Online Data Supplement

Four-gene pan-African blood signature predicts progression to tuberculosis

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Online supplement:

Supplementary Methods:

Study cohorts:

1. Household contact (HHC) cohorts:

The Grand Challenges 6-74 (GC6-74) parent cohort enrolled 4,466 HIV-negative household contacts (HHC) of an index TB case, aged 10-60 years, with no clinical signs of active TB disease at enrolment **(Figure 1 and Supplementary Table 2)**. Index TB cases were at least 15 years old, with confirmed positive sputum smear for acid-fast bacilli, diagnosed two months or less before enrolment of the HHC. HHC who progressed to active TB disease within 2 years of follow-up were considered "progressors" (**TB disease classifications A-K, Supplementary Table 10)**. Participants who were diagnosed with active TB within 3 months of enrolment were excluded to prevent inclusion of those with undiagnosed TB disease at time of exposure as progressors. Those with a positive HIV rapid test, current or previous anti-retroviral treatment, history of TB, pregnancy, participation in drug and/or vaccine clinical trials or a chronic disease diagnosis or immunosuppressive therapy within the past 6 months, or living in the study area for less than 3 months, were also excluded. Each progressor was matched to 4 HHC non-progressors/controls **(Supplementary Tables 11A and 11B)**, who remained healthy during follow-up, by site, age category, sex, and wherever possible, year of recruitment **(classifications R and S, Supplementary Table 10).** Age was sub-divided into 4 categories: <18, 18-25,

25-36, and >36 years of age, and year of enrolment into 3 categories: 2006/2007, 2008 and 2009/2010.

The South African GC6-74 cohort was recruited from the communities of Ravensmead, Uitsig, Adriaanse and Elsiesriver and clinical sites affiliated with the University of Stellenbosch in Cape Town, South Africa. South African participants did not receive isoniazid preventive treatment in accordance with national South African guidelines. Samples were collected from participants at enrolment (baseline samples), and 18 months. The Gambian GC6-74 cohort was recruited from the Greater Banjul area and Medical Research Council (MRC) outpatient departments in The Gambia. The Ethiopian cohort was recruited from Arada, T/Haimanot, Kirkos and W-23 clinical centers in Addis Ababa, Ethiopia. Finally, the Ugandan cohort was recruited from the Uganda National Tuberculosis and Leprosy Program treatment center at the Old Mulago Hospital and surrounding communities in Kampala, Uganda. Latently infected Ugandan, but not Ethiopian or Gambian, participants were offered isoniazid preventive treatment. For the Gambian, Ethiopian and Ugandan sites, samples were collected at enrolment (baseline), 6 and 18 months post-enrolment. Samples from all 4 sites were shipped to the University of Cape Town for standardized analysis.

2. Adolescents Cohort Study:

The Adolescents Cohort Study includes South African adolescents aged 12-18 years old, who had evidence of *M.tb* infection (IGRA+ and/or TST+) with no

clinical signs of active TB disease at enrolment. The selected participants were nested from a larger cohort of 6,363 adolescents at high schools in the town of Worcester, South Africa[2]. The study was approved by the Human Research Ethics Committee (HREC) of the University of Cape Town; approval no. 045/2005. The parents or legal guardians of participating adolescents provided written informed consent and adolescent provided written informed assent. Recruited adolescents were monitored for a 2-year follow-up period. During follow-up visits, whole blood samples were directly collected into PAXgene blood RNA tubes (PreAnalytiX, Hombrechtikon, Switzerland). Participants who developed intrathoracic TB disease with microbiological confirmation of *M.tb* in either two positive sputum smears for acid-fast bacilli or at least one positive sputum culture for *M.tb* were designated progressors. For each progressor, 2 non-progressors (controls), who remained healthy and did not develop clinical signs of active TB disease during follow-up, were matched by age, sex, race, previous history of TB and school attended at time of enrolment. Participants that developed active TB disease within 6 months of enrolment were excluded from analysis to prevent inclusion of those who had undiagnosed TB at enrolment.

Whole blood RNA sample processing and sequencing:

PAXgene blood RNA samples were collected before TB diagnosis in progressors. Non-progressor were samples matched to the pre-diagnosis time points of the corresponding progressor. RNA was extracted from blood RNA samples using the PAXgene Blood RNA kit (Qiagen, Germantown, MD, USA),

and separated into aliquots for local quality control, RNA-sequencing and qRT-PCR. Quantification of RNA and initial quality control were performed using a NanoDrop 2000^{TM} spectrophotometer (ThermoFisher Scientific, Waltham, MA, USA), followed by Agilent 2100 Bioanalyzer sampling (Agilent, Santa Clara, CA, USA) to determine RNA Integrity. RNA samples with a minimum of 200ng total RNA and RNA integrity number ≥7 were submitted for sequencing (see Figure 1 for QC exclusions).

For RNA-sequencing, globin transcript depletion (GlobinClear, ThermoFisher Scientific, MA, USA), cDNA library preparation (Illumina TruSeq Stranded mRNA; Illumina, CA, USA)), and RNA sequencing (60 million 50bp paired-end reads on HiSeq-4000 sequencers) were performed by Beijing Genomics Institute (Shenzhen, China).

Quality control and processing of RNA-Seq data:

Read pairs were preprocessed by adjusting base calls with phred scores < 5 to 'N' and removing for which either end had fewer than 30 unambiguous base calls. Read pairs were aligned to the human genome (hg19) using STAR (v2.3.1d)[29], taking as input the Ensembl GRCh37.74 splice junction table and allowing for novel splice junction detection. Gene expression was quantified in terms of splice junction counts to facilitate inter-conversion between RNA-Seq and qRT-PCR platforms, as previously described[27]. Junction-level expression values were standardized for each sample using a set of reference features, such that:

$$abundance_j = \log_2\left(counts_j + 1\right) - \sum_{r \in refs} \frac{\log_2(counts_r + 1)}{N_{refs}}$$

where $abudance_j$ is the standardized estimate of abundance for junction j, $counts_i$ is the raw number of reads aligning to junction I, and N_{refs} is the number of reference junctions used for standardization (here, N_{refs} = 20).

Quantitative real-time PCR (qRT-PCR):

Expression levels of genes of interest were analyzed by qRT-PCR using Taqman FAM-TAMRA gene expression primer-probe assays (Thermo Fisher Scientific, Waltham, MA) mapping to splice junctions selected by machine learning analysis. cDNA was synthesized using Superscript II reverse transcriptase (Thermo Fisher Scientific), followed by pre-amplification with primer-probe master mixes of 96 assays run on each chip as follows: 95°C for 10 minutes followed by 16 cycles of: 95°C for 15 seconds, then 60 minutes for 4 minutes and cooled to 4°C. Multiplex qRT-PCR reactions were performed on the BioMark HD (Fluidigm, San Francisco, CA) using microfluidic 96.96 gene expression chips (Fluidigm). Reaction Ct values were generated using Fluidigm Real-time PCR Analysis Software v.3.1.3 (Fluidigm), with a quality threshold of 0.65, linear derivative baseline correction method and auto global setting for Ct threshold determination.

Pair Ratios (PR) algorithm

Easily implementable host RNA-based signatures were derived from the RNA-seq and qRT-PCR measurements using the Pair Ratios algorithm (PR), which reduces the number of transcripts that need to be assayed by formulating the signatures in ratio-metric terms. This approach standardizes data using ratios of signal transcripts that are regulated in opposite directions during TB progression, to magnify TB-associated signals and simultaneously standardize.

The overall output of the PR signatures is a score between 0 and 1, which is the average over the scores from the individual pairs. One of the strengths of the signature is that it is robust to missing data, which often occurs in qRT-PCR measurements. If a particular assay fails on a given sample, then the score is computed by simply computing the average score from all ratios that do not involve that assay.

The only computational step in the signature is converting each transcript expression ratio into a score between 0 and 1. This is done by comparing the ratio to the distribution of ratios present in the training set. The ratio is compared to all ratios from TB progressors and controls in the training cohorts. The score for a particular sample is computed as the average over the percentage of progressor samples in the training set that have a ratio lower than the observed ratio and the percentage of control samples in the training set that have a ratio lower than the observed ratio. By separately considering the progressors and controls, we ensure that the conversion of the ratio to a score between 0 and 1 is independent of the relative numbers of progressors and controls in the training population.

For the RNA-seq discovery of the South Africa and Gambia signatures, we performed selection of pairs to include in the final signature in a two-step procedure. First, all exon-exon junctions were evaluated at the univariate level for the ability to predict progression. Due to the imbalance in progressors and non-progressors in the training sets, 500 re-sampled training sets were formed for both sites, each including all progressor samples plus one randomly-selected matching non-progressor sample for each. For each re-sampled training set, the ability of each junction to predict progression was evaluated using the Wilcoxon test, and those junctions with a sufficiently strong signal were carried forward to the pairwise selection step. The univariate selection criterion in South Africa was all junctions that had Wilcoxon $p<0.001$ in at least 70% of the re-sampled training sets, and in The Gambia the criterion was all junctions with Wilcoxon $p<0.001$ in at least 80% of re-sampled training sets. These cutoffs were determined by optimizing Leave-One-Out-Cross-Validation (LOOCV) results. Once a pool of exon-exon junctions was established through the univariate selection procedure, all possible pairs of junctions (where each pair involves one junction up-regulated and one junction down-regulated during progression) were formed, and their log-ratios computed. The ability of each junction pair to predict progression was measured in terms of sensitivity and specificity. All pairs with sensitivity and specificity above a fixed cutoff were included in the final ensemble. In South Africa, the pairwise cut-off was 80%, whereas in the Gambia it was 75%. Once again, the values of these cutoffs were determined by optimizing LOOCV performance.

For the final qRT-PCR based RISK4 signature, the pool of transcripts that formed the basis of the pairwise analysis comprised all transcripts selected in the South African and Gambian RNA-seq signatures. The final ensemble was then systematically constructed as described in the main text.

Adaptation of RNA-seq signatures to qRT-PCR

Taqman primer-probe assays were selected corresponding to all splice junctions in the signatures, when possible. A table showing the assays selected for each junction is given in **Supplementary Tables 12 and 13**. Pairwise linear discriminant models were trained using the qRT-PCR Cts for all of the pairs in the signatures in a direct search analogous to the method described above. Pairs including a junction without an available qRT-PCR assay were omitted. We started by identifying a single pair of transcripts that best fitted the entire training set and successively added the next best pair to the ensemble and re-assessed the predictive power at each stage. This procedure was carried out until addition of pairs led to no further increase in predictive power. The pairwise structure of the qRT-PCR versions of the RISK4 signature is given in **Supplementary Table 14**.

