained MD Anderson interviewers collected epidemiologic and demographic data through in-person interviews [12].

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UKCVD

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UKTWIN

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NHS

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PLCO

We thank the staff of the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial, and acknowledge the study participants for their contributions. This PLCO TL work was supported in part by the Intramural Research Program of the NIH, National Cancer Institute, Division of Cancer Epidemiology and Genetics.

MDACC

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Supplementary Table 1: AIDHS/SDS discovery and replication (Stage 1), Stage 2, and Stage 3 study cohorts (N=16,998)

Study	Ethnic Group	Replication Stage	Replication	Total (N)
AIDHS/SDS GWAS	Punjabi Sikh	Discovery Stage 1	-	1616
AIDHS/SDS	Punjabi Sikh	Stage 1		2397
UKCVD	CE	Stage 2		2952
UKTWIN	CE	Stage 3	Look-up	4899
NHS	CE	Stage 3	Look-up	1944
PLCO	CE	Stage 3	Look-up	1610
MDACC	CE	Stage 3	Look-up	1580

Supplementary Table 2A: Clinical characteristics of Punjabi Sikh Discovery and Stage 1 Replication (N= 4013)

	AIDS/SDS		<i>P</i>
	DISCOVERY	STAGE 1	
N	1616	2397	
Age (yrs)	53.1 (12.2)	51.2 (13.8)	5.2E-01
Gender (% males)	53.0	57.0	2.5E-01
SYBP (mmHg)	139 (23.4)	143.5 (12.1)	8.6E-01
DYSBP (mmHg)	83.6 (12.8)	83 (12.3)	9.7E-01
BMI (kg/m²)	26.8 (5.0)	26.8 (11.3)	8.1E-01
Waist (cm)	93.7 (11.9)	92.1 (12.2)	9.2E-01
WHR	0.95 (0.08)	0.94 (0.09)	9.3E-01
FBG (mg/dL)	123.3 (47.6)	127.7 (50.4)	9.5E-01
HOMA-IR	2.1 (1.9)	2.1 (2.0)	9.1E-01
%T2D	52	46	6.2E-01
% CHD	11	21	3.4E-02
Relative Telomere Length	1.95 (0.47)	1.04 (0.68)	2.7E-02

SYBP- systolic blood pressure, DYSBP-diastolic blood pressure, BMI-body mass index, WHR-waist to hip ratio, FBG-fasting blood glucose, T2D-type II diabetes, CHD-Coronary Heart Disease, HOMA-IR-Homeostatic Model Assessment-Insulin Resistance

Values in parentheses are geometric mean and SD.

Supplementary Table 2B: Clinical characteristics of AIDS/SDS and other populations (N=16,998)

	AIDS/SDS	UKCVD	P	UKTWIN	P	NHS	P	PLCO	P	MDACC	P
	N=4013	N=2952		N=4899		N=1944		N=1610		N=1580	
Age	51.9 (13.4)	51.6 (5.4)	9.5E-01	51.02 (13.2)	2.1E-01	58.5 (6.4)	9E-01	63.9 (5.0)	4E-01	62.7 (10.7)	5.2E-01
N-Males (%)	2219 (55.3)	2488 (84.2)		440 (9.0)		0 (0)		1610 (100)		1139 (72.1)	
BMI (Kg/m²)	26.8 (8.7)	26.6 (3.3)	1.8E-01	25.4 (4.7)	8.8E-01	-		-		27.6 (0.2)	9.2E-01
SYBP (mmHg)	141.4 (17.3)	127.9 (15.7)	5.6E-01	122.7(15.9)	4.2E-01	-				-	
N-Current Smokers (%)	-	259 (23.7)		756 (15.4)		258 (13.3)		160 (9.9)		295 (18.7)	
N-CHD (%)	678 (16.9)	527 (48.3)	6.9E-11	-		-		-		-	
Relative Telomere Length (COMBINED)	1.33 (0.78)	1.19 (0.37)	8.7E-01	3.71 (0.69)	4.3E-04	2.79 (0.35)	4.6E-02	2.58 (0.56)	2.5E-01	1.20 (0.40)	7.4E-01
Relative Telomere Length (HEALTHY)	1.67 (0.49)	1.28 (0.66)		3.46 (0.61)		2.82(0.37)		2.55(0.65)		1.37(0.31)	
N (HEALTHY)	1762	130 (Males only)		119 (Females only)		182 (Females only)		62 (Males only)		82	

BMI- Body Mass Index, SYBP- Systolic Blood Pressure, CHD- Coronary Heart Disease Values in parentheses are geometric mean and SD, HEALTHY- non-smokers, non-drinkers.

Supplementary Table 3: Primers used to measure relative telomere length

SINGLE COPY GENE	
36b4F	5'CAGCAAGTGGGAAGGTGTAATCC3'
36b4R	5'CCCATTCTATCATCAACGGGTACAA3'

TELOMERE	
tel1F	5'GGTTTTTGAGGGTGAGGGTGAGGGTGAGGGTGAGGGT3'
tel2R	5'TCCCGACTATCCCTATCCCTATCCCTATCCCTATCCCTA3'

Reference: Cawthon RM. Telomere measurement by quantitative pcr. Nucleic Acids Res 2002; 30:e47.

Supplementary Table 4: Punjabi Sikh Initial Discovery Analysis

SNP	Chr	Position	GENE	Strand	Genotyped	Info	effect_allele	base_allele	freq_effect	BETA	SE	P	N	HWE
16-58234260	16	58234260	CSNK2A2	+	0	0.92405	GA	G	0.179888	-0.46998	0.089254	1.40E-07	1478.93	0.18537
rs11076223	16	58239558	CSNK2A2	+	0	0.8797	G	T	0.174177	-0.48376	0.092736	1.82E-07	1478.99	0.20524
rs8058372	16	58238081	CSNK2A2	+	0	0.90006	A	C	0.17595	-0.4752	0.091274	1.93E-07	1478.93	0.20847
rs1834021	16	58234767	CSNK2A2	+	0	0.93393	C	T	0.176221	-0.46637	0.089581	1.93E-07	1478.95	0.2086
rs7196068	16	58234135	CSNK2A2	+	0	0.93805	A	G	0.176559	-0.46464	0.08931	1.97E-07	1478.92	0.20956
rs58553914	16	58233709	CSNK2A2	+	0	0.93331	C	T	0.176378	-0.46501	0.089591	2.10E-07	1479	0.20956
rs73549172	16	58181055	CSNK2A2	+	0	0.99137	A	G	0.186092	-0.44222	0.085524	2.33E-07	1479	0.3898
16-58139084	16	58139084		+	0	0.86028	A	AC	0.157648	-0.50124	0.097234	2.54E-07	1478.91	0.14033
16-58240273	16	58240273		+	0	0.86692	C	CTTTAT	0.165057	-0.49055	0.095301	2.64E-07	1478.99	0.18512
rs11860708	16	58178596	CSNK2A2	+	1	1	A	G	0.186613	-0.43861	0.085233	2.66E-07	1479	0.44087
16-58179843	16	58179843	CSNK2A2	+	0	0.99278	C	CA	0.185765	-0.43905	0.085504	2.82E-07	1479	0.38871
rs58588258	16	58189271	CSNK2A2	+	0	0.9929	A	C	0.18233	-0.44142	0.086025	2.88E-07	1478.99	0.29605
rs7185651	16	58187826	CSNK2A2	+	0	0.99314	G	A	0.182366	-0.44118	0.086027	2.92E-07	1479	0.38132
rs59165986	16	58186952	CSNK2A2	+	0	0.99331	T	C	0.182386	-0.44101	0.086028	2.95E-07	1479.01	0.38132
rs8044707	16	58240972	CSNK2A2	+	0	0.83798	T	C	0.159785	-0.50274	0.098269	3.12E-07	1478.95	0.20705
rs111234535	16	58137426	C16orf80	+	0	0.83258	A	G	0.1428	-0.52768	0.10353	3.45E-07	1478.95	0.28666
rs77762167	16	58141185	C16orf80	+	0	0.88594	G	T	0.160847	-0.47695	0.095018	5.18E-07	1478.95	0.12263
rs74019786	16	58141441	C16orf80	+	0	0.88824	G	A	0.161014	-0.47564	0.094855	5.32E-07	1478.96	0.12263
rs74019790	16	58141827	C16orf80	+	0	0.89149	C	T	0.161436	-0.47352	0.0946	5.57E-07	1478.98	0.14729
rs74019791	16	58141882	C16orf80	+	0	0.89214	G	A	0.161297	-0.47333	0.094581	5.60E-07	1478.96	0.14729
rs74019792	16	58141933	C16orf80	+	0	0.89256	A	G	0.161331	-0.47309	0.094552	5.63E-07	1478.93	0.14729
rs78955299	16	58141203	C16orf80	+	0	0.88065	T	C	0.161021	-0.4764	0.095259	5.70E-07	1478.98	0.12263
rs55990878	16	58142126	C16orf80	+	0	0.89428	C	T	0.161455	-0.47219	0.094432	5.72E-07	1478.94	0.14729
rs60765503	16	58144761	C16orf80	+	0	0.91474	G	A	0.161872	-0.46577	0.093272	5.92E-07	1478.96	0.12392
rs2098713	5	37144574	C5orf42	+	1	0.99904	T	C	0.470588	-0.33379	0.066939	6.15E-07	1479.01	0.75422
rs74019794	16	58144179	C16orf80	+	0	0.91168	C	G	0.161758	-0.46544	0.093449	6.34E-07	1478.96	0.12392
rs61535084	16	58143889	C16orf80	+	0	0.90953	G	T	0.161949	-0.46549	0.093518	6.44E-07	1478.92	0.12392
rs113577652	16	58232261		+	0	0.93279	A	C	0.165544	-0.45379	0.091168	6.44E-07	1478.98	0.072531
rs76411253	5	1.08E+08	FER	+	0	0.80217	A	G	0.077956	0.70129	0.1409	6.46E-07	1478.95	0.58828
rs10445026	16	58143253	C16orf80	+	0	0.90477	G	A	0.162145	-0.46641	0.093722	6.47E-07	1478.91	0.12481
rs74019793	16	58144117	C16orf80	+	0	0.90114	G	A	0.163483	-0.46385	0.093584	7.18E-07	1478.89	0.10581
rs57827735	16	58144938	C16orf80	+	0	0.92214	C	T	0.162169	-0.4599	0.092798	7.20E-07	1478.94	0.12402
rs75241789	16	58224666	CSNK2A2	+	0	0.98153	A	G	0.171146	-0.4346	0.087918	7.69E-07	1478.95	0.098147
rs149021498	16	58231487	CSNK2A2	+	0	0.96706	A	G	0.165296	-0.4439	0.089837	7.76E-07	1478.93	0.1074
rs74019837	16	58231266	CSNK2A2	+	0	0.96862	T	C	0.165424	-0.44336	0.089735	7.78E-07	1478.93	0.10811
rs77325010	16	58230324	CSNK2A2	+	0	0.97569	G	A	0.165989	-0.44056	0.089276	8.03E-07	1478.96	0.10943
rs57474112	16	58228856	CSNK2A2	+	0	0.98667	G	A	0.166865	-0.4362	0.088575	8.45E-07	1479.03	0.091713
rs55691416	16	58228735	CSNK2A2	+	0	0.98752	C	G	0.166942	-0.43587	0.088521	8.48E-07	1479.02	0.091713
rs74019833	16	58219939	CSNK2A2	+	0	0.99846	C	T	0.167861	-0.4314	0.08785	9.08E-07	1478.95	0.11173
16-58239268	16	58239268		+	0	0.88625	AT	A	0.160108	-0.46605	0.094926	9.12E-07	1478.94	0.080403
rs3743578	16	58217799	CSNK2A2	+	0	0.99869	T	C	0.1678	-0.43121	0.087848	9.17E-07	1478.99	0.11173
rs16959780	16	58217759	CSNK2A2	+	0	0.99869	A	T	0.167798	-0.43121	0.087848	9.17E-07	1478.98	0.11173
rs61667621	16	58217564	CSNK2A2	+	0	0.99869	C	T	0.1678	-0.43119	0.087848	9.18E-07	1478.99	0.11173
rs301869	5	37140597	C5orf42	+	0	0.97887	A	T	0.474587	-0.33489	0.068235	9.20E-07	1478.95	0.71505
rs12149696	16	58215752	CSNK2A2	+	0	0.99873	C	G	0.167824	-0.43102	0.087843	9.26E-07	1478.95	0.11173