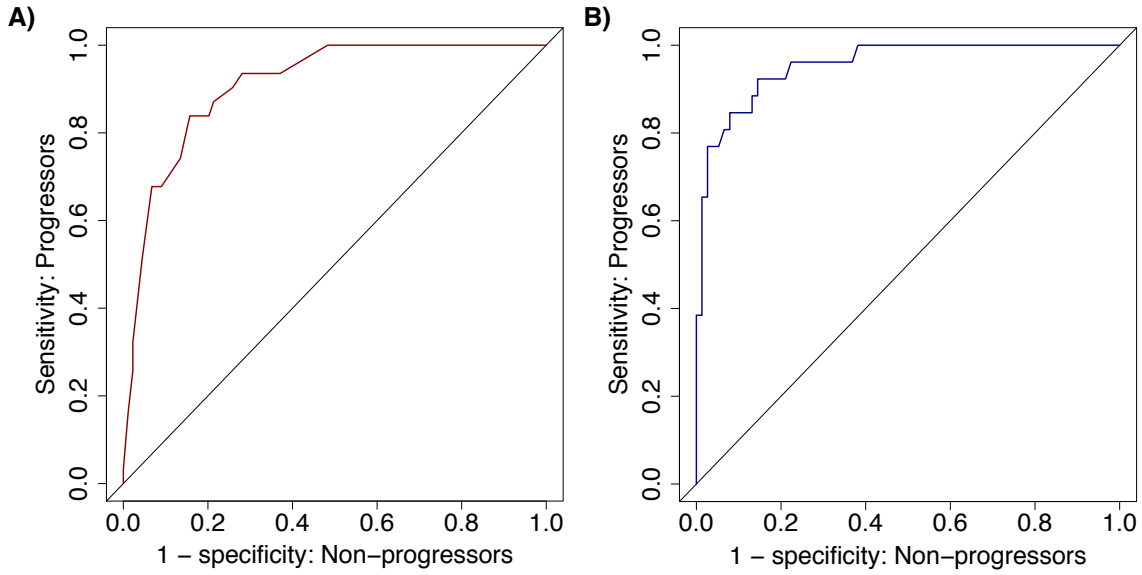
Meta-analysis of unblinded training and test cohorts

We first identified all splice junction counts that strongly predicted progression on any one of the three cohorts (**Supplementary Tables 17-18 and 24-26**; FDR <0.05). We then paired up-regulated splice junctions with down-regulated junctions to generate a set of expression-ratio pairs and assessed the ability of

each pair to predict progression in each GC6-74 cohort. The AUC of each pair on each cohort was computed, and we identified pairs that maximized predictive performance over the worst AUC that was observed in any of the three cohorts **(Supplementary Table 14)**. To determine whether other pairs were providing complementary or redundant information to the top pair, C1QC/TRAV27, for each of the other top 8 pairs, a logistic regression model was fit as PROGRESSION ~ 1 + C1QC/TRAV27 + SecondPair. The fit of this model was compared to the fit of the base PROGRESSION ~ 1 + C1QC/TRAV27 model using a chi-squared test.

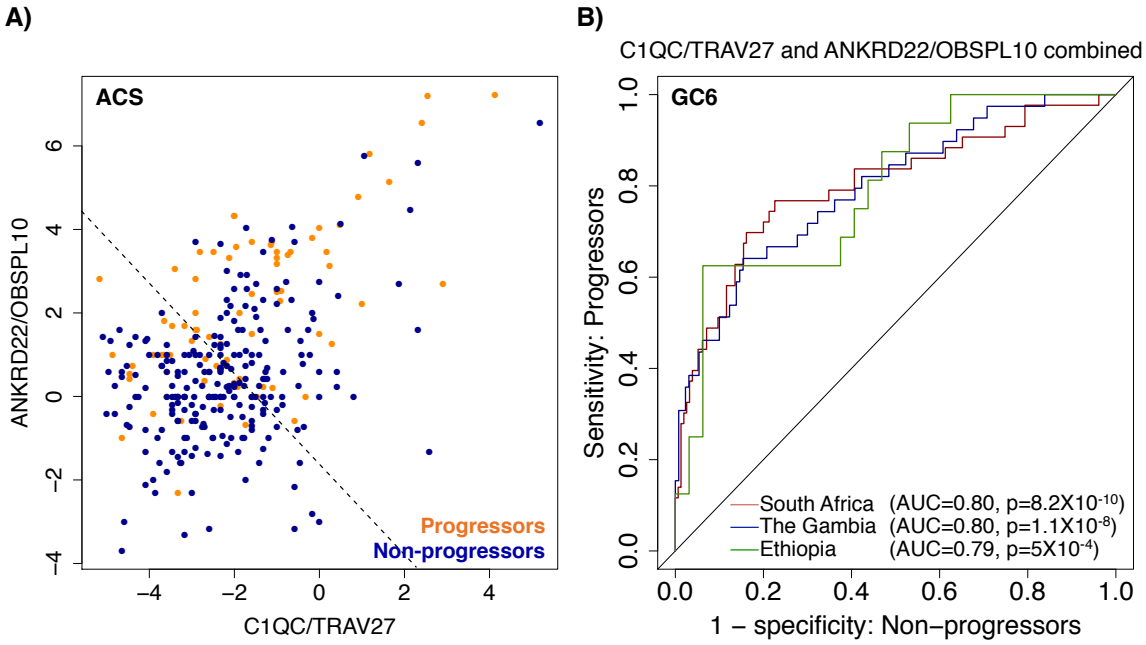
Supplementary Figures:

Supplementary Figure 1:



Translation of RNA-seq signatures to qRT-PCR: The RNA-seq signatures discovered using the South Africa training set (as shown in **Figure 1C**) and The Gambia training set (as shown in **Figure 1D**) were converted to qRT-PCR with minimal loss of fit to the training set. **A.** Receiver operating characteristic curve for the South Africa qRT-PCR signature fit to the South Africa training set. AUC [95% CI] = 0.91 [0.86-0.96]. **B.** Receiver operating characteristic curve for the Gambia qRT-PCR signature fit to the Gambia training set. AUC [95% CI] = 0.95 [0.92-0.99].

Supplementary Figure 2:



Complementation of pair ratios of C1QC/TRAV27 with ANKRD22/OBSPL10: Scatterplot of C1QC/TRAV27 complementation with the top pair ANKRD22/OBSPL10 on the natural history cohort of South African latently *M.tb*–infected adolescents (Adolescents Cohort Study: ACS; Zak, et al. *Lancet* 2016)

S2B: Area under the Receiver Operators Characteristics Curve corresponding to the linear combination of C1QC/TRAV27 and ANKRD22/OBSPL10 on each of the three African household contact cohorts separately: South Africa (red) with AUC=0.81 [0.72-0.88], $p=8.16X10^{-10}$; The Gambia (blue) with AUC=0.8 [0.71-0.88], $p=1.13X10^{-8}$; and Ethiopia (green) with AUC=0.79 [0.66-0.93], $p=5X10^{-4}$.

Supplementary Table 1: Institutional Review Boards that provided ethics approvals for the different GC6-74 sites

Site	Ethics Review Committee	Protocol no.
SUN	Stellenbosch University Institutional Review Board	N05/11/187
MRC	Joint Medical Research Council and Gambian Government	SCC.1141vs2
MAK	Uganda National Council for Science and Technology	MV 715
MAK	University Hospitals Case Medical Centre	12-95-08
AHRI	Armauer Hansen Research Institute (AHRI)/All Africa Leprosy, TB and Rehabilitation Training Center (ALERT)	P015/10
UCT (GC6)	University of Cape Town Human Research Ethics Committee HREC	013/2013
UCT (ACS)	University of Cape Town Human Research Ethics Committee HREC	045/2005

Supplementary Table 2: GC6-74 recruitment and follow up dates

Site	Cohort	Study Design	First date of enrolment	Last date of enrolment	Last date of follow-up	Number of Index cases	Number of Household Contacts
South Africa	SUN	Household Contact	February 27th, 2006	December 14th, 2010	November 28th, 2012	209	1 197
The Gambia	MRC	Household Contact	March 5th, 2007	October 21st, 2010	October 22nd, 2012	402	1 948
Uganda	MAK	Household Contact	June 1st, 2006	June 8th, 2010	May 4th, 2012	181	499
Ethiopia	AHRI	Household Contact	February 12th, 2007	August 3rd, 2011	August 16th, 2012	154	818
South Africa	ACS	Natural History	July 6th, 2005	April 23rd, 2007	February 19th, 2009	NA	NA

Supplementary Table S3 - Pairwise **s**tructure of RISK 4 signature

Pair number	Primer-probe ID #1	Primer-probe ID #2
1	GAS6_NM_000820_10_11	CD1C_Hs00957534_g1
2	SEPT4_Hs00910208_g1	BLK_Hs01017452_m1
3	SEPT4_Hs00910208_g1	CD1C_Hs00957534_g1
4	GAS6_NM_000820_10_11	BLK_Hs01017452_m1

Supplementary Table S8: Adaptation of the DIAG3 signature to qRT-PCR

Gene	Primer-Probe ID	Regulation	Custom sequence	Custom target
GBP5	Hs00369472_m1	Up-regulation		
DUSP3	Hs01115776_m1	Up-regulation		
KLF2	CUSTOM	Down-regulation	CGCTGGCCGCGCGCCC	816

Supplementary Table S9: Adaptation of the DIAG4 signature to qRT-PCR

Gene	Primer-Probe ID	Regulation
GBP1	Hs00977005_m1	Up-regulation
IFITM3	Hs03057129_s1	Up-regulation
P2RY14	Hs01848195_s1	Up-regulation
ID3	Hs00954037_g1	Down-regulation

Supplementary Table 10: Criteria for tuberculosis diagnosis in GC6-74 progressors

Category	Culture 1	Culture 2*	AFB 1	AFB 2*	CXR	Symptoms	TB Treatment Response	Failed AB	Diagnostic Class
A	+	+							Definite
B	+				+				Definite
C	+		+						Definite
D			+	+	+				Probable
E			+	+		+			Probable
F			+		+				Probable
G	+					+	+		Probable
H	+					+			Possible
I			+	+			+		Possible
J			+			+			Possible
K					+	+	+	+	Possible
L	+								Questionable
M			+	+					Questionable
N			+						Questionable
O					+	+			Questionable
P					+				Questionable
Q						+			Questionable
R	*Neg/ND*	*Neg/ND*	*Neg/ND*	*Neg/ND*	*Neg/ND*	+	Rx not started		Non-TB case
S	*Neg/ND*	*Neg/ND*	*Neg/ND*	*Neg/ND*	*Neg/ND*	*Neg/ND*	Rx not started		Non-TB case

Culture *Either liquid or solid agar positive with confirmed speciation for M.tuberculosis complex*
AFB *Acid-fast bacilli: sputum smear ≥scanty (≥1-9 acid-fast organisms per 100x oil field)*
CXR *Chest X-ray compatible with active TB*
Failed AB *Failed antibiotics treatment; no response of symptoms to a 7-day, broad spectrum oral or IV antibiotics*
***** *Positivity on a separate sample of culture or AFB (not an aliquot of the same sample) provided by the participant preferrably but not necessarily on separate days*

Note: Questionable classification is excluded in both progressors and non-progressors

Supplementary Table 11A: Diagnosis and demographic characterists for all progressors in the GC6-74 household contact cohorts

	Progressor Participant ID	RNA Sample ID			Demographics				
		BL	M6	M18	Age at enrolment	Gender	Enrolment Year	Time to TB from Enrolment (months)	Training/Test Split (RNA-seq)
SOUTH AFRICA	2	715			13	M	2006	17	Training
	19	735			21	F	2006	11	Test
	63	719			19	F	2006	17	Test
	87	722			25	F	2006	5	Test
	93	721			52	F	2006	17	Test
	149	741		891	15	M	2006	5	Test
	165	752			17	F	2006	4	Training
	184	750			17	F	2006	14	Training
	196	753			45	F	2006	6	Test
	204	746		904	47	F	2006	23	Training
	299	754		917	35	M	2006	19	Training
	317	755			31	M	2006	6	Test
	375	761			24	M	2006	5	Training
	450	760			26	M	2006	5	Training
	479	778			57	F	2007	5	Training
	507	793			24	F	2007	5	Training
	650	777			19	F	2007	5	Training
	769	718			45	F	2007	5	Training
	878	825			24	F	2007	5	Test
	886	805			27	M	2007	10	Test
	921				17	M	2007	7	
	938	822			39	M	2007	18	Training
	1051			197	43	M	2007	23	Test
	1115	819			60	M	2007	5	Test
	1151				52	M	2007	5	
	1371	836			38	F	2007	5	Test
	1445	834			15	F	2007	13	Test
	1552	839		173	45	M	2008	19	Training
	1590	842			47	F	2008	17	Training
	2123	179			53	M	2008	5	Training
	2129	186			25	M	2008	3.5	Training
	2693	866			24	F	2008	17	Training
	2847	124			30	F	2008	5	Training
	2864	864		159	16	F	2008	23	Training
	3011	857			27	M	2008	6	Training
	3099			157	22	F	2008	23	Training
	3102	865			14	F	2008	5	Training
	5662	73		96	17	F	2010	23	Training
	6290				15	F	2010	5	
	6313	165			38	M	2010	17	Training
	6665	142			14	F	2010	17	Training
	6675	52			19	F	2010	23	Training
	6907	49			22	M	2010	17	Training
THE GAM	2007/G123	532			31	F	2007	15	QC failed
	2007/G213	236			34	M	2007	14	QC failed
	2007/G225	489		490	17	M	2007	19	QC failed
	2007/G300	248			26	M	2007	10	Training
	2007/G437	543			18	F	2007	9	QC failed
	2007/G438				16	M	2007	7	
	2007/G468	259	260		52	M	2007	18	QC failed
	2008/G245		272	273	16	M	2008	21	Training
	2008/G249		285	286	22	M	2008	24	Test
	2008/G260	297	298		37	F	2008	14	Training
	2008/G367	502	503		56	M	2008	10	Training
	2008/G423	309	310		21	F	2008	10	Training
	2008/G433	565	566	567	26	F	2008	24	Training
	2008/G493	322	323		37	F	2008	8	Training
	2008/G494	334	335		30	F	2008	9	Training
	2008/G606	578	579	580	21	F	2008	22	Training
	2008/G762	348	349	350	23	M	2008	21	Test
	2008/G800	361			20	M	2008	12	Training
	2008/G814	517			20	F	2008	4	Training

	Progressor Participant ID	RNA Sample ID			Demographics				
		BL	M6	M18	Age at enrolment	Gender	Enrolment Year	Time to TB from Enrolment (months)	Training/Test Split (RNA-seq)
BIA	2008/G876	373	374		20	F	2008	7	Test
	2009/G262				26	F	2009	3.5	
	2009/G280		591		32	F	2009	12	Test
	2009/G340				28	M	2009	6	
	2009/G367	398	399		56	M	2009	10	Training
	2009/G497	613			22	M	2009	3	Training
	2009/G524	413			26	F	2009	19	Training
	2010/G139	426		427	17	M	2010	21	Training
	2010/G178	437			26	F	2010	11	Training
	2010/G215	449	450		20	F	2010	7	Training
	2010/G261	626			38	F	2010	3	Test
	2010/G279	463	464	465	21	F	2010	19	Test
	2010/G289	640	641		16	F	2010	6	Test
	2010/G369	477	478		22	M	2010	11	Test
	2010/G407	655	656		22	F	2010	7	Training
ETHIOPIA	ARHHC63	987	235		20	F	2010	15	Test
	DZHHC78	929		233	19	M	2008	21	Test
	DZHHC96	977			25	F	2009	12	Test
	KFHHC21	1011			35	F	2007	7	Test
	KHHC121	963			18	F	2009	4	Test
	KHHC151	974	231		21	F	2010	14	Test
	KHHC26	1019	1020		25	M	2007	7	Test
	KHHC68	954	983		35	F	2008	15	Test
	KHHC78	1027			26	F	2008	4	Test
	MOHHC04	1029	935		30	F	2007	8	Test
	W23HHC08		1042	951	20	M	2007	18	Test
	W23HHC132	1002			18	M	2009	5	Test
UGANDA	90953				23	F	2008	11	
	92227				18	M	2008	7	
	92245	672*			32	F	2008	6	
	92663				18	F	2009	11	
	92957				18	F	2010	15	
	89902105				17	M	2006	3	
	90292102				40	M	2006	5	
	90749102				30	M	2007	3	
	90753104				52	M	2007	16	
	90850102				40	M	2007	5	
	91505506				15	F	2008	9	

	Progressor Participant ID	TB diagnosis								
		Culture+ (n)	Smear+ (n)	Chest X-Ray	Symptoms (n)	Other	Classification	Category	TB Strain of Index Case	TB Strain of Progressor
SOUTH AFRICA	2	1x speciated	none	no	1x	none	Possible	H	ND	ND
	19	none	, one AFB pos c	Yes	2x	Rx respons	Probable	D	ND	ND
	63	1x speciated	none	Yes	none	Rx respons	Definite	B	ND	ND
	87	2x speciated	none	no	1x	none	Definite	A	ND	ND
	93	1x speciated	none	Yes	1x	none	Definite	B	w	ND
	149	1x speciated	xpos 3+,3+,scan	Yes	3x	Rx respons	Definite	B	ND	ND
	165	ND	2xpos 1+	Yes	3x	Rx response	Probable	D	ND	ND
	184	1x speciated	2xpos 1+, 1+	no	none	Rx respons	Definite	C	ND	ND
	196	none	1x pos	Yes	none	none	Probable	F	ND	ND
	204	1x speciated	3xpos scanty, 1+, 3+	ND	No symptoms recorded	none	Definite	C	ND	ND
	299	1x speciated	none	Yes	3x	Rx respons	Definite	B	ND	ND
	317	1x speciated	2xpos 1+, 3+	Yes	none	Rx respons	Definite	B	ND	ND
	375	1x speciated	ND	yes	none		Definite	B	ND	ND
	450	1x speciated	3xpos 3+,3+,3+	Yes	none	Rx respons	Definite	B	ND	ND
	479	1x speciated	none	no	3x	none	Possible	H	ND	ND
	507	1x speciated	2xpos scanty, 2+	Yes	1x	Rx respons	Definite	B	ND	ND
	650	1x speciated	none	Yes	1x	Rx respons	Definite	B	ND	ND
	769	1x speciated	none	no	none	none	Definite	A	ND	ND
	878	1x speciated	ND	no	3x	none	Possible	H	ND	ND
	886	1x speciated	xpos scanty, 1+,	Yes	3x	none	Definite	B	ND	ND
	921	none	3xpos 1+,1+,3+	no	3x	Rx response	Probable	E	ND	ND
	938	1x speciated	2x pos 1+, 3+	no	1x (Hemoptysis)	Rx response	Definite	B	ND	ND
	1051	1x speciated	none	no	x2	none	Possible	H	ND	ND
	1115	1x speciated	2xpos 3+,3+	no	1x	Rx respons	Definite	C	ND	ND
	1151	1x speciated	neg	Yes	3x	none	Definite	C	ND	ND
	1371	1x speciated	none	no	3x	none	Definite	A	ND	ND
	1445	1x speciated	1xpos 2+	yes	3x	Rx response	Definite	B	ND	ND
	1552	1x speciated	2xpos 1+, 2+	Yes	2x	Rx respons	Definite	B	ND	ND
	1590	1x speciated	neg	no	1x	none	Possible	H	ND	ND
	2123	1x speciated	1xpos 3+	Yes	2x	Rx respons	Definite	B	ND	ND
	2129	1x speciated	xpos -2xscanty,	no	1x	Rx respons	Definite	C	ND	ND
	2693	1x speciated	neg	Yes	3x	none	Definite	B	ND	ND
	2847	1x speciated	2xpos 3+, 2+	Yes	2x	Rx respons	Definite	B	ND	ND
	2864	1x speciated	2xpos 1+, 2+	Yes	3x	Rx response	Definite	B	ND	ND
	3011	1x speciated	none	no	2x	Rx respons	Probable	G	ND	ND
	3099	2x speciated	2xpos - culture AFB & 2+	Yes	3x	Rx response	Definite	A	ND	ND
	3102	1x speciated	2xpos 1+, 3+	no	1x	Rx respons	Definite	C	ND	ND
	5662	2x speciated	neg	Yes	2x	none	Definite	A	ND	ND
	6290	1x speciated	neg	no	2x	none	Possible	K	ND	ND
	6313	2x speciated	neg	no	none	none	Definite	A	ND	ND
	6665	2x speciated	neg	no	none	none	Definite	A	ND	ND
	6675	2x speciated	1xpos 1+	no	1x	none	Definite	A	ND	ND
	6907	2x speciated	none	no	none	none	Definite	A	ND	ND
THE	2007/G123	none	2xpos 1+,1+	no	4x	Rx respons	Probable	E		ND
	2007/G213	2x speciated	none	Yes	5x	none	Definite	A		ND
	2007/G225	none	none	Yes	4x	sponse, AB	Possible	K		ND
	2007/G300	2x speciated	none	Yes	5x	none	Definite	A	M.tb	M.tb
	2007/G437	none	2xpos 1+,2+	no	1x	none	Probable	E		ND
	2007/G438	none	2xpos 1+,2+	Yes	4x	Rx respons	Probable	D		ND
	2007/G468	2x speciated	none	no	4x	none	Definite	A		ND
	2008/G245	1x speciated	none	Yes	5x	none	Definite	B	M.tb	M.tb
	2008/G249	1x speciated	2xpos 3+,3+	Yes	4x	none	Definite	B	M.tb	M.tb
	2008/G260	1x speciated	none	Yes	4x	AB failed	Definite	B	M.tb	M.tb
	2008/G367	none	none	Yes	4x	sponse, AB	Possible	K	M.Africanum	ND
	2008/G423	1x speciated	none	Yes	4x	AB failed	Definite	B	M.tb	M.tb
	2008/G433	neg	2xpos 1+,1+	Yes	5x	none	Probable	D	M.Africanum	ND
	2008/G493	2x speciated	none	Yes	5x	none	Definite	A	M.Africanum	M.Africanum
	2008/G494	2x speciated	none	Yes	4x	none	Definite	A	M.Africanum	M.Africanum
	2008/G606	neg	2xpos 2+, 3+	Yes	5x	none	Probable	D	M.Africanum	M.Africanum