16-58193808	16	58193808	CSNK2A2	+	0	0.98885	G	GT	0.168759	-0.43288	0.088344	9.59E-07	1478.99	0.13736
rs112480836	16	58232237	CSNK2A2	+	0	0.95553	A	C	0.161282	-0.44527	0.091048	1.01E-06	1478.92	0.067025
rs301872	5	37137858	C5orf42	+	0	0.97429	G	C	0.475614	-0.33489	0.068504	1.02E-06	1478.94	0.60236
rs74019829	16	58209316	CSNK2A2	+	0	0.99967	C	T	0.167977	-0.42908	0.08778	1.02E-06	1478.97	0.11173
rs117382243	16	58224034	CSNK2A2	+	0	0.98661	T	A	0.164562	-0.43666	0.089332	1.02E-06	1478.96	0.12978
rs117776647	16	58224035	CSNK2A2	+	0	0.98661	C	A	0.164562	-0.43666	0.089332	1.02E-06	1478.96	0.12978
rs74019828	16	58209274	CSNK2A2	+	0	0.99968	A	G	0.167977	-0.42907	0.087779	1.02E-06	1478.97	0.11173
rs1875525	16	58201849	CSNK2A2	+	1	0.9827	T	C	0.16802	-0.4294	0.087854	1.02E-06	1478.96	0.024991
rs1875524	16	58201931	CSNK2A2	+	0	0.99997	C	T	0.16801	-0.42862	0.087762	1.04E-06	1478.96	0.092897
rs1875523	16	58202084	CSNK2A2	+	0	0.99997	T	A	0.16801	-0.42862	0.087762	1.04E-06	1478.96	0.092897
rs112724982	16	58203280	CSNK2A2	+	0	0.99997	G	A	0.16801	-0.42862	0.087762	1.04E-06	1478.96	0.092897
rs74019824	16	58206406	CSNK2A2	+	0	0.99997	G	T	0.16801	-0.42862	0.087762	1.04E-06	1478.96	0.092897
16-58197412	16	58197412	CSNK2A2	+	0	0.99336	TAC	T	0.168496	-0.43014	0.088078	1.04E-06	1478.95	0.13618
rs1875522	16	58202107	CSNK2A2	+	1	0.99814	T	C	0.168022	-0.42863	0.087773	1.04E-06	1478.96	0.092897
rs113103741	16	58225498	CSNK2A2	+	0	0.9579	C	G	0.167283	-0.44103	0.090432	1.08E-06	1479	0.2624
rs1393203	16	58207203	CSNK2A2	+	1	0.99936	C	A	0.168016	-0.42745	0.087653	1.08E-06	1479.04	0.07653
rs59804790	16	58216261	CSNK2A2	+	0	0.99335	G	A	0.170365	-0.42767	0.08777	1.10E-06	1478.95	0.14
rs74989935	16	58224042	CSNK2A2	+	0	0.99707	A	G	0.169031	-0.42753	0.087789	1.12E-06	1478.99	0.11432
rs74019835	16	58222531	CSNK2A2	+	0	0.99709	C	G	0.169004	-0.42752	0.08779	1.12E-06	1479.02	0.11432
rs74019834	16	58222102	CSNK2A2	+	0	0.99709	G	A	0.169004	-0.42752	0.08779	1.12E-06	1479.02	0.11432
rs74019836	16	58224062	CSNK2A2	+	0	0.99685	C	A	0.168959	-0.42755	0.087811	1.12E-06	1479.01	0.13633
rs76255078	16	58216428	CSNK2A2	+	0	0.99702	T	C	0.16896	-0.4275	0.087801	1.12E-06	1478.99	0.13633
rs74019832	16	58219280	CSNK2A2	+	0	0.99738	A	T	0.168997	-0.42717	0.087779	1.14E-06	1478.99	0.11432
rs74019831	16	58218489	CSNK2A2	+	0	0.99738	A	G	0.168997	-0.42716	0.087779	1.14E-06	1478.99	0.11432
rs16959778	16	58217701	CSNK2A2	+	0	0.99737	C	T	0.168999	-0.42715	0.087779	1.14E-06	1479	0.11432
rs11076224	16	58239644	CSNK2A2	+	0	0.89976	C	A	0.155136	-0.4635	0.095252	1.14E-06	1478.95	0.058462
rs16942468	16	58217323	CSNK2A2	+	0	0.99738	C	T	0.168999	-0.42712	0.087779	1.14E-06	1479	0.11432
16-58216075	16	58216075	CSNK2A2	+	0	0.99736	GA	G	0.169022	-0.427	0.087777	1.15E-06	1478.95	0.11432
rs58770507	16	58190770	CSNK2A2	+	0	0.992	T	G	0.168522	-0.42926	0.088269	1.16E-06	1479	0.16348
rs61268955	16	58214346	CSNK2A2	+	0	0.99737	C	T	0.169033	-0.42671	0.087775	1.17E-06	1479	0.11511
16-58187598	16	58187598		+	0	0.99185	CT	C	0.168609	-0.42895	0.088297	1.19E-06	1479	0.19231
16-58187595	16	58187595		+	0	0.99186	AC	A	0.168611	-0.42894	0.088297	1.19E-06	1479.01	0.19231
rs113236023	16	58186446	CSNK2A2	+	0	0.99186	G	A	0.168649	-0.42881	0.088305	1.20E-06	1478.96	0.19246
rs112628469	16	58186451	CSNK2A2	+	0	0.99182	G	A	0.168658	-0.42881	0.088305	1.20E-06	1479	0.19246
rs55998300	16	58212393	CSNK2A2	+	0	0.99748	C	T	0.169072	-0.42609	0.087767	1.21E-06	1479.02	0.11511
16-58238603	16	58238603	LOC390739	+	0	0.90086	G	GC	0.154291	-0.46298	0.095377	1.21E-06	1478.96	0.057008
rs3826095	16	58217784	CSNK2A2	+	0	0.99585	T	C	0.168727	-0.42654	0.087879	1.21E-06	1479.04	0.13633
rs16959811	16	58241399	CSNK2A2	+	0	0.79049	G	A	0.155957	-0.49355	0.1018	1.25E-06	1478.94	0.11261
rs58415199	16	58200617	CSNK2A2	+	0	0.99809	C	A	0.169004	-0.42534	0.087746	1.25E-06	1479.02	0.11432
rs3784914	16	58209396	CSNK2A2	+	0	0.99779	G	C	0.16913	-0.42521	0.087747	1.26E-06	1478.97	0.11511
rs3736397	16	58208536	CSNK2A2	+	0	0.99788	C	T	0.169136	-0.42503	0.087742	1.27E-06	1479	0.11511
rs74019825	16	58206621	CSNK2A2	+	0	0.998	C	T	0.169145	-0.42478	0.087736	1.29E-06	1479.04	0.11511
rs60571175	16	58206650	CSNK2A2	+	0	0.998	A	G	0.169145	-0.42478	0.087736	1.29E-06	1479.04	0.11511
rs76387456	16	58204430	CSNK2A2	+	0	0.99798	G	A	0.169146	-0.42477	0.087736	1.29E-06	1479.04	0.11511
rs59638837	16	58145291	C16orf80	+	0	0.91225	G	A	0.162721	-0.44977	0.093119	1.36E-06	1478.95	0.12497
rs301873	5	37136998	C5orf42	+	0	0.96706	G	C	0.476176	-0.33243	0.068858	1.38E-06	1478.95	0.5661
rs16959799	16	58229628	CSNK2A2	+	0	0.96423	A	G	0.161013	-0.43955	0.091106	1.40E-06	1478.96	0.14719
16-58229403	16	58229403		+	0	0.95305	CT	C	0.15804	-0.44073	0.092232	1.77E-06	1478.92	0.11645
16-58229402	16	58229402		+	0	0.95305	T	TC	0.15804	-0.44072	0.092232	1.77E-06	1478.92	0.11645