GAMBIA	2008/G762	2x speciated	none	Yes	4x	none	Definite	A	ND	M.tb
	2008/G800	2x speciated	none	Yes	3x	none	Definite	A	M.tb	M.Africanum
	2008/G814	none	none	Yes	4x	sponse, AB	Possible	K	ND	ND
	2008/G876	2x speciated	none	Yes	5x	none	Definite	A	M.tb	M.tb
	2009/G262	2x speciated	none	Yes	4x	none	Definite	A		ND
	2009/G280	none	2xpos 2+,2+	Yes	5x	none	Probable	D	M.Africanum	ND
	2009/G340	neg	2xpos 2+, 2+	Yes	3x	none	Probable	D		ND
	2009/G367	1x speciated	none	yes	4x	none	Definite	B	M.Africanum	M.tb
	2009/G497	neg	2xpos 3+, 2+	Yes	4x	none	Probable	D	M.Africanum	ND
	2009/G524	2x speciated	none	yes	4x	none	Definite	A	M.tb	M.tb
	2010/G139	2x speciated	none	yes	4x	none	Definite	A	M.tb	M.tb
	2010/G178	2x speciated	none	yes	4x	none	Definite	A	M.tb	M.tb
	2010/G215	2x speciated	none	yes	3x	none	Definite	A	M.tb	M.tb
	2010/G261	none	2xpos 1+,2+	yes	4x	none	Probable	D	ND	ND
	2010/G279	2x speciated	none	yes	4x	none	Definite	A	M.tb	M.tb
	2010/G289	none	2xpos 2+	yes	5x	none	Probable	D	M.tb	ND
	2010/G369	1x speciated	none	yes	4x	none	Definite	A	M.Africanum	M.tb
	2010/G407	neg	2xpos 2+	yes	4x	AB failed	Probable	D	M.Africanum	M.Africanum
ETHIOPIA	ARHHC63	none	3xpos 3+	no	1x	failed, Rx r	Probable	E	ND	ND
	DZHHC78	none	neg	Yes	4x	failed, Rx r	Possible	K	ND	ND
	DZHHC96	1x speciated	none	no	2x	failed, Rx r	Probable	G	ND	ND
	KFHHC21	none	neg	yes	3x	failed, Rx r	Possible	K	ND	ND
	KHHC121	neg	2xpos	no	3x	failed, Rx r	Probable	E	ND	ND
	KHHC151	1x speciated	none	Yes	4x	failed, Rx r	Definite	B	ND	ND
	KHHC26	1x speciated	3xpos 3+	yes	3x	failed, Rx r	Definite	B	ND	ND
	KHHC68	neg	none	yes	1x	failed, Rx r	Possible	K	ND	ND
	KHHC78	none	none	yes	3x	failed, Rx r	Possible	K	ND	ND
	MOHHC04	none	3xpos 3+	yes	3x	failed, Rx r	Probable	D	ND	ND
	W23HHC08	none	3xpos 3+	yes	3x	failed, Rx r	Probable	D	ND	ND
	W23HHC132	1x speciated	3xpos 3+	yes	3x	failed, Rx r	Definite	B	ND	ND
UGANDA	90953	2x speciated	4xpos 3+	no	x1	failed, Rx r	Definite	A	ND	ND
	92227	1x speciated	none	yes	none	failed, Rx r	Definite	B	ND	ND
	92245	1x speciated	**2xpos, 20+**	yes	x2	failed, Rx r	Definite	B	ND	ND
	92663	1x speciated	2xpos, 1+	no	x1	Rx respons	Definite	C	ND	ND
	92957	2x speciated	1xpos 3+	no	x3	Rx respons	Definite	A	ND	ND
	89902105	2x speciated	**1xpos 20+**	yes	none	failed, Rx r	Definite	A	ND	ND
	90292102	1x speciated	none	no	x3	failed, Rx r	Probable	G	ND	ND
	90749102	none	1xpos 1+	yes	x3	AB trial faile	Probable	F	ND	ND
	90753104	2x speciated	1xpos 3+	yes	x1	failed, Rx r	Definite	A	ND	ND
	90850102	1x speciated	none	no	x1	Rx respons	Probable	G	ND	ND
	91505506	1x speciated	2xpos 3+	no	x1	failed, Rx r	Definite	C	ND	ND

Sample numbers refer to samples collected at baseline following household exposure (BL), 6 months (M6), or 18 months (M18) after household contact
Shaded rows correspond to participants that did not have available RNA samples for this analysis
ND: Not done
***Note**: Uganda RNA samples were sequenced and included in biological network analysis, but not predictive modelling analysis

Supplementary Table 11B: Diagnosis and demographic characterists for all progressors in the GC6-74 household contact cohorts

Non-Progressor Participant ID	RNA Sample ID			Demographics					Category
	BL	M6	M18	Age at enrolment	Gender	Enrolment Year	Training/ Test Split (RNA-seq)	Matched Progressor ID	
1				25	M	2006		317	R
6	716			18	M	2006	Test	Unmatched	S
8				21	F	2006		87	R
15	726			15	M	2006	Test	149	R
45	736			23	F	2006	Test	19	S
46	717			15	M	2006	Test	149	S
53	737			21	F	2006	Test	87	R
62				29	F	2006		712	R
70	738			45	F	2006	Test	1371	S
72	727			23	F	2006	Test	878	R
76	732			25	M	2006	Test	317	R
79				40	M	2006		1149	S
89	730			23	F	2006	Test	63	R
92	729			27	M	2006	Test	886	S
96	733			12	M	2006	Test	149	R
99	734			14	M	2006	Test	921	R
100	739			13	F	2006	Training	165	S
108	720			22	M	2006	Test	375	R
122	723			19	M	2006	Test	Unmatched	R
124	724			18	F	2006	Test	19	R
134	740		897	47	F	2006	Training	204	S
140	731			17	M	2006	Test	149	S
145	743			20	F	2006	Test	878	R
150				39	M	2006		1149	S
161	744			17	F	2006	Training	184	R
198	745			15	F	2006	Test	165	S
217			217	38	F	2006	Training	204	R
290	748		219	20	F	2006	Test	650	S
294				23	F	2006		878	S
301	749			13	F	2006	Test	1445	S
315	751		220	56	F	2006	Test	479	S
353	771			19	F	2007	Test	63	S
355	871			42	F	2007	Test	1371	R
357	758			42	F	2006	Training	479	R
358	756			12	M	2006	Test	921	S
359	757			8	F	2006	Test	184	R
374	759			11	M	2006	Training	Unmatched	R
376	376			46	M	2006	Test	1151	R
380	766			27	M	2006	Test	317	R
381				29	F	2006		712	R
393	767		906	25	M	2006	Training	299	S
405	762			53	M	2006	Test	938	R
447	764			23	F	2006	Test	Unmatched	R
455	763			19	M	2006	Training	375	S
458				13	M	2006		2	S
460	768			24	F	2007	Training	507	S
461	769			18	F	2006	Training	507	R
463	772			14	F	2007	Training	184	R
465	774			56	F	2007	Test	196	R
468	773			37	F	2007	Test	1371	R
481	779			46	M	2007	Training	938	R
483	784			18	F	2007	Test	87	R
495	791			15	M	2007	Test	2	R
496	801			16	M	2007	Training	2	R
497	790			26	M	2007	Training	450	R
498	792			48	F	2007	Training	Unmatched	R
503	802			15	F	2007	Test	1445	S
513	742			49	F	2007	Training	Unmatched	R
524	804			27	M	2007	Test	1151	S
529	803		193	30	M	2007	Training	299	R

SOUTH AFRICA	621	776			37	F	2007	Training	479	S
	624	775			13	F	2007	Training	184	S
	636	780			32	M	2007	Training	450	R
	647	783			17	F	2007	Training	165	R
	649	781			52	F	2007	Test	196	R
	654				12	M	2007		921	S
	656	782			36	M	2007	Training	450	S
	657	808			21	F	2007	Training	507	R
	659	794			31	M	2007	Test	317	S
	671	786			55	F	2007	Test	1371	R
	716				49	F	2007		196	R
	724	788			14	F	2007	Training	165	S
	728	795			48	M	2007	Training	938	R
	729	789			30	M	2007	Test	1151	S
	730	796			15	M	2007	Test	921	S
	741	799			21	F	2007	Test	63	R
	752	798			45	F	2007	Test	93	S
	758	800			26	M	2007	Test	886	S
	765	728			42	F	2007	Training	Unmatched	R
	875				29	F	2007		712	R
	890	806			37	F	2007	Training	204	S
	907	809			53	F	2007	Test	93	S
	918	770			52	F	2007	Test	Unmatched	S
	919	821		914	26	M	2007	Test	299	R
	925	812			18	F	2007	Training	650	R
	940	823			12	M	2007	Training	2	R
	945	848			24	F	2007	Test	19	S
	1000				26	F	2007		712	S
	1007	813			24	F	2007	Test	878	R
	1008	811		921	27	M	2007	Training	299	S
	1014				51	M	2007		1149	S
	1019	833			47	F	2007	Training	479	R
	1021	828			23	M	2007	Training	375	R
	1023			131	24	M	2007	Test	1051	S
	1056	826			24	F	2007	Training	650	R
	1064	846			51	F	2007	Test	93	R
	1066	810			57	M	2007	Test	1151	S
	1072	872			20	M	2007	Training	375	S
	1074	849			30	M	2007	Test	886	R
	1075	829			19	F	2007	Training	650	R
	1114	818			15	F	2007	Test	1445	R
	1116	820			21	F	2007	Test	507	S
	1126	815			32	M	2007	Test	886	S
	1130	814			29	M	2007	Test	450	R
	1148			195	37	F	2007	Training	204	R
	1222	830			51	M	2007	Training	938	S
	1231	816			18	F	2007	Test	87	S
	1233	827			48	F	2007	Test	196	R
	1237				47	M	2007		1149	R
	1239	831			19	F	2007	Test	63	S
	1241			104	24	M	2007	Test	1051	R
	1243	785			37	F	2007	Training	Unmatched	S
	1355				51	F	2007		93	R
	1363				17	F	2007		1445	S
	1448	835			18	F	2007	Test	19	R
	1457	840			17	F	2008	Training	3102	S
	1460	838			31	F	2008	Training	2847	R
	1463	844			49	M	2008	Training	2123	R
	1554				18	F	2008		3099	R
	1556	213			27	F	2008	Test	2847	R
	1570				50	F	2008		1773	R
	1587	845			22	M	2008	Training	Unmatched	R
	1588			79	22	F	2008	Training	Unmatched	S
	1594	841			23	F	2008	Training	2693	S
	1750	852			55	F	2008	Training	1590	R
	1755	843			31	F	2008	Training	2847	R
	1756	211			19	M	2008	Training	2129	R
	1769			175	15	F	2008	Training	2864	S