rs77474474	16	58205405	CSNK2A2	+	0	0.98873	T	C	0.170229	-0.41891	0.087718	1.79E-06	1479.05	0.096088
rs112020835	5	1.08E+08	FER	+	0	0.97339	A	G	0.08054	0.60203	0.12636	1.89E-06	1479.04	0.48107
rs649653	4	1.06E+08	CXXC4	+	0	0.7691	G	A	0.193831	-0.45652	0.095838	1.90E-06	1478.93	0.50534
rs78869517	5	1.08E+08	FER	+	0	0.97329	G	C	0.080486	0.59989	0.12646	2.10E-06	1478.97	0.48107
rs244731	5	1.77E+08	FGFR4	+	1	0.99538	A	G	0.236647	0.3803	0.080327	2.20E-06	1478.99	0.24858
rs78341307	5	1.08E+08	FER	+	0	0.97171	G	C	0.080391	0.59778	0.12667	2.37E-06	1478.97	0.28767
rs111465548	5	1.08E+08	FER	+	0	0.93718	G	C	0.081231	0.60653	0.12886	2.51E-06	1479.01	0.29027
rs73220177	5	1.08E+08	FER	+	0	0.95757	A	G	0.082031	0.5927	0.12595	2.53E-06	1478.95	0.606
rs9322459	6	1.55E+08	IPCEF1	+	0	0.91347	T	C	0.808849	0.42174	0.089753	2.62E-06	1478.87	0.67423
rs244730	5	1.77E+08	NSD1	+	0	0.96711	A	G	0.233813	0.38415	0.081913	2.74E-06	1478.9	0.21748
rs3784912	16	58148246	C16orf80	+	0	0.95845	A	G	0.175839	-0.41371	0.088309	2.80E-06	1478.96	0.17695
rs4568379	5	1.77E+08	MXD3	+	0	0.90488	C	G	0.223383	0.40564	0.086608	2.82E-06	1478.92	0.08475
rs301863	5	37133558	C5orf42	+	0	0.95198	T	C	0.482968	-0.32652	0.069824	2.92E-06	1478.96	0.27409
rs7758731	6	1.55E+08	IPCEF1	+	0	0.79826	A	G	0.759107	0.40988	0.088043	3.23E-06	1478.85	0.83135
rs4409879	12	27739993	PPFIBP1	+	1	0.72291	A	G	0.178135	-0.45847	0.098494	3.24E-06	1478.84	0.00048
rs8036711	15	37171699	LOC145845	+	0	0.96615	T	A	0.280808	0.3512	0.075608	3.40E-06	1478.91	0.74761
rs16959786	16	58228064	CSNK2A2	+	0	0.94104	C	T	0.145573	-0.44453	0.095824	3.50E-06	1479.01	0.093219
rs11634677	15	37171459	LOC145845	+	0	0.9536	G	A	0.280491	0.35312	0.076162	3.55E-06	1478.89	0.79659
rs78004902	16	58242919	CSNK2A2	+	0	0.77115	T	C	0.128366	-0.51707	0.11155	3.56E-06	1478.93	0.08009
rs79409628	5	1.08E+08	FER	+	0	0.95733	T	G	0.081697	0.58834	0.12704	3.63E-06	1478.96	0.22471
rs10445014	16	58160974	C16orf80	+	1	0.98724	G	A	0.170384	-0.40701	0.087892	3.64E-06	1479	0.11666
rs8036656	15	37172064	LOC145845	+	1	0.97724	A	C	0.279917	0.34583	0.074762	3.73E-06	1478.99	0.43847
1-69341239	1	69341239		+	0	0.7216	GT	G	0.122431	-0.55251	0.11956	3.81E-06	1478.85	0.62614
rs12898227	15	87225439	AGBL1	+	0	0.9604	C	T	0.462102	-0.31471	0.068298	4.07E-06	1478.98	0.71413
rs75815475	5	1.08E+08	FER	+	0	0.95189	A	C	0.081511	0.58855	0.12779	4.11E-06	1478.99	0.22476
rs186663369	16	58231677	CSNK2A2	+	0	0.80678	A	G	0.201188	-0.42185	0.091637	4.16E-06	1478.86	0.22413
rs9783726	15	87225075	AGBL1	+	0	0.96021	G	A	0.462565	-0.31432	0.068284	4.16E-06	1478.97	0.67586
rs74019800	16	58159888	C16orf80	+	0	0.98374	G	A	0.174504	-0.4023	0.087516	4.29E-06	1479.02	0.20437
rs72813185	5	1.77E+08	MXD3	+	0	0.92659	A	C	0.230082	0.38617	0.084023	4.31E-06	1478.94	0.27006
rs75360637	5	1.08E+08	FER	+	0	0.97309	C	T	0.078741	0.58879	0.12812	4.31E-06	1478.98	0.36605
rs79621178	5	1.08E+08	FER	+	0	0.96046	C	G	0.082734	0.58023	0.12626	4.32E-06	1479	0.22524
rs112668446	5	1.08E+08	FER	+	0	0.96015	A	G	0.082791	0.58031	0.12629	4.33E-06	1479.04	0.22524
rs71592765	5	1.08E+08	FER	+	0	0.96034	G	C	0.082723	0.58029	0.12629	4.33E-06	1478.98	0.22524
rs79980741	5	1.08E+08	FER	+	0	0.9602	A	G	0.082803	0.58025	0.12628	4.33E-06	1478.97	0.22609
rs62397242	5	1.77E+08	MXD3	+	0	0.91246	A	C	0.234406	0.38668	0.084157	4.33E-06	1478.91	0.2764
rs77630811	5	1.08E+08	FER	+	0	0.96051	G	A	0.08283	0.58	0.12627	4.36E-06	1478.99	0.22609
rs112472930	5	1.08E+08	FER	+	0	0.96082	G	A	0.082849	0.57982	0.12625	4.38E-06	1478.96	0.22609
rs76325227	5	1.08E+08	FER	+	0	0.96112	A	T	0.082857	0.5797	0.12623	4.38E-06	1479.01	0.22609
rs113792119	5	1.08E+08	FER	+	0	0.96123	G	T	0.082862	0.57961	0.12622	4.39E-06	1479.03	0.22609
rs79243757	5	1.08E+08	FER	+	0	0.96115	G	A	0.082974	0.57892	0.1262	4.49E-06	1479.02	0.22617
rs74019802	16	58162210	C16orf80	+	0	0.99235	A	T	0.170509	-0.40372	0.088009	4.49E-06	1479.04	0.19678
rs77606373	5	1.08E+08	FER	+	0	0.96198	C	A	0.082899	0.57882	0.12619	4.50E-06	1479	0.22609
rs113193866	5	1.08E+08	FER	+	0	0.96212	G	A	0.0829	0.57874	0.12618	4.50E-06	1478.99	0.22609
rs112828293	5	1.08E+08	FER	+	0	0.96215	T	G	0.082899	0.57871	0.12618	4.51E-06	1478.99	0.22609
rs112949822	5	1.08E+08	FER	+	0	0.96114	A	G	0.083078	0.57853	0.12614	4.51E-06	1479.04	0.22735
rs79001324	5	1.08E+08	FER	+	0	0.9618	C	A	0.082899	0.57863	0.12621	4.55E-06	1479.01	0.22609
rs113728457	5	1.08E+08	FER	+	0	0.96176	C	G	0.082891	0.57829	0.12623	4.62E-06	1479.02	0.22609
rs77163552	16	58137888	C16orf80	+	0	0.83099	C	T	0.158045	-0.4537	0.099038	4.63E-06	1478.94	0.17063
rs75955236	5	1.08E+08	FER	+	0	0.95546	C	T	0.085392	0.57314	0.12517	4.67E-06	1478.97	0.13318

rs79536589	5	1.08E+08	FER	+	0	0.96174	A	G	0.082889	0.57794	0.12624	4.70E-06	1479.04	0.22609
rs73220190	5	1.08E+08	FER	+	0	0.95548	C	T	0.081424	0.57976	0.1268	4.82E-06	1478.97	0.48189
rs301867	5	S 37130856	C5orf42	+	0	0.94166	C	A	0.48715	-0.32155	0.070396	4.93E-06	1478.95	0.17585
rs6930716	6	u 1.55E+08	IPCEF1	+	1	0.99632	C	T	0.831303	0.4095	0.08967	4.95E-06	1478.96	1
rs11258300	10	p 13316312	PHYH	+	0	0.60488	T	G	0.362672	0.41195	0.09022	4.97E-06	1478.94	0.69349
rs7171195	15	p 37171230	LOC145845	+	0	0.94112	G	A	0.281686	0.34868	0.076393	5.01E-06	1478.9	0.69944
rs11738226	5	l 76716430	PDE8B	+	0	0.85728	T	A	0.41797	0.34241	0.07505	5.06E-06	1478.98	0.10878
rs111636466	5	e 1.08E+08	FER	+	0	0.96232	G	A	0.082954	0.57562	0.12621	5.09E-06	1478.97	0.22617
rs78492167	5	m 1.08E+08	FER	+	0	0.96276	T	C	0.082944	0.57519	0.12618	5.16E-06	1478.94	0.22617
rs7912768	10	e 50884092	C10orf53	+	0	0.9078	T	C	0.411416	0.33103	0.072627	5.17E-06	1478.93	0.25926
rs12859492	13	n 71905552	DACH1	+	0	0.88856	C	T	0.321708	-0.34039	0.074772	5.30E-06	1478.92	0.15278
rs75271047	5	t 1.08E+08	FER	+	0	0.96418	A	G	0.082908	0.57403	0.12614	5.34E-06	1478.98	0.22617
5-37168326	5	a 37168326		+	0	0.93967	A	AT	0.492725	-0.32076	0.07052	5.40E-06	1478.96	0.16002
rs73549151	16	r 58144187	C16orf80	+	0	0.89886	G	A	0.183056	-0.40555	0.089191	5.44E-06	1478.91	0.045736
5-108074449	5	y 1.08E+08		+	0	0.96495	AT	A	0.08289	0.57335	0.12611	5.45E-06	1478.95	0.22617
10-50884075	10	T 50884075		+	0	0.90316	TCA	T	0.412479	0.33117	0.072845	5.46E-06	1478.91	0.23781
rs77844865	5	a 1.08E+08	FER	+	0	0.96507	C	T	0.08289	0.57322	0.1261	5.48E-06	1478.94	0.22617
rs13379594	15	b 37172558	LOC145845	+	0	0.95901	C	G	0.276727	0.34652	0.076234	5.48E-06	1478.95	0.7948
rs7180198	15	i 87228075	AGBL1	+	0	0.95595	C	T	0.459705	-0.31031	0.068455	5.81E-06	1478.98	0.71384
rs113427433	5	e 1.08E+08	FER	+	0	0.93498	A	G	0.081275	0.5816	0.12853	6.04E-06	1478.98	0.48293
rs10004325	4	s 1.77E+08	SPATA4	+	0	0.93974	C	G	0.161804	0.42285	0.093572	6.21E-06	1479	0.77313
rs8043203	15	5 87224199	AGBL1	+	0	0.95141	C	A	0.462896	-0.30998	0.068631	6.28E-06	1478.96	0.71446
rs1553738	15	: 56370951	RFXDC2	+	0	0.83657	G	T	0.066757	0.66522	0.14771	6.68E-06	1478.97	0.67567
rs10073054	5	37172383	C5orf42	+	0	0.92009	G	A	0.503073	-0.31978	0.071054	6.78E-06	1478.95	0.23156
rs11630710	15	l 56364758	RFXDC2	+	0	0.78882	T	G	0.066079	0.69058	0.15351	6.84E-06	1478.98	0.39985
rs1553737	15	m 56370492	RFXDC2	+	0	0.83387	T	C	0.066364	0.66664	0.1483	6.95E-06	1479.02	0.67574
rs28457856	4	p 1.77E+08	SPATA4	+	0	0.95753	A	G	0.291493	0.33736	0.075142	7.13E-06	1478.97	0.80126
rs76712141	15	a 56501134	RFX7	+	0	0.8198	C	T	0.054823	0.73961	0.16489	7.28E-06	1479.03	0.31414
rs75421844	5	c 1.08E+08	FER	+	0	0.94137	C	T	0.082352	0.57264	0.12772	7.34E-06	1479.01	0.22469
rs72736501	15	56423061	RFX7	+	0	0.89742	A	C	0.064856	0.64796	0.14465	7.48E-06	1479.04	0.82891
rs116140504	15	56410918	RFX7	+	0	0.89603	G	A	0.065215	0.64662	0.1444	7.54E-06	1478.93	0.82931
rs72736484	15	56408168	RFX7	+	0	0.89594	G	T	0.065221	0.64661	0.1444	7.54E-06	1478.95	0.82931
rs113877323	5	1.08E+08	FER	+	0	0.96976	C	A	0.08036	0.56961	0.12735	7.72E-06	1478.98	0.28816
rs2065415	6	1.69E+08	THBS2	+	0	0.74107	G	A	0.811543	0.44432	0.099401	7.82E-06	1478.89	0.93209
rs75475720	5	1.08E+08	FER	+	0	0.9403	G	C	0.082275	0.56993	0.12784	8.27E-06	1478.98	0.22468
rs9746214	16	58179472	CSNK2A2	+	0	0.74539	C	T	0.089175	-0.60439	0.13583	8.60E-06	1478.98	0.87192
rs571880	4	1.06E+08	CXXC4	+	0	0.95135	A	T	0.230691	-0.35927	0.080852	8.85E-06	1478.94	0.50858
rs4392004	15	56548922	RFXDC2	+	0	0.88918	G	A	0.063626	0.65005	0.14643	9.02E-06	1478.98	0.82856
rs7175969	15	56371998	RFXDC2	+	0	0.85348	T	C	0.93362	-0.65064	0.1466	9.07E-06	1479	0.67574
rs60621000	16	17329849	XYLT1	+	0	0.56347	A	G	0.145279	0.56413	0.12711	9.07E-06	1478.9	0.91647
rs139758543	8	97063079	GAPDHP30	+	0	0.57191	A	G	0.075335	0.74863	0.16888	9.29E-06	1478.98	0.85051
rs181139921	15	56426852	RFX7	+	0	0.8799	T	A	0.061559	0.66211	0.14948	9.45E-06	1479.03	0.65124
rs488076	4	1.06E+08	CXXC4	+	0	0.94039	A	C	0.229521	-0.36074	0.081482	9.55E-06	1478.95	0.50786
rs78579945	5	1.08E+08	FER	+	0	0.99088	G	T	0.079362	0.55982	0.12658	9.75E-06	1479.03	0.28804
rs76112574	5	1.08E+08	FER	+	0	0.99063	T	C	0.079393	0.55915	0.12658	9.99E-06	1479.02	0.28804

Supplementary Table 5. Effect of Relative Telomere Length on Quantitative Traits

	BETA(SE)	P (Not adjusted)	BETA(SE)	P	MODEL
Cardio Vascular traits					
SYBP(mmHg)	-1.20(.17)	4E-03	-1.03(.07)	2E-03	SEX,AGE,BMI,T2D
DYSBP(mmHg)	-0.55(.21)	7.6E-02	-0.68(.15)	2E-03	SEX,AGE,BMI,T2D
Mean Arterial pressure(mmHg)	-0.76(.26)	2.4E-02	-0.83(.13)	5.8E-02	SEX,AGE,BMI,T2D
MCP-1(pg/ml)	-0.17(.04)	7E-06	-0.05(.14)	7E-07	SEX,AGE,BMI,T2D
Metabolic traits					
FBG(mg/dl)	-0.12(.06)	4.3E-01	-0.24(.13)	2.7E-01	SEX,AGE,BMI,CONTROLS ONLY
HOMA-B	0.11(.05)	3E-04	0.16(.09)	1E-04	SEX,AGE,BMI,T2D

SE- Standard Error, SYBP- systolic blood pressure, DYSBP-diastolic blood pressure, FBG-fasting blood glucose, HOMA-β - Homeostatic Model Assessment- beta, MCP-1- Monocyte chemoattractant protein 1

Supplementary Table 6. Association of Previously Established Risk Variants for Relative Telomere Length in Sikh Discovery GWAS

SNP	Gene	Chr	Position	Genotyped/imputed	effect allele	base allele	freq	effect	BETA	SE	P	N	HWE	CONSISTENT
rs10936599	<i>TERC</i>	3	169492101	g	T	C	0.30	0.19	0.07	9.74E-03	1478.99	0.90	NO	
rs8105767	<i>ZNF208</i>	19	22215441	i	G	A	0.40	-0.04	0.07	0.54	1479.00	0.45	NO	
rs7675998	<i>NAF1</i>	4	164007820	i	G	A	0.82	-0.04	0.09	0.67	1478.99	0.07	NO	
rs9420907	<i>OBCF1</i>	10	105676465	g	A	C	0.91	-0.04	0.11	0.70	1479.03	0.36	YES	
rs2736100	<i>TERT</i>	5	1286516	g	A	C	0.38	-0.02	0.07	0.78	1478.98	1.00	YES	
rs11125529	<i>ACYP2</i>	2	54475866	i	A	C	0.11	0.00	0.11	0.98	1479.02	0.60	YES	

All imputed SNPs on the list were imputed with info >0.95

Supplementary Table 7: Punjabi Sikh Discovery and Stage 1 Replication Meta-analysis Results

SNP	CHR	BP	GENE	Allele1	Allele2	Effect	SE	P-value	Direction	HetChiSq	HetDf	HetPVal
rs74019828	16	58209274	CSNK2A2	a	g	-0.3818	0.0698	4.52E-08	--	0.79	1	0.3741
rs2098713	5	37144574	C5orf42/TERT	t	c	-0.249	0.0536	3.35E-06	--	4.46	1	0.0347
rs10004325	4	177106289	SPATA4	c	g	0.3153	0.0738	1.95E-05	++	3.502	1	0.0613
rs78869517	5	108050074	FER	c	g	-0.4151	0.099	2.78E-05	--	5.525	1	0.01874
rs4409879	12	27739993	PPFIBP1	a	g	-0.3168	0.0764	3.36E-05	--	5.188	1	0.02274
rs244731	5	176539679	NA	a	g	0.2577	0.0634	4.82E-05	++	6.18	1	0.01292
rs9988609	1	69087816	NA	a	g	-0.3577	0.0889	5.78E-05	--	2.666	1	0.1025
rs112020835	5	103218341	FER	a	g	0.3812	0.098	1E-04	++	7.66	1	0.005646
rs8036656	15	37172064	LOC145845	a	c	0.2101	0.0593	3.9E-04	+-	8.872	1	0.002896
rs11738226	5	76716430	PDE8B	a	t	-0.1788	0.057	1.6E-03	-+	11.206	1	0.0008152
rs12859492	13	71905552	NA	t	c	0.1355	0.0593	2.2E-02	+-	20.241	1	6.83E-06

Supplementary Table 8A: Punjabi Sikh Initial Discovery analysis adjusting for age, gender and BMI

SNP	CHR	BP	EFFECT_ALLELE	BASE_ALLELE	FREQ_EFFECT	BETA	SE	P
16-58234260	16	58234260	GA	G	0.1801	-0.46367	0.089178	2.00E-07
rs11076223	16	58239558	G	T	0.1744	-0.47677	0.092634	2.65E-07
rs1834021	16	58234767	C	T	0.1764	-0.45968	0.089493	2.80E-07
rs8058372	16	58238081	A	C	0.1761	-0.46832	0.091179	2.80E-07
rs7196068	16	58234135	A	G	0.1768	-0.45796	0.089224	2.86E-07
rs58553914	16	58233709	C	T	0.1766	-0.45819	0.089509	3.07E-07
rs73549172	16	58181055	A	G	0.1863	-0.43647	0.085464	3.27E-07
16-58139084	16	58139084	A	AC	0.1579	-0.49511	0.097088	3.40E-07
rs11860708	16	58178596	A	G	0.1868	-0.43308	0.085179	3.69E-07
16-58240273	16	58240273	C	CTTTAT	0.1653	-0.48285	0.095176	3.91E-07
16-58179843	16	58179843	C	CA	0.1859	-0.43335	0.085444	3.94E-07
rs58588258	16	58189271	A	C	0.1825	-0.43487	0.08598	4.24E-07
rs7185651	16	58187826	G	A	0.1825	-0.43465	0.085982	4.30E-07
rs59165986	16	58186952	T	C	0.1826	-0.43449	0.085982	4.34E-07
rs8044707	16	58240972	T	C	0.16	-0.49479	0.098123	4.59E-07
rs111234535	16	58137426	A	G	0.1431	-0.5211	0.10335	4.60E-07
rs2098713	5	37144574	T	C	0.4707	-0.33293	0.066886	6.44E-07
rs77762167	16	58141185	G	T	0.1611	-0.47182	0.094903	6.64E-07
rs74019786	16	58141441	G	A	0.1613	-0.47055	0.094742	6.81E-07
rs74019791	16	58141882	G	A	0.1616	-0.46829	0.094471	7.16E-07
rs74019790	16	58141827	C	T	0.1617	-0.46835	0.094489	7.17E-07
rs74019792	16	58141933	A	G	0.1616	-0.46806	0.094441	7.19E-07
rs78955299	16	58141203	T	C	0.1613	-0.47127	0.095145	7.30E-07
rs55990878	16	58142126	C	T	0.1617	-0.46717	0.094322	7.31E-07
rs76411253	5	1.08E+08	A	G	0.07848	0.6948	0.14043	7.51E-07
rs60765503	16	58144761	G	A	0.1621	-0.46073	0.093172	7.62E-07
rs113577652	16	58232261	A	C	0.1658	-0.44953	0.091099	8.03E-07
rs74019794	16	58144179	C	G	0.162	-0.46051	0.09335	8.09E-07
rs61535084	16	58143889	G	T	0.1622	-0.46059	0.093418	8.21E-07
rs10445026	16	58143253	G	A	0.1624	-0.46155	0.09362	8.22E-07
rs74019793	16	58144117	G	A	0.1638	-0.45898	0.093474	9.10E-07
rs57827735	16	58144938	C	T	0.1624	-0.45484	0.092709	9.29E-07
rs301869	5	37140597	A	T	0.4747	-0.33429	0.068191	9.47E-07
rs149021498	16	58231487	A	G	0.1655	-0.43891	0.089751	1.01E-06
rs74019837	16	58231266	T	C	0.1657	-0.43837	0.08965	1.01E-06
rs77325010	16	58230324	G	A	0.1662	-0.43559	0.089194	1.04E-06
rs301872	5	37137858	G	C	0.4757	-0.33434	0.068462	1.04E-06
rs75241789	16	58224666	A	G	0.1714	-0.42847	0.087854	1.08E-06
rs57474112	16	58228856	G	A	0.1671	-0.43127	0.088496	1.10E-06