	1771				20	F	2008		2693	S
	1772			168	38	M	2008	Training	1552	R
	1778	221			24	F	2008	Training	Unmatched	R
	2077	853			16	F	2008	Test	3102	R
	2082	129			30	F	2008	Training	2847	S
	2092	183			59	M	2008	Test	1552	R
	2097	188		77	14	F	2008	Training	2864	S
	2102	187			16	F	2008	Training	2864	S
	2133	181			30	M	2008	Training	3011	R
	2224				44	F	2008		1773	S
	2227				47	M	2008		2123	S
	2228	120			13	F	2008	Training	3102	S
	2274	184		61	11	F	2008	Training	2864	R
	2276				18	F	2008		2693	R
	2688	861			21	M	2008	Training	2129	R
	2696				44	F	2008		1773	R
	2700	119		155	31	M	2008	Test	1552	S
	2713	862			32	M	2008	Test	3011	S
	2856	869			19	M	2008	Test	2129	S
	2857			158	24	F	2008	Training	3099	S
	2858	868			48	F	2008	Training	1590	R
	2861	30			52	F	2008	Training	1590	S
	2993	130			25	M	2008	Training	3011	R
	2994	125			21	M	2008	Training	Unmatched	R
	3004	33			53	F	2008	Test	1590	R
	3005	205			23	M	2008	Training	2129	S
	3007	208			23	F	2008	Training	2693	S
	3010				45	F	2008		1773	S
	3012			174	48	M	2008	Training	1552	R
	3092	128			40	M	2008	Training	2123	S
	3094	859		78	15	F	2008	Training	Unmatched	S
	3095				53	M	2008		2123	R
	3106			109	19	F	2008	Training	3099	S
	3110	207			10	F	2008	Training	3102	S
	3221				24	F	2008		3099	R
	3237	863			35	M	2008	Test	3011	S
	5319	116			48	M	2009	Test	1115	R
	5326	59			22	F	2009	Training	Unmatched	S
	5357	90		45	15	F	2009	Training	Unmatched	S
	5358	87			15	F	2009	Test	6290	R
	5359	88			10	F	2009	Training	Unmatched	R
	5360	89			40	M	2009	Test	1115	S
	5362	86			39	M	2009	Training	1115	S
	5365	118			49	M	2009	Test	1115	S
	5434	80			21	M	2009	Test	Unmatched	S
	5442	170			35	M	2009	Training	1051	S
	5551	111		67	33	M	2009	Test	1051	S
	5553				14	F	2009		Unmatched	S
	5554	113			19	M	2009	Training	Unmatched	S
	5561				17	F	2009		6290	R
	5563				13	F	2009		6290	R
	5572	146			21	F	2009	Test	Unmatched	S
	5661	114			22	M	2009	Training	Unmatched	R
	5674			98	12	F	2009	Training	Unmatched	R
	5677	224			14	F	2010	Training	Unmatched	S
	5918	145			13	F	2009	Training	Unmatched	S
	6074	223			11	F	2010	Training	Unmatched	S
	6302	94			12	F	2010	Training	Unmatched	S
	6303				17	F	2010		6290	S
	6565	68			22	M	2010	Training	Unmatched	R
	6686	143			21	F	2010	Training	Unmatched	S
	07/G119				26	F	2007		07/G123	S
	07/G155				25	M	2007		07/G300	R
	07/G182				27	M	2007		07/G300	S
	07/G189		548		22	F	2007	Training	07/G437	S
	07/G197				16	M	2007		07/G438	S
	07/G253				16	M	2007		07/G225	S
	07/G255				34	M	2007		07/G213	S

	07/G274			498	17	M	2007	Training	07/G225	S
	07/G277	544			20	F	2007	Training	07/G437	S
	07/G322				41	M	2007		07/G468	S
	07/G328		539		25	F	2007	Test	07/G123	S
	07/G335				27	M	2007		07/G300	R
	07/G351		494	495	17	M	2007	Training	07/G225	R
	07/G354	267			37	M	2007	Training	07/G468	S
	07/G356				16	M	2007		07/G438	S
	07/G359				30	M	2007		07/G213	S
	07/G368	560			15	M	2007	Training	07/G438	S
	07/G369				18	F	2007		07/G437	S
	07/G370			492	17	M	2007	Training	07/G225	S
	07/G372				17	M	2007		07/G438	S
	07/G411				27	M	2007		07/G213	S
	07/G414				28	M	2007		07/G213	S
	07/G419	270			52	M	2007	Training	07/G468	S
	07/G474				19	F	2007		07/G437	S
	07/G475				25	F	2007		07/G123	S
	07/G479				39	M	2007		07/G468	S
	07/G491				27	M	2007		07/G300	R
	07/G493				35	F	2007		07/G123	S
	08/G109			313	22	F	2008	Test	08/G423	S
	08/G131	320			22	F	2008	Test	08/G423	S
	08/G136	529			22	F	2008	Training	08/G814	S
	08/G141	365			19	M	2008	Training	08/G800	S
	08/G143	287	288		21	M	2008	Test	08/G249	S
	08/G154	380			18	F	2008	Test	08/G876	S
	08/G160	523			18	F	2008	Training	08/G814	S
	08/G191				60	M	2008		08/G367	R
	08/G196			284	17	M	2008	Test	08/G245	S
	08/G198	585		587	18	F	2008	Test	08/G606	R
	08/G324	568	569	570	35	F	2008	Training	08/G433	S
	08/G329		318		24	F	2008	Test	08/G423	R
	08/G333		304		51	F	2008	Training	08/G260	S
	08/G340				16	M	2008		08/G245	S
	08/G343		306		47	F	2008	Training	08/G260	S
	08/G344				24	F	2008		08/G876	S
	08/G372		577		36	F	2008	Test	08/G433	S
	08/G400		280	281	15	M	2008	Training	08/G245	S
	08/G407		512		57	M	2008	Training	08/G367	S
	08/G415		341		32	F	2008	Training	08/G494	S
	08/G424		344		26	F	2008	Training	08/G494	S
	08/G434	294	295		21	M	2008	Test	08/G249	S
	08/G496		356	357	24	M	2008	Test	08/G762	S
	08/G506		290	291	19	M	2008	Test	08/G249	S
	08/G517				19	F	2008		08/G876	S
	08/G541		384		18	F	2008	Training	08/G876	S
	08/G568		354		24	M	2008	Test	08/G762	S
	08/G587		509		55	M	2008	Training	08/G367	S
	08/G588				58	F	2008		08/G260	S
	08/G593		293		22	M	2008	Test	08/G249	R
	08/G595		352		18	M	2008	Test	08/G762	S
	08/G596		521		20	F	2008	Training	08/G814	S
	08/G613		277	278	15	M	2008	Training	08/G245	S
	08/G643		589		22	F	2008	Training	08/G606	S
	08/G647				40	F	2008		08/G493	S
T	08/G652	514	515		51	M	2008	Training	08/G367	S
H	08/G654	345			26	F	2008	Training	08/G494	S
E	08/G695		301		55	F	2008	Training	08/G260	S
	08/G701		338		28	F	2008	Training	08/G494	S
G	08/G703	325	326		60	F	2008	Training	08/G493	S
A	08/G714		332		44	F	2008	Training	08/G493	S
M	08/G715		527		20	F	2008	Training	08/G814	S
B	08/G726		329		48	F	2008	Training	08/G493	S
I	08/G782	368			18	M	2008	Training	08/G800	S
A	08/G788	363			18	M	2008	Training	08/G800	S
	08/G797	571	572	573	28	F	2008	Training	08/G433	S
	08/G802	358	359	360	24	M	2008	Test	08/G762	R

	08/G810		582		21	F	2008	Training	08/G606	S
	08/G812				22	F	2008		08/G606	S
	08/G826	314			24	F	2008	Test	08/G423	R
	08/G828	370	371	372	18	M	2008	Test	08/G800	R
	08/G893	574		575	29	F	2008	Training	08/G433	S
	09/G106	482	483		18	M	2009	Test	10/G369	S
	09/G110		487	488	24	M	2009	Test	10/G369	S
	09/G111				30	F	2009		09/G262	S
	09/G112	629			39	F	2009	Test	10/G261	S
	09/G113	634			39	F	2009	Test	10/G261	S
	09/G117				31	F	2009		09/G280	R
	09/G120	441			29	F	2009	Training	10/G178	S
	09/G130				20	F	2009		10/G215	S
	09/G131			434	16	M	2009	Test	10/G139	S
	09/G133	420			34	F	2009	Training	09/G524	S
	09/G135	443			26	F	2009	Training	10/G178	S
	09/G143		593		25	F	2009	Test	09/G280	S
	09/G145				22	F	2009		10/G215	R
	09/G162	610	611		30	M	2009	Test	09/G340	R
	09/G168	446			31	F	2009	Test	10/G178	S
	09/G169	623	624		18	M	2009	Test	09/G497	S
	09/G172				18	F	2009		10/G407	S
	09/G179	410	411		57	M	2009	Training	09/G367	R
	09/G187	479	480		21	M	2009	Test	10/G369	S
	09/G188	452	453		18	F	2009	Training	10/G215	S
	09/G196	616			19	M	2009	Training	09/G497	S
	09/G199				27	F	2009		09/G280	S
	09/G202	474	475		18	F	2009	Training	10/G279	S
	09/G204	401	402		49	M	2009	Training	09/G367	S
	09/G209				25	F	2009		09/G262	S
	09/G212	485			21	M	2009	Test	10/G369	R
	09/G222				16	F	2009		10/G289	S
	09/G223	407	408		52	M	2009	Training	09/G367	S
	09/G224	605			35	M	2009	Training	09/G340	R
	09/G228	618			18	M	2009	Training	09/G497	S
	09/G237				27	F	2009		09/G262	S
	09/G238	657			24	F	2009	Test	10/G407	S
	09/G247	607			25	M	2009	Training	09/G340	S
	09/G252	602	603	604	28	M	2009	Test	09/G340	S
	09/G258		424	425	29	F	2009	Test	09/G524	S
	09/G371	404	405		56	M	2009	Training	09/G367	S
	09/G377	660			23	F	2009	Training	10/G407	S
	09/G384	637			40	F	2009	Test	10/G261	R
	09/G388	417			29	F	2009	Training	09/G524	R
	09/G389	414			30	F	2009	Training	09/G524	R
	09/G390	663			21	F	2009	Training	10/G407	S
	09/G391	466	467	468	23	F	2009	Test	10/G279	S
	09/G397	596	597		35	F	2009	Test	09/G280	S
	09/G400				28	F	2009		10/G178	S
	09/G401	469	470		18	F	2009	Test	10/G279	R
	09/G403		647		17	F	2009	Test	10/G289	S
	09/G431	428			16	M	2009	Test	10/G139	S
	09/G435	621			18	M	2009	Training	09/G497	S
	09/G442	435			16	M	2009	Training	10/G139	S
	09/G445	430		432	16	M	2009	Training	10/G139	S
	09/G449	649			16	F	2009	Test	10/G289	S
	09/G450	652			16	F	2009	Test	10/G289	S
	09/G455	631			45	F	2009		10/G261	S
	09/G476	390			30	F	2009		09/G262	S
	09/G477	455	456		18	F	2009	Training	10/G215	S
	09/G482	471	472	473	23	F	2009	Test	10/G279	S
	ARHHC16	1058			60	M	2007	Test	unmatched	S
	ARHHC34				29	F	2008		DZHHC96	R
	ARHHC35			229	22	M	2008	Test	DZHHC78	S
	ARHHC45	952	938		30	F	2008	Test	KHHC68	R
	ARHHC46	962			18	M	2009	Test	W23HHC132	S
	DZHHC06	1060	1061		24	F	2007	Test	Unmatched	S
	DZHHC10		1062		19	M	2007	Test	Unmatched	S