Supplementary Table 8B: Punjabi Sikh initial discovery analysis for BMI < 25

SNP	CHR	BP	EFFECT_ALLELE	BASE_ALLELE	FREQ_EFFECT	BETA	SE	P
rs301872	5	37137858	G	C	0.4925	-0.57874	0.10642	5.38E-08
rs301869	5	37140597	A	T	0.4913	-0.57579	0.10595	5.49E-08
rs301873	5	37136998	G	C	0.4935	-0.58156	0.10723	5.85E-08
rs111851553	8	15216403	A	G	0.06561	1.2644	0.23387	6.43E-08
rs301863	5	37133558	T	C	0.5018	-0.58367	0.1088	8.12E-08
rs2098713	5	37144574	T	C	0.4874	-0.55408	0.10342	8.44E-08
rs301867	5	37130856	C	A	0.5059	-0.5824	0.10928	9.84E-08
5-37094419	5	37094419	TTAAC	T	0.4746	-0.6099	0.11744	2.06E-07
rs9693907	8	15154598	T	G	0.1453	0.85291	0.16523	2.44E-07
rs301906	5	37105606	T	C	0.5	-0.58575	0.11366	2.56E-07
5-37168326	5	37168326	A	AT	0.5126	-0.5644	0.11028	3.09E-07
rs301908	5	37103806	T	A	0.5001	-0.58186	0.1139	3.24E-07
rs301909	5	37102627	T	C	0.4995	-0.58076	0.11399	3.49E-07
rs301878	5	37097138	T	C	0.4983	-0.57968	0.11473	4.36E-07
rs10073054	5	37172383	G	A	0.5279	-0.56205	0.11142	4.55E-07
rs301874	5	37094291	G	A	0.4904	-0.58519	0.11629	4.85E-07
rs7017139	8	15205895	C	T	0.1039	0.94929	0.19099	6.68E-07
5-37176864	5	37176864	CT	C	0.5258	-0.61297	0.12451	8.51E-07
rs11727182	4	1.51E+08	A	G	0.3973	-0.5453	0.11097	8.93E-07
rs6887958	5	37189819	G	A	0.52	-0.54727	0.11233	1.11E-06
rs6451313	5	37182310	T	C	0.521	-0.54546	0.11227	1.18E-06
rs6860727	5	37179341	A	G	0.5204	-0.54472	0.11213	1.19E-06
5-169525862	5	1.7E+08	G	GT	0.05028	2.2235	0.32697	1.24E-06
rs6993454	8	15205901	T	C	0.1043	0.9117	0.18904	1.42E-06
rs56092751	8	15205204	T	G	0.1412	0.75212	0.15665	1.58E-06
rs7715883	5	37238262	C	T	0.5049	-0.54045	0.11261	1.59E-06
rs7729404	5	37238050	G	A	0.505	-0.54021	0.11263	1.62E-06
rs301905	5	37111383	C	T	0.4733	-0.54645	0.11431	1.75E-06
rs4498539	8	15185883	T	A	0.1468	0.71428	0.15013	1.96E-06
rs61652782	8	15200617	A	G	0.141	0.73356	0.1546	2.08E-06
rs6987496	8	15204533	T	C	0.1425	0.72531	0.15313	2.18E-06
rs62499923	8	15204065	T	G	0.1425	0.72358	0.15285	2.20E-06
rs6982651	8	15203869	T	C	0.1427	0.72226	0.15265	2.23E-06
rs11991432	8	15203469	C	G	0.1426	0.72033	0.15241	2.29E-06
rs1930219	13	96908722	A	G	0.5135	-0.48259	0.10216	2.32E-06
rs7006627	8	15204240	G	A	0.1433	0.72173	0.15286	2.34E-06
rs6886108	5	37252939	C	T	0.5059	-0.58179	0.12323	2.34E-06
rs28621423	8	15169185	G	T	0.147	0.70616	0.14971	2.40E-06
rs12114950	8	15169007	G	A	0.1472	0.70394	0.14925	2.40E-06

Supplementary Table 8C: Punjabi Sikh Initial Discovery analysis for BMI > 25

SNP	CHR	BP	EFFECT_ALLELE	BASE_ALLELE	FREQ_EFFECT	BETA	SE	P
rs11634677	15	37171459	G	A	0.2726	0.46329	0.098036	2.29E-06
rs8036711	15	37171699	T	A	0.273	0.45814	0.097172	2.42E-06
rs114508985	6	32900018	G	C	0.7518	0.57875	0.12338	2.72E-06
rs8036656	15	37172064	A	C	0.2718	0.45069	0.096116	2.74E-06
rs7171195	15	37171230	G	A	0.274	0.46042	0.098309	2.82E-06
5-97298072	5	97298072	TA	T	0.3239	-0.50307	0.108	3.19E-06
rs12909623	15	37173147	G	T	0.4751	0.4243	0.092098	4.08E-06
15-95721821	15	95721821	A	AT	0.2049	-0.61981	0.1346	4.13E-06
rs60077625	1	1.72E+08	A	G	0.2701	0.48251	0.10479	4.14E-06
rs2070886	12	6094065	T	C	0.1764	-0.52036	0.11332	4.39E-06
rs13379594	15	37172558	C	G	0.2685	0.44894	0.09793	4.56E-06
rs2568838	3	71309259	C	G	0.4286	0.42808	0.093915	5.16E-06
rs2256864	7	1.51E+08	A	G	0.3563	-0.46031	0.1012	5.40E-06
rs11070169	15	39320011	T	C	0.3289	0.4142	0.091081	5.43E-06
rs12904358	15	37172926	T	C	0.4695	0.41551	0.091431	5.51E-06
rs12904352	15	37172918	G	C	0.2719	0.44165	0.098353	7.11E-06
rs4725398	7	1.51E+08	G	A	0.3493	-0.45581	0.1017	7.40E-06
15-37173119	15	37173119	AT	A	0.4701	0.40918	0.091315	7.43E-06
5-97298080	5	97298080	TC	T	0.3383	-0.46789	0.10498	8.31E-06
15-79220928	15	79220928	A	AAAAG	0.09559	-0.72596	0.16361	9.12E-06
rs12903788	15	37173267	A	G	0.4713	0.40439	0.09132	9.50E-06
rs2118381	2	19368078	A	G	0.6755	0.40296	0.091435	1.05E-05
rs12495693	3	71337856	C	T	0.2487	-0.44098	0.10035	1.11E-05
rs6103674	20	42826710	T	C	0.1588	-0.51625	0.11757	1.13E-05
7-17119073	7	17119073	TA	T	0.8615	-0.62744	0.1429	1.13E-05
rs78040573	15	95725639	A	G	0.2264	-0.53367	0.1216	1.14E-05
rs1870238	7	1.51E+08	G	C	0.3489	-0.43365	0.099317	1.26E-05
rs3097978	11	1.26E+08	A	G	0.2529	-0.47533	0.10902	1.30E-05
rs10893595	11	99483734	C	T	0.1874	0.49155	0.11278	1.31E-05
rs4666323	2	19328111	A	G	0.6819	0.39706	0.09114	1.32E-05
11-74422845	11	74422845	AT	A	0.09201	0.84733	0.19464	1.34E-05
rs536344	11	1.26E+08	A	G	0.2701	-0.45576	0.10474	1.35E-05
rs6031450	20	42830192	T	A	0.7537	-0.42937	0.098689	1.36E-05
rs11853413	15	39319573	G	A	0.3251	0.3884	0.089467	1.42E-05
rs10851378	15	39322422	G	A	0.327	0.42649	0.098366	1.45E-05
rs62001260	15	33064635	T	C	0.4425	0.40526	0.09378	1.55E-05
rs61137448	15	95729571	C	T	0.2295	-0.53155	0.12301	1.55E-05
rs78045666	15	95725068	T	C	0.2219	-0.54463	0.1261	1.57E-05
rs144790127	15	95727316	A	G	0.2284	-0.53026	0.12294	1.61E-05

Supplementary Table 9A: Punjabi Sikh Discovery and Stage 1(Replication) meta-analysis with age, gender and BMI as covariates

CHR	BP	SNP	A1	A2	P	OR	Q	I ²
5	37144574	rs2098713	T	C	1.63E-08	0.7479	0.1584	49.72
16	58209274	rs74019828	A	G	5.51E-07	0.6973	0.1935	40.87

Supplementary Table 9B: Punjabi Sikh Discovery and Stage 1(Replication) meta-analysis for BMI < 25

CHR	BP	SNP	A1	A2	P	OR	Q	I ²
5	37144574	rs2098713	T	C	2.22E-05	0.6206	0.4523	0

Supplementary Table 9C: Punjabi Sikh Discovery and Stage 1(Replication) meta-analysis for BMI > 25

CHR	BP	SNP	A1	A2	P	OR	Q	I ²
16	58209274	rs74019828	A	G	2.15E-04	0.5787	0.2207	33.32

Supplementary Table 10: Punjabi Sikh Discovery and Stage 1 (Replication) meta-analysis with different models

SNP	POSITION	GENE	ALLELES	MODEL	P	β,SE
rs74019828	16 58209274	CSNK2A2	A/G	ADDITIVE	4.52 × 10 ⁻⁰⁸	-0.38,0.06
				DOMINANT	1.16 × 10 ⁻⁰⁵	-0.34,0.10
				RECESSIVE	3.80 × 10 ⁻⁰⁴	-0.73,0.12
rs2098713	5 37144574	C5orf42 (Near TERT)	T/C	ADDITIVE	3.35 × 10 ⁻⁰⁶	-0.25,0.05
				DOMINANT	6.36 × 10 ⁻⁰⁶	-0.33,0.08
				RECESSIVE	4.28 × 10 ⁻⁰⁴	-0.30,0.15
rs78869517	5 108050074	FER	C/G	ADDITIVE	2.78 × 10 ⁻⁰⁵	0.41,0.09
				DOMINANT	8.52 × 10 ⁻⁰⁷	0.63,0.17
				RECESSIVE	6.85 × 10 ⁻⁰¹	0.16,0.11

Supplementary Table 11: AIDHS/SDS and UKCVD Meta-analysis Results

SNP	CHR	BP	GENE	Allele1	Allele2	Effect	StdErr	P-value	Direction	HetChiSq	HetDf	HetPVal
rs74019828	16	58209274	CSNK2A2	a	g	-0.0588	0.0164	3.2E-04	---	23.446	2	8.11E-06
rs112020835	5	103218341	FER	a	g	0.0267	0.0151	7.8E-02	+++	21.073	2	2.66E-05

Supplementary Table 12A: Multi-Ethnic Meta-analysis Results

SNP	CHR	BP	GENE	Allele1	Allele2	Effect	StdErr	P-value	Direction	HetChiSq	HetDf	HetPVal
rs74019828	16	58209274	CSNK2A2	a	g	-0.0317	0.0103	2.1E-03	---+++-	30.053	8	0.0002069
rs117119920	20	22325663	LOC284788	t	g	0.0692	0.0226	2.2E-03	+++???	11.286	4	0.02353
rs12935153	16	79667015	MAF	a	g	0.0193	0.0076	1E-02	+++++0	16.202	6	0.01271
rs11154619	6	131428095	AKAP7	a	g	0.0299	0.0122	1.4E-02	+++???	21.662	4	0.000234
rs4502258	17	65445711	PITPNC1	t	c	0.0242	0.0101	1.6E-02	+++???	16.671	4	0.002239
rs10065850	5	32067398	PDZD2	a	g	-0.0212	0.0095	2.5E-02	++-+--	26.511	6	0.0001788
rs11199695	10	122754470	BRWD2	t	g	0.0156	0.0074	3.4E-02	++-++++	18.952	6	0.004245
rs12516673	5	149105605	PPARGC1B	a	t	-0.018	0.0089	4.4E-02	-??-----	16.974	6	0.009379
rs12043296	1	220569966	LOC127086	a	c	-0.0147	0.0073	4.4E-02	-??-+--	15.85	6	0.01458
rs649653	4	105518376	CXXC4	a	g	0.0234	0.0117	4.5E-02	+++???	28.917	4	8.13E-06
rs146122959	1	106217141	VAV3	t	c	-0.0342	0.0172	4.7E-02	-??-??-	13.768	4	0.008073

Supplementary Table 12B: GWAS, replication, and meta-analysis results of RTL loci identified in Punjabi Sikhs

SNP	Chromosome Position	Nearest gene	Effect/ Other Allele	EAF	Punjabi Sikh Discovery GWAS	Punjabi Sikh Replication (Stage 1)	EAF	UK CVDS (Stage 2)	EAF	UK TWINS (Stage 3)	EAF	NHS (Stage 3)	EAF	PLCO (Stage 3)	EAF	MDACC (Stage 3)	EAF	Sikh Meta- analysis	Sikh- UK CVDS Meta- analysis	Multi- ethnic Meta- analysis
					β ,SE	β ,SE		β ,SE		β ,SE		β ,SE		β ,SE		β ,SE		β ,SE	β ,SE	
					<i>P</i> value	<i>P</i> value		<i>P</i> value		<i>P</i> value		<i>P</i> value		<i>P</i> value		<i>P</i> value		<i>P</i> value	<i>P</i> value	
				SIKH			UK CVD		UK TWINS		NHS		PLCO		MDACC					
				CEU																
rs74019828	16 58209274	CSNK2A2	A/G	0.16 0.03	-0.43,0.09 1.02×10^{-06}	-0.27, 0.13 2.62×10^{-02}	0.07	-0.04, 0.03 4.00×10^{-02}	0.07	-0.03, 0.03* 2.54×10^{-01}	0.07	-0.02,0.02* 2.57×10^{-01}	0.07	0.001, 0.03* 9.81×10^{-01}	0.07	0.04,0.07* 5.20×10^{-01}		-0.38,0.06 4.52×10^{-08}	-0.06, 0.02 3.20×10^{-04}	-0.03, 0.01 2.10×10^{-03}
rs2098713	5 37144574	CSorf42 (Near TERT)	T/C	0.47 0.35	-0.33,0.07 6.15×10^{-07}	-0.15,0.09 1.26×10^{-01}	N/A	N/A	0.35	-0.01,0.01 3.61×10^{-01}	0.39	-0.01,0.01 5.34×10^{-01}	0.37	0.02,0.02 2.54×10^{-01}	0.35	-0.06,.04 1.29×10^{-01}		-0.25,0.05 3.35×10^{-06}	N/A	-0.01,0.01 4.93×10^{-01}
rs10004325	4 177106289	SPATA4	G/C	0.84 0.75	-0.42,0.09 6.21×10^{-06}	-0.04,0.13 7.27×10^{-01}	N/A	N/A	0.23	0.01,0.02 6.85×10^{-01}	0.21	0.03,0.01 2.70×10^{-02}	0.21	0.03,0.02 2.63×10^{-01}	0.24	0.04,0.05 3.67×10^{-01}		-0.31,0.08 1.95×10^{-05}	N/A	-0.02,0.01 6.00×10^{-02}
rs78869517	5 108050074	FER	C/G	0.92 0.94	-0.59,0.13 2.10×10^{-06}	0.09,0.17 5.89×10^{-01}	0.88	0.01,0.03 3.20×10^{-01}	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A		-0.41,0.09 2.78×10^{-05}	0.02,0.02 7.80×10^{-02}	N/A
rs4409879	12 27739993	PTFIBP1	A/G	0.17 0.32	-0.45,0.09 3.24×10^{-06}	-0.08,0.13 5.31×10^{-01}	N/A	N/A	0.29	0.02,0.01 1.86×10^{-01}	0.28	0.002,0.01 8.17×10^{-01}	0.27	0.03,0.02 1.23×10^{-01}	0.30	0.001,0.04 9.83×10^{-01}		-0.31,0.07 3.36×10^{-05}	N/A	-0.01,0.001 1.37×10^{-01}
rs244731	5 176539679	unknown	A/G	0.23 0.28	0.38,0.08 2.20×10^{-06}	0.07,0.11 4.88×10^{-01}	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A		0.25,0.06 4.82×10^{-05}	N/A	N/A
rs9988609	1 69315228	unknown	A/G	0.10 0.11	-0.47,0.11 2.67×10^{-05}	-0.22,0.16 1.72×10^{-01}	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A		-0.36,0.08 5.78×10^{-05}	N/A	N/A

All P values are two sided. CEU- Euro-Caucasians, EAF-Effect Allele Frequency, SE-Standard Error

*data from rs1393203 is a proxy for rs74019828

Supplementary Table 13. Nominal Association of RTL Loci and of Genetic Risk Score of Previously Identified RTL Loci with Cardiometabolic Traits

Cardiometabolic Trait	SNP	Chr	Basepair	Imputation Info	Telomere shortening allele	other allele	Effect Allele frequency	Beta	SE	P	N	HWE
Total cholesterol (mmol/L)	rs10936599 (TERC)	3	169492101	0.97978	T	C	0.30	-4.89	2.01	0.0152	1507	0.90
Triglyceride (mmol/L)	rs10936599 (TERC)	3	169492101	0.98095	T	C	0.30	-0.06	0.02	0.0188	1492	1.00
DYSBP (cases)(mmHg)	rs2736100 (TERT)	5	1339516	1	A	C	0.37	-1.85	0.67	0.0060	777	0.49
SYBP (controls)(mmHg)	rs2736100 (TERT)	5	1339516	1	A	C	0.39	-3.57	1.19	0.0027	726	1.00
MAP (cases)(mmHg)	rs2736100 (TERT)	5	1339516	1	A	C	0.37	-1.62	0.75	0.0314	777	0.49
MAP (controls)(mmHg)	rs2736100 (TERT)	5	1339516	1	A	C	0.39	-1.80	0.80	0.0239	726	1.00
PP (controls)(mmHg)	rs2736100 (TERT)	5	1339516	1	A	C	0.39	-2.65	0.85	0.0019	726	1.00
Triglyceride (mmol/L)	rs9420907 (OBFC1)	10	105676465	0.98819	A	C	0.91	0.08	0.04	0.0225	1492	0.22

Cardiometabolic Trait	SNP	Telomere shortening allele	Beta	SE	P	N	Phet
Triglyceride (mmol/L)	genotype risk score	yes	0.16	0.15	0.2907	1492	0.057
CHD	genotype risk score	yes	-0.26	0.79	0.7458	1604	0.850
DYSBP_cases (mmHg)	genotype risk score	yes	6.74	4.34	0.1204	787	0.297
DYSBP_controls (mmHg)	genotype risk score	yes	2.93	4.64	0.5270	736	0.343
HDL-cholesterol (mmol/L)	genotype risk score	yes	-1.70	3.36	0.6128	1490	0.630
LDL-cholesterol (mmol/L)	genotype risk score	yes	9.52	9.83	0.3331	1399	0.652
MAP_cases (mmHg)	genotype risk score	yes	6.22	4.86	0.2001	787	0.478
MAP_controls (mmHg)	genotype risk score	yes	6.08	5.24	0.2457	736	0.089
PP_cases (mmHg)	genotype risk score	yes	-1.55	6.14	0.8006	787	0.807
PP_controls (mmHg)	genotype risk score	yes	9.72	5.63	0.0839	736	0.011
SYBP_cases (mmHg)	genotype risk score	yes	5.19	7.63	0.4961	787	0.771
SYBP_controls (mmHg)	genotype risk score	yes	12.37	7.78	0.1118	736	0.015
Total cholesterol (mmol/L)	genotype risk score	yes	23.20	12.49	0.0633	1507	0.326

DYSBP- Diastolic Blood Pressure, SYBP- Systolic Blood Pressure, MAP- Mean Arterial Pressure, PP-Pulse Pressure, CHD - Coronary Heart Disease, HDL- High Density Lipids, LDL-Low Density Lipids, SE- Standard Error