ETHIOPIA	DZHHC12				27	F	2007		KFHHC21	S
	DZHHC26	1006	1007		32	F	2008	Test	KHHC68	S
	DZHHC38	1065			18	F	2008	Test	Unmatched	S
	DZHHC59				28	F	2008		KHHC78	S
	DZHHC68			953	20	M	2008	Test	DZHHC78	S
	DZHHC69	1009	997		35	F	2008	Test	KHHC68	S
	DZHHC70	1010	995		42	F	2008	Test	ARHHC63	S
	DZHHC84	956			18	F	2008	Test	ARHHC63	S
	KAZHHC04				19	F	2008		KHHC151	R
	KAZHHC23			1194	18	F	2008	Test	Unmatched	S
	KAZHHC50	939			30	F	2010	Test	DZHHC96	S
	KAZHHC54				24	F	2010		KHHC121	S
	KFHHC04				25	F	2007		KFHHC21	S
	KFHHC15	1067			30	M	2007	Test	Unmatched	S
	KHHC03				31	F	2007		MOHHC04	S
	KHHC04	1070			30	M	2007	Test	Unmatched	S
	KHHC05	1014			30	F	2007	Test	KFHHC21	S
	KHHC09				36	F	2007		MOHHC04	S
	KHHC10	1016			23	M	2007		KHHC26	S
	KHHC11				21	M	2007		KHHC26	S
	KHHC17			957	22	M	2007	Test	W23HHC08	S
	KHHC32		1076		19	F	2007	Test	Unmatched	R
	KHHC36	1077			45	F	2007	Test	Unmatched	S
	KHHC41	1078			37	F	2007	Test	Unmatched	S
	KHHC42				29	F	2007		MOHHC04	S
	KHHC43				32	F	2007		MOHHC04	S
	KHHC47		964		42	F	2008	Test	KHHC151	S
	KHHC71				23	F	2008		ARHHC63	S
	KHHC87	932		994	40	F	2008	Test	KHHC121	S
	LDHHC09	1028			50	F	2008	Test	KHHC121	S
	LDHHC10			1183	26	M	2008		unmatched	S
	LDHHC12				28	F	2008		KHHC78	S
	LDHHC18	961			19	F	2009	Test	KHHC151	S
	MESHHC04		1082		43	F	2007	Test	Unmatched	S
	MOHHC21	1030	927		22	F	2008	Test	KHHC151	S
	TEKHHC04	1084			19	M	2007	Test	Unmatched	S
	TEKHHC08		1031		19	M	2007	Test	W23HHC08	S
	TEKHHC10	1032	1033		22	M	2007	Test	KHHC26	S
	TEKHHC105	1034			44	F	2008	Test	DZHHC96	S
	TEKHHC53				46	F	2008		ARHHC63	S
	TEKHHC74	1037			35	F	2008	Test	KHHC78	S
	TEKHHC81	1039			25	F	2008	Test	KHHC68	S
	TEKHHC89	1040			18	M	2008	Test	DZHHC78	S
	TEKHHC94				21	M	2008		DZHHC78	S
	TEKHHC98				18	M	2008		W23HHC132	S
	TEKHHC99				50	F	2008		DZHHC96	S
	W23HHC03	1198			18	F	2007	Test	Unmatched	S
	W23HHC04	1103			40	F	2007	Test	Unmatched	S
	W23HHC107				23	M	2008		W23HHC132	S
	W23HHC113			992	21	M	2008	Test	W23HHC132	S
	W23HHC15		1045		18	M	2007	Test	W23HHC08	S
	W23HHC21		1046		24	M	2007	Test	KHHC26	S
	W23HHC27				36	F	2007		KFHHC21	S
	W23HHC29		1049	984	18	M	2007	Test	W23HHC08	S
	W23HHC58	1164			18	M	2008	Test	Unmatched	S
	W23HHC61	1050			35	F	2008	Test	KHHC78	S
	W23HHC77				52	F	2008		KHHC121	S
	W23HHC78		1196		23	F	2008	Test	Unmatched	S
	91124103				16	M	2007		89902105	S
	92274102				17	M	2008		89902105	S
	91545104				17	M	2008		89902105	S
	91675103				15	M	2008		89902105	S
	91938102				41	M	2008		90753104	S
	91959102				47	M	2008		90753104	S
	92020102				46	M	2008		90753104	S
	92274104				52	M	2008		90753104	S
	91958102				23	F	2008		90953	S
	92139102				23	F	2008		90953	S

	90934102				23	F	2008		90953	S
	92025102				22	F	2008		90953	R
	91152110				20	F	2007		91505506	S
	91118502				18	F	2007		91505506	S
	91152105				16	F	2007		91505506	S
	91237105				17	F	2007		91505506	S
	91956102				18	M	2008		92227	S
	91235102				18	M	2007		92227	S
	90963				22	M	2008		92227	S
U	91836102				19	M	2008		92227	S
G	91268102				20	F	2007		92663	S
A	90939				19	F	2008		92663	S
N	92145				19	F	2008		92663	S
D	91698102				19	F	2008		92663	S
A	91565102				35	F	2008		92957	S
	91949109				25	F	2008		92957	S
	91552102				29	F	2008		92957	S
	92272102				27	F	2008		92957	S
	92655				47	M	2009		90292102	S
	92756				42	M	2009		90292102	S
	90493102				58	M	2006		90292102	S
	92608107				46	M	2009		90292102	S
	91269106				32	M	2007		90749102	R
	91633102				27	M	2008		90749102	S
	92045102				35	M	2008		90749102	S
	91395102				31	M	2008		90749102	S
	91148502				38	M	2007		90850102	R
	91013102				41	M	2007		90850102	S
	91050102				46	M	2007		90850102	S
	90897104				48	M	2007		90850102	S
	90936				35	F	2008		92245	S
	91451104	695			28	F	2008	Not included*	92245	S
	91512102				33	F	2008		92245	S
	91420103	694			34	F	2008	Not included*	92245	R

*Note: Ughanda RNA samples were sequenced and included in biological network analysis, but not predictive modelling analysis

Participant does not have RNA-seq data

Supplementary Table 12: Junctions and genes in the SUN signature

Gene	Splice Junction	Primer/Probe Set
C14orf159	chr14:91681900-91691027.+	Hs01061063_m1
C1orf131	chr1:231360160-231361216.-	Hs01098493_m1
CD63	chr12:56122136-56122736.-	Hs01041232_g1
CRTAM	chr11:122722553-122724650.+	NA
DCAF17	chr2:172330485-172333369.+	Hs00980525_m1
DDX47;APOLD1	chr12:12976950-12977473.+	Hs01033153_g1
DGCR8	chr22:20074844-20077191.+	Hs00256062_m1
DOCK9	chr13:99538085-99538785.-	Hs00324508_m1
IGFLR1;AD000671.6	chr19:36230527-36230610.-	Hs01033814_g1
KIAA0586	chr14:58965678-58975272.+	Hs00914947_m1
KLRK1;KLRC4-KLRK1	chr12:10532391-10539501.-	Hs00183683_m1
KNTC1	chr12:123103092-123105025.+	Hs00938581_g1
LINC00969	chr3:195435712-195451550.+	ENST599566_2_3
LZTFL1	chr3:45870107-45872404.-	Hs00947902_m1
MFSD7	chr4:677156-677397.-	Hs01003911_g1
MMP8	chr11:102592257-102592344.-	NM_002424_3_4
MMP8	chr11:102589306-102592131.-	NM_002424_4_5
MMP8	chr11:102586168-102587032.-	NA
MSRB2	chr10:23384655-23393072.+	Hs00969344_m1
NR1H2	chr19:50883136-50885222.+	Hs00173195_m1
OMA1	chr1:58996401-58999624.-	Hs00377025_m1
OXNAD1	chr3:16343375-16344146.+	Hs00976485_m1
PLAUR	chr19:44150700-44156376.-	NM_001005376_6_7
POLA1	chrX:24830980-24833095.+	Hs01102681_m1
PSMB10	chr16:67968851-67969322.-	Hs00160620_m1
QRSL1	chr6:107103607-107110854.+	Hs00733915_m1
RBCK1	chr20:401675-402770.+	NA
RBCK1	chr20:402882-407956.+	Hs00246291_m1
RBCK1	chr20:408136-409134.+	Hs00934612_m1
RBCK1	chr20:409233-409594.+	Hs00934613_g1
RBCK1	chr20:409738-410993.+	Hs00934604_m1
RENBP	chrX:153208531-153208997.-	Hs01031135_g1
RENBP	chrX:153209422-153209531.-	Hs00234138_m1
SIPA1L1	chr14:72202108-72204957.+	Hs01553889_m1
SLC2A5	chr1:9107793-9117506.-	Hs01086389_m1
THUMPD2	chr2:39983100-39984387.-	Hs00903142_m1
ZNF14	chr19:19825296-19843764.-	Hs00221420_m1

ZNF286A	chr17:15604554-15609700.+	Hs00276637_m1

NA: Not annotated; custom designed

Supplementary Table 13: Junctions and genes in the MRC signature

Gene	Splice Junction	Primer/Probe Set
ACBD4	chr17:43215355-43216387.+	Hs00963320_m1
ADAMTSL4	chr1:150531641-150531762.+	Hs01120107_g1
ANKRD22	chr10:90588423-90591591.-	Hs00944015_m1
BLK	chr8:11403612-11405540.+	Hs01017452_m1
BLK	chr8:11412398-11412840.+	Hs01017461_g1
CD1C	chr1:158262664-158263001.+	Hs00957534_g1
CD1C	chr1:158263092-158263244.+	Hs00416803_g1
DRAM2	chr1:111680208-111682659.-	Hs01070227_m1
DUSP3	chr17:41847182-41852079.-	Hs00187940_m1
DUSP3	chr17:41852306-41856167.-	Hs01115776_m1
ENO2	chr12:7031565-7031893.+	Hs01102367_g1
FAM20A	chr17:66538306-66538834.-	Hs01034072_g1
FCGR1B	chr1:120927417-120930038.-	Hs02341825_m1
FFAR3	chr19:35849551-35849781.+	Hs02519193_g1
FLVCR2	chr14:76088563-76090954.+	Hs00900390_m1
GAS6	chr13:114523991-114524930.-	Hs01090305_m1
GAS6	chr13:114531684-114535271.-	NM_000820_10_11
GAS6	chr13:114535461-114535606.-	Hs00181323_m1
GAS6	chr13:114535725-114537523.-	NA
GAS6	chr13:114541164-114542700.-	NM_000820_5_6
HAUS5	chr19:36103794-36104631.+	Hs01042094_m1
NA_1	chr14:106213948-106214178.-	NA
NRG1	chr8:32585596-32599525.+	Hs01103794_m1
PHF1	chr6:33383106-33383366.+	Hs00984678_g1
PHF1	chr6:33382921-33383011.+	Hs00984676_g1
RASGRP2	chr11:64506948-64507107.-	Hs01057128_g1
RASGRP2	chr11:64509584-64510265.-	Hs01057123_m1
SEPT4	chr17:56599462-56602438.-	Hs00910208_g1
SEPT4	chr17:56603142-56603580.-	Hs04408432_m1
SLC22A17	chr14:23817880-23818480.-	Hs00539432_m1
SLC26A8	chr6:35928689-35928769.-	Hs01122045_g1
SORT1	chr1:109865743-109867520.-	Hs00361760_m1
SPHK1	chr17:74382218-74382301.+	Hs01116530_g1
VCAN	chr5:82850857-82868234.+	Hs01007928_m1
VCAN	chr5:82868379-82875798.+	Hs00171642_m1

NA: Not annotated; custom designed

Supplementary Table 14: Construction of GC6-4 signature through progressive addition of pairs

# pairs	Pair added		Training Set Fit - AUC
1	GAS6_NM_000820_10_11	CD1C_Hs00957534_g1	0,762
2	SEPT4_Hs00910208_g1	BLK_Hs01017452_m1	0,779
3	SEPT4_Hs00910208_g1	CD1C_Hs00957534_g1	0,785
4	GAS6_NM_000820_10_11	BLK_Hs01017452_m1	0,791
5	SEPT4_Hs00910208_g1	CD1C_Hs00416803_g1	0,786

Supplementary Table 15: P-values of one-sided comaprison of the AUC of RISK4 against PCR-adapted published signatures

	Test Set:			
RISK4 vs:	**All**	**SUN**	**MRC**	**AHRI**
DIAG3	0.58	0.32	0.18	0.92
DIAG4	0.32	0.63	0.06	0.43
ACSCOR	0.42	0.79	0.11	0.30

Supplementary Table 16: The pair SEPT4/BLK closely reproduces the results from the full GC64 signature

	SUN Test	MRC Test	AHRI Test	All Test
RISK4	0.72	0.72	0.67	0.67
SEPT4/BLK	0.72	0.74	0.65	0.68
SEPT4/CD1C	0.77	0.68	0.59	0.63
GAS6/BLK	0.64	0.72	0.78	0.70
GAS6/CD1C	0.68	0.64	0.65	0.61

Supplementary Table 17: Up-regulated splice junctions used for pairwise meta-analysis. All junctions had FDR<0.05 in at least one site.