Supplementary Table 14A : Correlation of Beta and Power

Table 14A. Power to detect the association effect within a given population		BETA	POWER
additive		0.32	0.6305
MAF	0.17	0.33	0.6967
Mean	1.9587	0.34	0.7569
Stdev	1.8655	0.35	0.8101
N	4013	0.36	0.8554
p	5E-08	0.37	0.8929
		0.38	0.9227
		0.39	0.9458
		0.40	0.9631
		0.41	0.9756
		0.42	0.9843
		0.43	0.9902
		0.44	0.9941

Table 14B. Sample size needed (in Caucasians) to detect significant effect of same size as sikh population

additive	
MAF	0.07
MEAN	1.9587
Stdev	1.8655
p	5E-08

	POWER	N (p=5E-08)	N (P=0.05)
Beta	0.32	63%	8,723
		80%	10,328
		80%	7,318
		80%	5,453
			1,370
			2,047
			1,450
			1,081

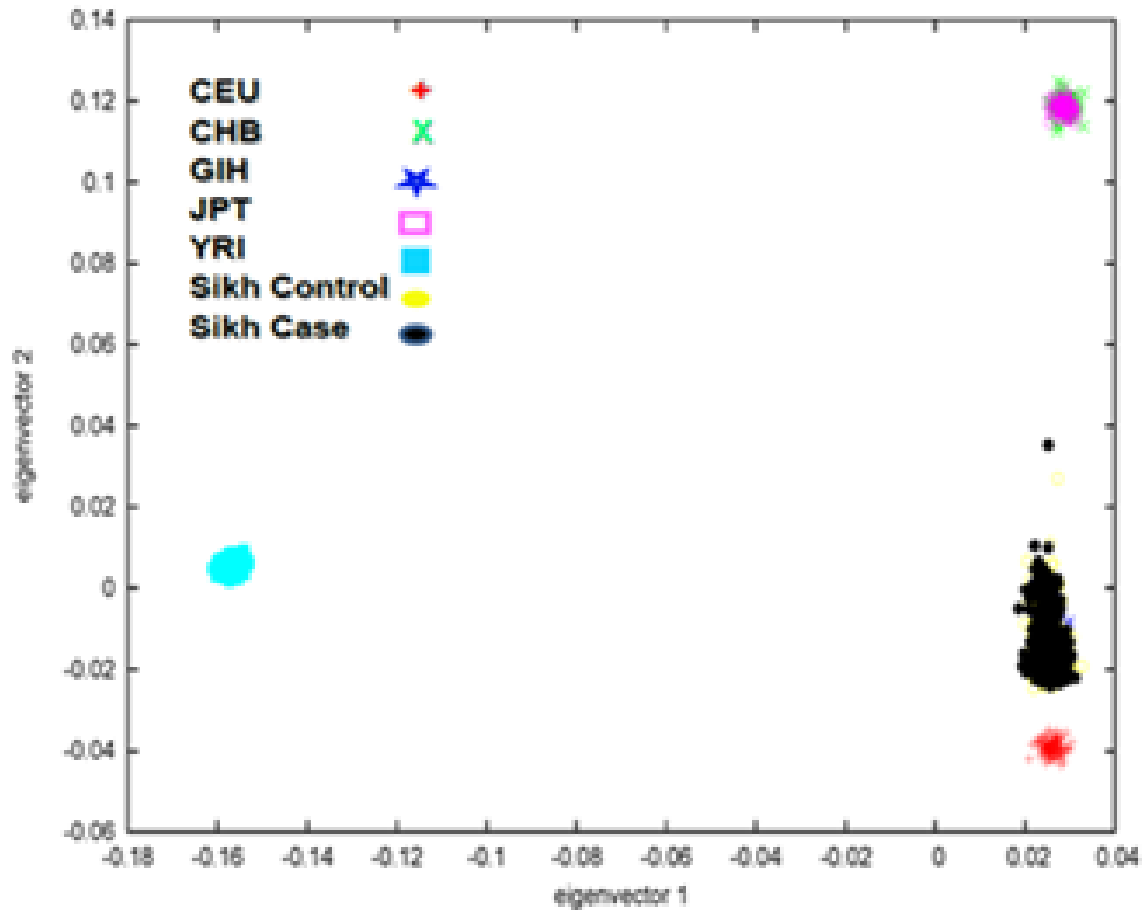
Supplementary Table 15: Association of CSNK2A2 rs74019828 snp with quantitative traits

		rs74019828		
	MODEL	BETA(SE)	<i>P</i> (Not adjusted)	<i>P</i>
CARDIOVASCULAR TRAITS				
CHD	SEX,AGE,BMI,DISEASE	-0.02(0.15)	8.8E-01	7.3E-01
SYBP	SEX,AGE,BMI,CONTROLS ONLY	0.01(0.21)	8.5E-01	9E-01
DYSBP	SEX,AGE,BMI,CONTROLS ONLY	-0.03(0.57)	2.3E-01	2.6E-01
SYBP	SEX,AGE,BMI,DISEASE	0.09(0.13)	4.2E-01	3.7E-01
DYSBP	SEX,AGE,BMI,DISEASE	-0.12(0.06)	5.8E-01	4.3E-01
METABOLIC TRAITS				
T2D	SEX,AGE,BMI	-0.03(0.09)	7.7E-01	5.8E-01
T2D Onset	SEX,AGE,BMI	0.01(0.47)	7.3E-01	2.1E-01
FBG	SEX,AGE,BMI,CONTROLS ONLY	0.05(0.27)	4.6E-01	3.2E-01
HOMA-IR	SEX,AGE,BMI,CONTROLS ONLY	0.03(0.33)	3.1E-01	2.8E-01
FBG	SEX,AGE,BMI,DISEASE	0.12(0.23)	1.7E-01	1.1E-01
HOMA-IR	SEX,AGE,BMI,DISEASE	0.08(0.16)	2.1E-01	1.3E-01

SE- Standard Error, CHD- Coronary Heart Disease, SYBP- systolic blood pressure, DYSBP-diastolic blood pressure,T2D- Type II Diabetes, FBG-fasting blood glucose, HOMA-IR- Homeostatic Model Assessment-Insulin Resistance, HOMA-β - Homeostatic Model Assessment-beta

Supplementary Figure 1

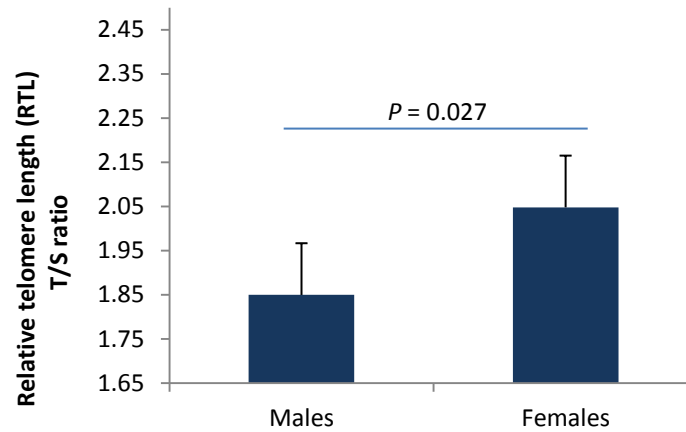
Principle component analysis of Sikh GWAS and HapMap 3 founder populations GIH, CEU, CHB, JPT, and YRI. Eigenvectors demonstrate the close proximity of the Sikh GWAS population to the GIH and CEU populations, and the close matching of cases and controls.



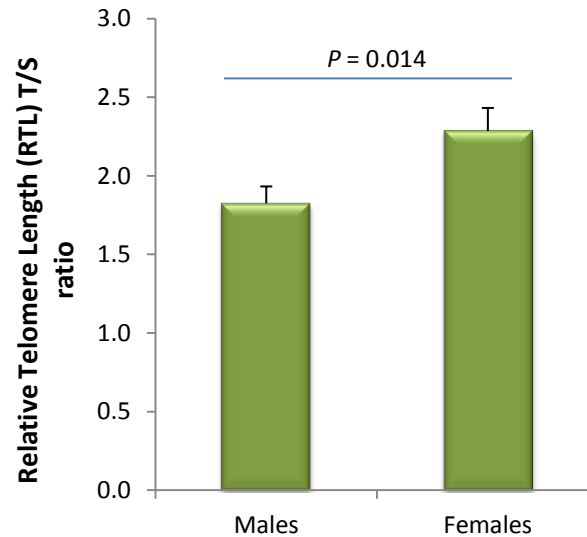
Supplementary Figure 2

Distribution of RTL with gender in AIDHS/SDS (Discovery GWAS) and combined (Discovery and Stage 1 Replication) cohorts

GWAS

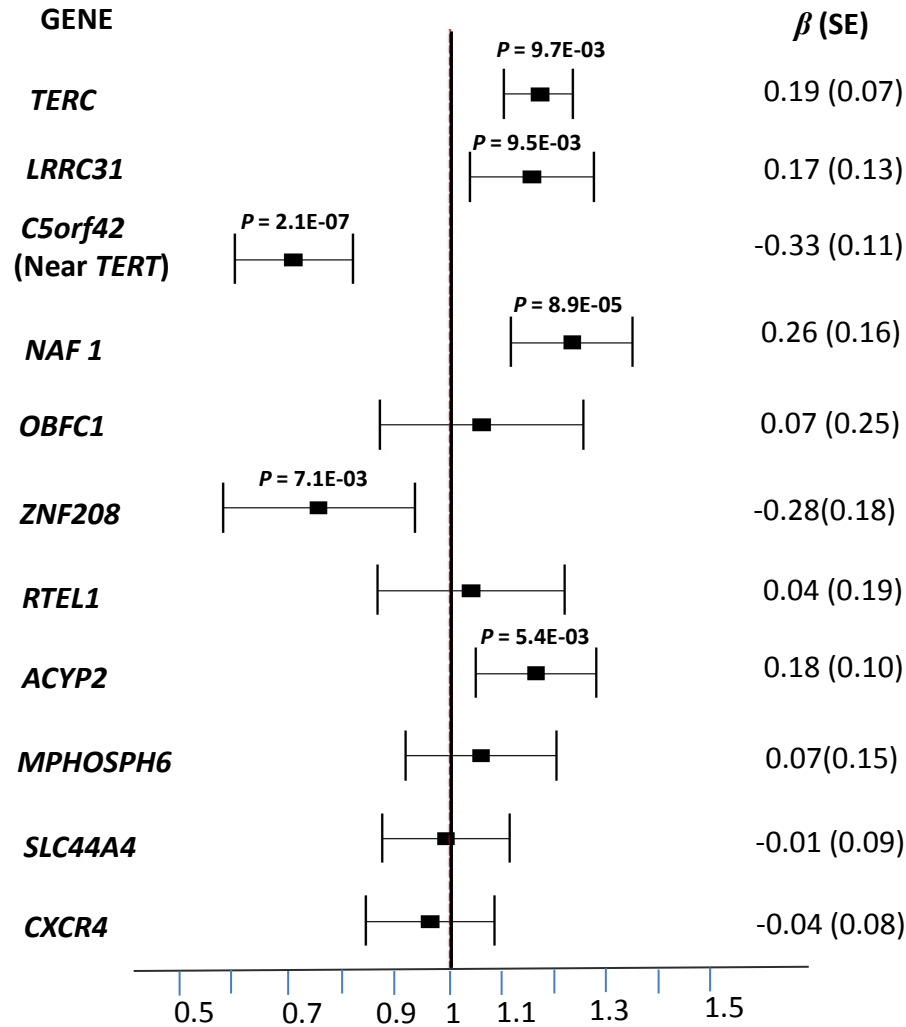


Combined (GWAS & Replication)