Junction	Gene	Sites with up-regulation
chr10:90588423-90591591.-	ANKRD22	SUN, MRC
chr1:22970207-22970503.+	C1QC	SUN, MRC
chr1:22970697-22973719.+	C1QC	SUN, MRC
chr20:44525679-44526355.+	CTSA	SUN, MRC
chr1:11729001-11731322.+	FBXO6	SUN, MRC
chr1:11732080-11733333.+	FBXO6	SUN, MRC
chr1:89573974-89575359.-	GBP2	SUN, MRC
chr1:89575553-89575846.-	GBP2	SUN, MRC
chr1:89575949-89578154.-	GBP2	SUN, MRC
chr1:89579979-89582674.-	GBP2	SUN, MRC
chr1:89582917-89583259.-	GBP2	SUN, MRC
chr1:89583456-89585861.-	GBP2	SUN, MRC
chr1:89585971-89586825.-	GBP2	SUN, MRC
chr6:30460213-30460317.+	HLA-E	SUN, MRC
chr19:18284783-18285849.+	IFI30;PIK3R2	SUN, MRC
chr19:18286032-18286120.+	IFI30;PIK3R2	SUN, MRC
chr19:18286195-18286414.+	IFI30;PIK3R2	SUN, MRC
chr19:18286507-18287949.+	IFI30;PIK3R2	SUN, MRC
chr19:18288102-18288520.+	IFI30;PIK3R2	SUN, MRC
chr19:18288574-18288658.+	IFI30;PIK3R2	SUN, MRC
chr4:676679-676998.-	MFSD7	SUN, MRC
chr4:678388-678507.-	MFSD7	SUN, MRC
chr14:74951290-74953031.-	NPC2	SUN, MRC
chr14:74953139-74959895.-	NPC2	SUN, MRC
chr19:49414509-49416267.+	NUCB1	SUN, MRC
chr19:49422379-49422450.+	NUCB1	SUN, MRC
chr19:49425189-49425574.+	NUCB1	SUN, MRC
chr22:50969281-50969365.-	ODF3B	SUN, MRC
chr19:44150700-44156376.-	PLAUR	SUN, MRC
chr19:44153295-44156376.-	PLAUR	SUN, MRC
chr19:44156523-44159590.-	PLAUR	SUN, MRC
chr19:44159725-44160630.-	PLAUR	SUN, MRC
chr19:44160792-44169467.-	PLAUR	SUN, MRC
chr19:44169611-44171732.-	PLAUR	SUN, MRC
chr19:44171843-44174217.-	PLAUR	SUN, MRC
chr17:80280246-80280753.-	SECTM1	SUN, MRC
chr17:80280887-80282457.-	SECTM1	SUN, MRC
chr17:80282766-80285022.-	SECTM1	SUN, MRC
chr17:80285168-80291575.-	SECTM1	SUN, MRC
chr7:150939064-150939222.-	SMARCD3	SUN, MRC
chr1:28203239-28211805.+	THEMIS2	SUN, MRC
chr17:76853728-76866979.-	TIMP2	SUN, MRC
chr12:112580099-112583389.+	TRAFD1	SUN, MRC
chr22:50965712-50966016.-	TYMP	SUN, MRC
chr22:50966146-50966940.-	TYMP	SUN, MRC
chr22:50967039-50967564.-	TYMP	SUN, MRC
chr22:50967767-50967924.-	TYMP	SUN, MRC
chr22:50968148-50968332.-	TYMP	SUN, MRC
chr22:50968160-50968332.-	TYMP	SUN, MRC
chr16:89778930-89779012.-	VPS9D1	SUN, MRC
chr6:31655321-31655418.-	ABHD16A;XXbac-BPG32J3.20	SUN
chr6:31655517-31655600.-	ABHD16A;XXbac-BPG32J3.20	SUN
chr6:31659457-31659580.-	ABHD16A;XXbac-BPG32J3.20	SUN
chr6:31659695-31660803.-	ABHD16A;XXbac-BPG32J3.20	SUN
chr9:139568379-139569186.-	AGPAT2	SUN
chr9:139569259-139571036.-	AGPAT2	SUN

chr1:11808667-11810133.+	AGTRAP	SUN
chr13:31309812-31318196.+	ALOX5AP	SUN
chr13:31318296-31326188.+	ALOX5AP	SUN
chr13:31326259-31330080.+	ALOX5AP	SUN
chr13:31330162-31338080.+	ALOX5AP	SUN
chr16:28509670-28509756.+	APOBR	SUN
chr22:36653182-36653364.+	APOL1	SUN
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chr2:238896634-238903385.+	UBE2F;UBE2F-SCLY	AHRI
chr22:21965332-21975803.+	UBE2L3	AHRI
chr15:42749356-42758250.-	ZNF106	AHRI
chr6:32550008-32551885.-		AHRI
chr13:27744466-27745728.-		AHRI

chr14:106206530-106235581.-		AHRI
chr22:37627430-37628840.-		AHRI
chr1:79094684-79101021.+		AHRI
chr19:48744320-48745290.-		AHRI
chr6:31236778-31321823.+		AHRI
chr6:29760082-29855731.+		AHRI

Supplementary Table 18: Down-regulated splice junctions used for pairwise meta-analysis. All junctions had FDR<0.05 in at least one site.

Junction	Gene	Sites with down-regulation
chr3:31703608-31705570.-	OSBPL10	SUN, MRC
chr12:112375047-112375964.-	TMEM116	SUN, MRC
chr19:17885096-17885202.+		SUN, MRC
chr4:146044509-146044629.+	ABCE1	SUN
chr2:87274429-87276711.-	AC125232.1	SUN
chr16:16427741-16429908.+	AC138969.4	SUN
chr3:132322171-132323941.-	ACAD11;NPHP3	SUN
chr3:132324049-132337477.-	ACAD11;NPHP3	SUN
chr1:180461500-180464595.-	ACBD6	SUN
chr10:76360251-76429940.+	ADK	SUN
chr16:90057411-90059128.+	AFG3L1P	SUN
chr12:121769231-121773335.-	ANAPC5	SUN
chr2:241463798-241465101.-	ANKMY1	SUN
chr9:101552888-101558414.-	ANKS6	SUN
chr15:35189906-35192822.-	AQR	SUN
chr12:27077416-27078693.-	ASUN	SUN
chr15:25932975-25936861.-	ATP10A	SUN
chr15:25940293-25947062.-	ATP10A	SUN
chr15:25947247-25953122.-	ATP10A	SUN
chr22:46085783-46088875.+	ATXN10	SUN
chr19:1993175-1997342.-	BTBD2	SUN
chr3:112185230-112188604.-	BTLA	SUN
chr10:124914628-124915173.+	BUB3	SUN
chr12:88429515-88433924.+	C12orf29	SUN
chr12:88434042-88436601.+	C12orf29	SUN
chr17:30660539-30661487.-	C17orf75	SUN
chr2:70392324-70392659.-	C2orf42	SUN
chr2:27455562-27455909.+	CAD	SUN
chr5:110814205-110818482.+	CAMK4	SUN
chr14:74523961-74531390.+	CCDC176	SUN
chr8:27606115-27610028.-	CCDC25	SUN
chr3:56651633-56652199.+	CCDC66	SUN
chr3:45928147-45936397.+	CCR9	SUN
chr12:69981396-69981709.+	CCT2	SUN
chr12:69981786-69981929.+	CCT2	SUN
chr11:118221398-118222342.+	CD3G	SUN
chr5:137528077-137528192.-	CDC23	SUN
chr19:42259610-42260507.+	CEACAM6	SUN
chr19:42266131-42270090.+	CEACAM6	SUN
chr19:43085505-43087357.-	CEACAM8	SUN
chr19:43093190-43093608.-	CEACAM8	SUN
chr19:43093887-43097692.-	CEACAM8	SUN
chr19:43098052-43098916.-	CEACAM8	SUN
chr9:80880459-80880774.+	CEP78	SUN
chr17:62517645-62518819.+	CEP95	SUN
chr13:53039600-53042412.+	CKAP2	SUN
chr19:14707973-14710528.+	CLEC17A	SUN
chr7:130295981-130297022.-	COPG2	SUN
chr7:130337788-130347806.-	COPG2	SUN
chr7:130347878-130351688.-	COPG2	SUN
chr17:17150874-17152239.-	COPS3	SUN
chr17:17152353-17158172.-	COPS3	SUN
chr17:17158259-17163614.-	COPS3	SUN
chr17:17168295-17171198.-	COPS3	SUN
chr17:17171291-17174071.-	COPS3	SUN
chr2:238004527-238005464.+	COPS8	SUN
chr6:36710263-36711465.-	CPNE5	SUN