Supplementary Figure 3

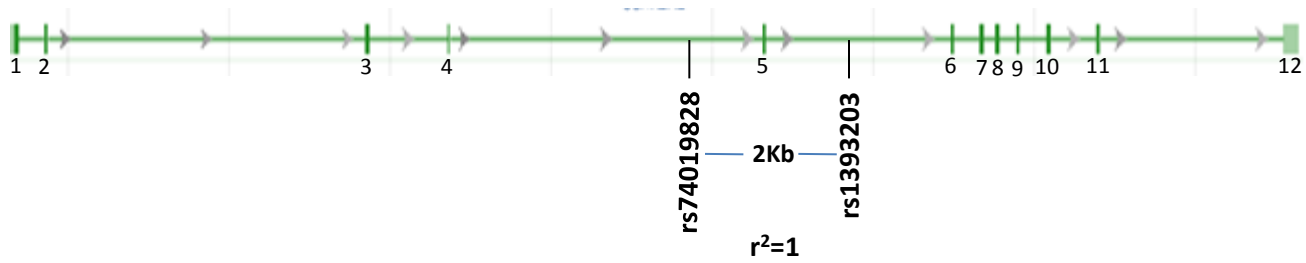
Forest plot shows significant association of previously reported genes with RTL using other variants in Sikhs.



Supplementary Figure 4

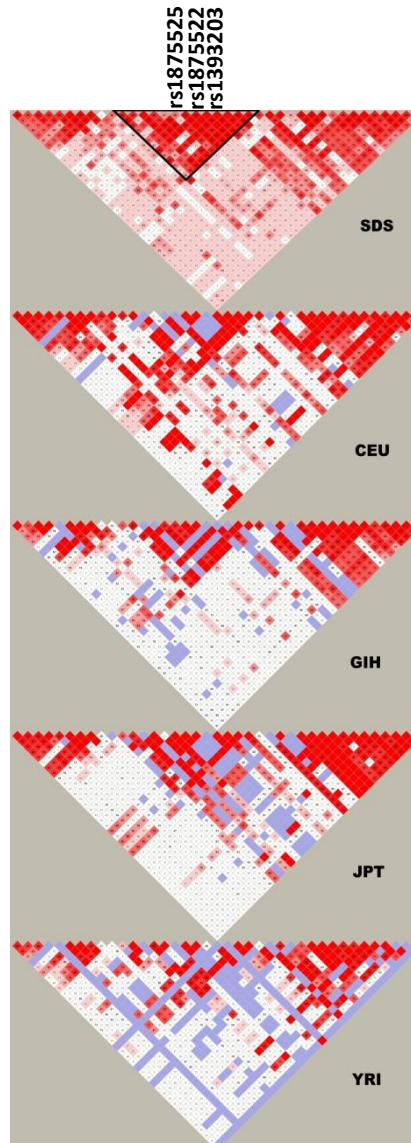
CSNK2A2 gene locus representing the positions of key variants rs74019828 and rs1393203 in the *CSNK2A2* introns.

CSNK2A2



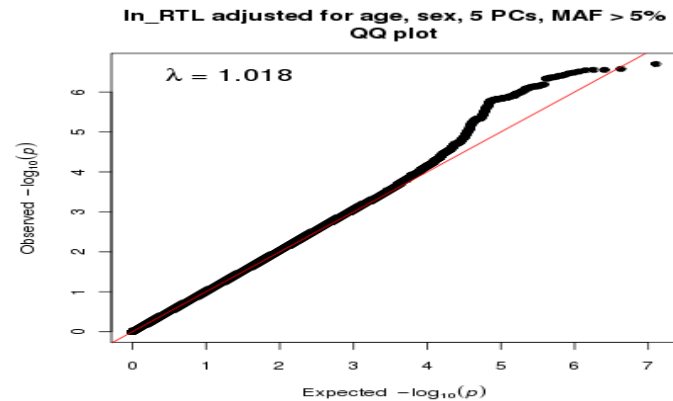
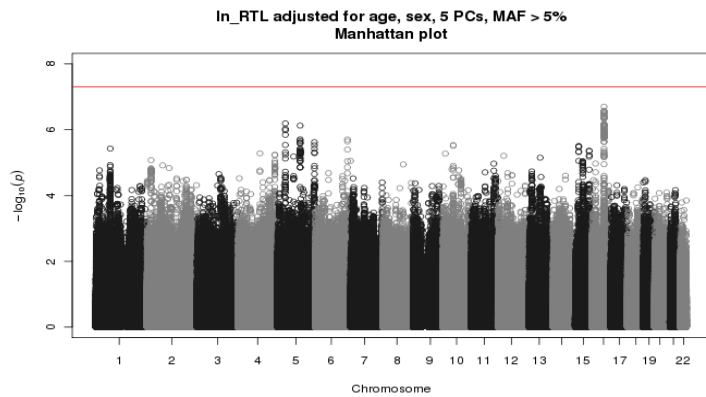
Supplementary Figure 5

The association of *CSNK2A2* locus represented by the three top SNPs showing strong association with RTL (Meta-analysis $P=4.4 \times 10^{-7}$). LD maps of the SNPs in the *CSNK2A2* locus showing patterns of pair-wise LD between Sikhs, Gujarati Indians (GIH), Caucasians (CEU), Japanese (JPT), and Africans (YRI).

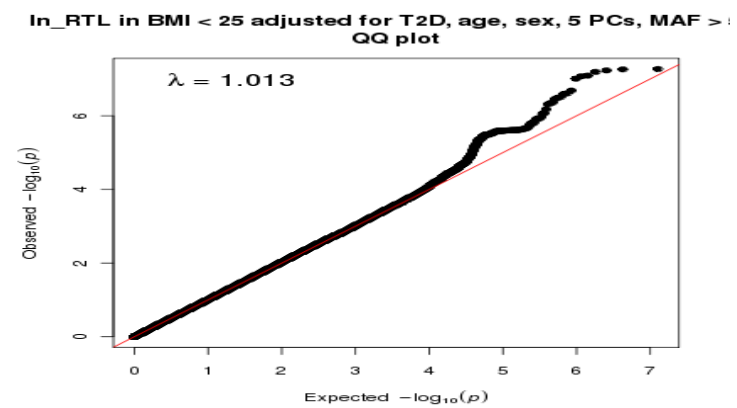
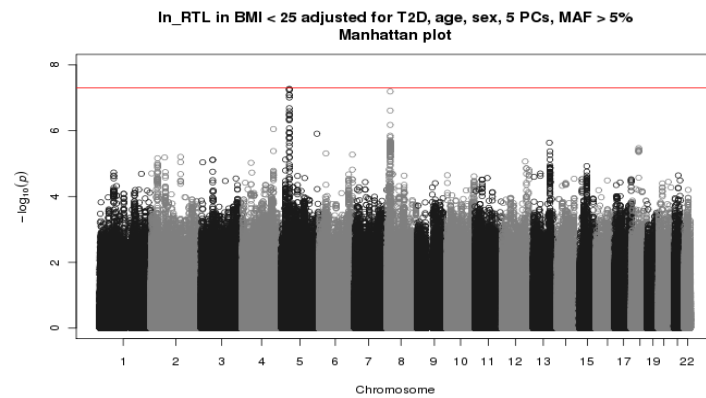


Supplementary Figure 6

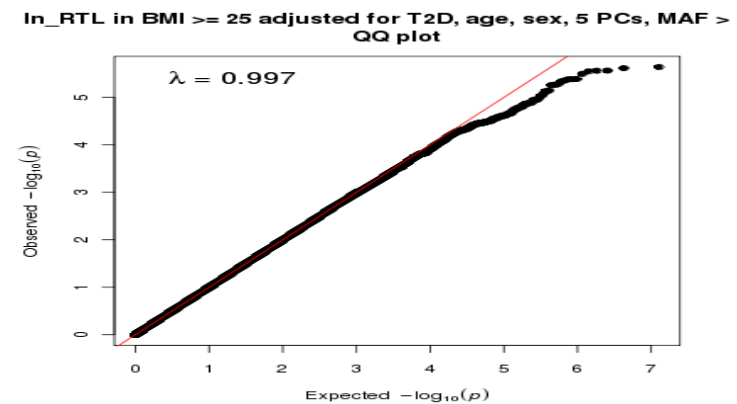
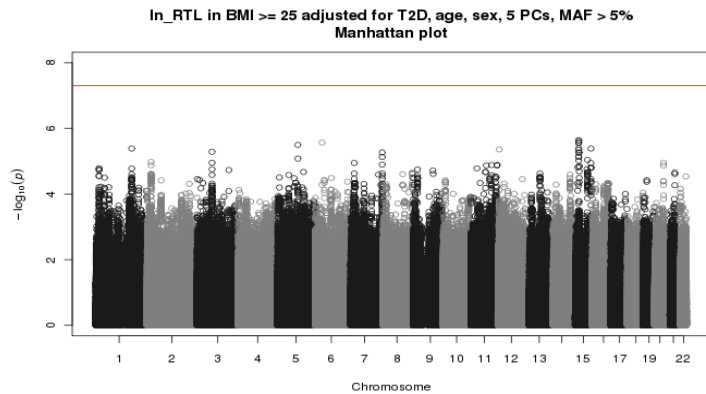
A



B



C



- A:** Manhattan and QQ plots displaying the association of RTL with SNPs without adjusting for Type 2 Diabetes (T2D)
B: Manhattan and QQ plots showing the association of RTL with SNPs in BMI<25 adjusted for T2D, age, sex and 5 PCs
C: Manhattan and QQ plots showing the association of RTL with SNPs in BMI>25 adjusted for T2D, age, sex and 5 PCs