chr12:69653323-69653823.+	CPSF6	SUN
chr6:49696570-49698875.-	CRISP3	SUN
chr6:49701005-49701415.-	CRISP3	SUN
chr6:49701561-49703216.-	CRISP3	SUN
chr6:49703304-49704103.-	CRISP3	SUN
chr6:49704220-49705037.-	CRISP3	SUN
chr6:49698964-49700907.-	CRISP3	SUN
chr11:122722553-122724650.+	CRTAM	SUN
chr11:122738807-122741976.+	CRTAM	SUN
chr8:68092161-68102884.+	CSPP1	SUN
chr1:41456920-41457436.+	CTPS1	SUN
chr10:35299370-35300775.-	CUL2	SUN
chr1:167974031-167992225.+	DCAF6	SUN
chr12:12974330-12974588.+	DDX47;APOLD1	SUN
chr12:12976950-12977473.+	DDX47;APOLD1	SUN
chr12:12979004-12980179.+	DDX47;APOLD1	SUN
chr12:125449552-125450213.-	DHX37	SUN
chrX:69720430-69720747.+	DLG3	SUN
chr10:75005934-75006445.-	DNAJC9	SUN
chr13:99538085-99538785.-	DOCK9	SUN
chr3:108393028-108394632.+	DZIP3	SUN
chr3:108396445-108403062.+	DZIP3	SUN
chr3:108403188-108405291.+	DZIP3	SUN
chr3:108407771-108409633.+	DZIP3	SUN
chrX:129771384-129790554.-	ENOX2	SUN
chr14:74449864-74453516.-	ENTPD5	SUN
chr13:37582972-37583320.+	EXOSC8	SUN
chr15:31222874-31229321.+	FAN1	SUN
chr22:32871385-32874967.+	FBXO7	SUN
chr6:52958359-52958682.+	FBXO9	SUN
chr6:52960462-52962519.+	FBXO9	SUN
chr1:157646558-157648384.-	FCRL3	SUN
chr1:157648763-157650491.-	FCRL3	SUN
chr1:157653034-157659587.-	FCRL3	SUN
chr1:157668419-157669481.-	FCRL3	SUN
chr18:55238772-55240477.-	FECH	SUN
chr14:66096324-66135960.+	FUT8	SUN
chr1:38034903-38039943.-	GNL2	SUN
chr10:96353372-96354451.+	HELLS	SUN
chr13:31725328-31725745.-	HSPH1	SUN
chr9:139327038-139327407.-	INPP5E	SUN
chr13:98634837-98637674.+	IPO5	SUN
chr6:33648231-33648331.+	ITPR3	SUN
chr5:78612133-78617428.+	JMY	SUN
chr6:149954052-149959521.-	KATNA1	SUN
chr9:2834166-2837179.-	KIAA0020	SUN
chr14:58965678-58975272.+	KIAA0586	SUN
chr12:10544490-10546408.-	KLRC4-KLRK1	SUN
chr12:123103092-123105025.+	KNTC1	SUN
chr4:129003460-129012155.+	LARP1B	SUN
chr9:130911942-130912516.+	LCN2	SUN
chr9:130912653-130913916.+	LCN2	SUN
chr9:130913996-130914184.+	LCN2	SUN
chr1:25880555-25881350.+	LDLRAP1	SUN
chr19:39294191-39294381.-	LGALS4	SUN
chr4:39462582-39463815.+	LIAS	SUN
chr12:50594667-50598334.-	LIMA1	SUN
chr12:50599851-50615803.-	LIMA1	SUN
chr3:45707209-45709785.+	LIMD1	SUN
chr3:195435712-195451550.+	LINC00969	SUN

chr1:145498180-145498535.+	LIX1L	SUN
chr13:76416119-76416986.+	LMO7	SUN
chr3:46477720-46479430.-	LTF	SUN
chr3:46479620-46480786.-	LTF	SUN
chr3:46480971-46482906.-	LTF	SUN
chr3:46482974-46484931.-	LTF	SUN
chr3:46485073-46486771.-	LTF	SUN
chr3:46486927-46487930.-	LTF	SUN
chr3:46487984-46488798.-	LTF	SUN
chr3:46488889-46490353.-	LTF	SUN
chr3:46490508-46491343.-	LTF	SUN
chr3:46491518-46491984.-	LTF	SUN
chr3:46492163-46495794.-	LTF	SUN
chr3:46495850-46496784.-	LTF	SUN
chr3:46496932-46497285.-	LTF	SUN
chr3:46497468-46497779.-	LTF	SUN
chr3:46497888-46501145.-	LTF	SUN
chr3:46501309-46506314.-	LTF	SUN
chr3:45870107-45872404.-	LZTFL1	SUN
chr3:45872630-45874541.-	LZTFL1	SUN
chr2:149241704-149243310.+	MBD5	SUN
chr5:89757369-89769655.-	MBLAC2	SUN
chr14:21966513-21967168.-	METTL3	SUN
chr14:21967946-21968636.-	METTL3	SUN
chr7:7636092-7645572.+	MIOS	SUN
chr3:12618240-12623306.+	MKRN2	SUN
chr9:20456784-20620652.-	MLLT3	SUN
chr11:102586168-102587032.-	MMP8	SUN
chr11:102589306-102592131.-	MMP8	SUN
chr11:102592257-102592344.-	MMP8	SUN
chr11:102592493-102593159.-	MMP8	SUN
chr11:102584188-102584484.-	MMP8	SUN
chr11:102587150-102589144.-	MMP8	SUN
chr10:99230618-99236439.-	MMS19	SUN
chr2:216810457-216811745.-	MREG	SUN
chr8:145278133-145293658.+	MROH1	SUN
chr6:24415391-24416624.+	MRS2	SUN
chr7:91509427-91509970.-	MTERF	SUN
chr1:21795078-21795180.+	NBPF3	SUN
chr1:21800078-21801392.+	NBPF3	SUN
chr1:21806716-21807422.+	NBPF3	SUN
chr11:134051079-134054531.-	NCAPD3	SUN
chr1:54291609-54293671.-	NDC1	SUN
chr12:44914012-44915782.-	NELL2	SUN
chr12:44915959-44917073.-	NELL2	SUN
chr12:44917267-44926363.-	NELL2	SUN
chr12:45004753-45059266.-	NELL2	SUN
chr12:45097637-45105074.-	NELL2	SUN
chr12:45105177-45108432.-	NELL2	SUN
chr12:45108524-45168529.-	NELL2	SUN
chr12:45168632-45169804.-	NELL2	SUN
chr12:45169933-45170824.-	NELL2	SUN
chr12:45170907-45171024.-	NELL2	SUN
chr12:45171097-45173445.-	NELL2	SUN
chr12:45173542-45173631.-	NELL2	SUN
chr12:45173805-45209768.-	NELL2	SUN
chr12:45209919-45269007.-	NELL2	SUN
chr12:45269136-45269597.-	NELL2	SUN
chr9:33338587-33342743.+	NFX1	SUN
chr12:95434373-95442843.-	NR2C1	SUN

chr10:123724900-123727169.-	NSMCE4A	SUN
chr5:37299670-37301538.-	NUP155	SUN
chr17:5291224-5292121.-	NUP88	SUN
chr13:53603175-53608482.+	OLFM4	SUN
chr2:201785116-201785715.-	ORC2	SUN
chr6:88367736-88372720.+	ORC3	SUN
chr7:103777340-103801519.-	ORC5	SUN
chr3:31744000-31774748.-	OSBPL10	SUN
chr4:57319927-57325537.+	PAICS	SUN
chr2:242076679-242077367.-	PASK	SUN
chr1:233136281-233137282.-	PCNXL2	SUN
chr1:233137427-233150410.-	PCNXL2	SUN
chr15:65411178-65411713.-	PDCD7	SUN
chr1:144922047-144922186.-	PDE4DIP	SUN
chr1:204419145-204423796.-	PIK3C2B	SUN
chr10:22898646-23003111.-	PIP4K2A	SUN
chr20:43218507-43243174.+	PKIG	SUN
chr4:155469005-155469980.-	PLRG1	SUN
chr14:20942734-20942931.+	PNP	SUN
chr9:140400212-140400434.-	PNPLA7	SUN
chr12:42778798-42781257.+	PPHLN1	SUN
chr12:42781337-42787371.+	PPHLN1	SUN
chrX:106888580-106890835.+	PRPS1	SUN
chr17:18814564-18827226.+	PRPSAP2	SUN
chr2:54092710-54093221.-	PSME4	SUN
chr2:54163964-54164527.-	PSME4	SUN
chr2:86360379-86360468.+	PTCD3	SUN
chr2:120639725-120640078.+	PTPN4	SUN
chr2:120702816-120703916.+	PTPN4	SUN
chr12:108079748-108082224.+	PWP1	SUN
chr12:108082579-108086590.+	PWP1	SUN
chr1:158914832-158946490.+	PYHIN1	SUN
chr6:107103607-107110854.+	QRSL1	SUN
chr16:67760461-67761229.-	RANBP10	SUN
chrX:16867424-16870168.-	RBBP7	SUN
chr3:186509639-186510278.-	RFC4	SUN
chr8:87500868-87519223.-	RMDN1	SUN
chr2:88991501-88998001.+	RPIA	SUN
chr2:89028855-89034068.+	RPIA	SUN
chr2:89036193-89037493.+	RPIA	SUN
chr11:126079617-126080784.-	RPUSD4	SUN
chr2:219457125-219457338.+	RQCD1	SUN
chr18:67721520-67724977.-	RTTN	SUN
chr19:47634285-47646750.+	SAE1	SUN
chr20:62606885-62607044.-	SAMD10	SUN
chr20:62608759-62611206.-	SAMD10	SUN
chr6:108026529-108029069.-	SCML4	SUN
chr5:1574410-1576293.-	SDHAP3	SUN
chr11:94918656-94922942.-	SESN3	SUN
chr11:94923125-94924567.-	SESN3	SUN
chr11:94924765-94926620.-	SESN3	SUN
chr11:94926686-94963946.-	SESN3	SUN
chr17:79683885-79684031.+	SLC25A10	SUN
chr2:172666786-172669848.-	SLC25A12	SUN
chr1:43396877-43408896.-	SLC2A1	SUN
chr1:9107793-9117506.-	SLC2A5	SUN
chr16:68307807-68308593.+	SLC7A6	SUN
chr11:62622688-62622895.-	SNHG1	SUN
chr4:186278891-186283077.+	SNX25	SUN
chr4:123978443-124011733.+	SPATA5	SUN

chr22:26882029-26883994.+	SRRD	SUN
chr22:26884254-26884355.+	SRRD	SUN
chr22:26884454-26886009.+	SRRD	SUN
chr22:26887036-26887428.+	SRRD	SUN
chr9:125887952-125890492.-	STRBP	SUN
chr9:125895247-125898319.-	STRBP	SUN
chr9:125898794-125901807.-	STRBP	SUN
chr9:125909333-125910056.-	STRBP	SUN
chr9:125920402-125920610.-	STRBP	SUN
chr9:125922741-125923255.-	STRBP	SUN
chr3:67571058-67578555.-	SUCLG2	SUN
chr1:234527491-234528161.-	TARBP1	SUN
chr1:234528298-234529107.-	TARBP1	SUN
chr15:102202019-102211688.-	TARSL2	SUN
chr15:102224440-102226098.-	TARSL2	SUN
chr13:75880607-75884077.-	TBC1D4	SUN
chr14:92258902-92264128.-	TC2N	SUN
chr5:145863192-145872482.+	TCERG1	SUN
chr19:1619473-1619778.-	TCF3	SUN
chr19:1621190-1621836.-	TCF3	SUN
chr19:1621969-1622052.-	TCF3	SUN
chr19:1622414-1623949.-	TCF3	SUN
chr19:1646426-1650175.-	TCF3	SUN
chr10:97447112-97447348.-	TCTN3	SUN
chr14:90459827-90485659.+	TDP1	SUN
chr1:151746980-151747185.-	TDRKH	SUN
chr12:48359128-48359620.+	TMEM106C	SUN
chr16:75575353-75576499.-	TMEM231;RP11-77K12.8	SUN
chr3:100093996-100096548.-	TOMM70A	SUN
chr18:34398936-34408645.-	TPGS2	SUN
chr1:211526799-211527751.+	TRAF5	SUN
chr3:49869501-49877204.-	TRAIP	SUN
chr1:40315933-40318402.-	TRIT1	SUN
chr17:3480486-3480891.-	TRPV1;SHPK	SUN
chr15:77344810-77345118.-	TSPAN3	SUN
chr21:38559446-38560795.+	TTC3	SUN
chr21:38560896-38563634.+	TTC3	SUN
chr21:38569997-38570182.+	TTC3	SUN
chr5:94845391-94848180.-	TTC37	SUN
chr9:15267946-15307081.-	TTC39B	SUN
chr17:40762238-40762440.+	TUBG1	SUN
chr4:48082145-48088482.-	TXK	SUN
chr3:132390725-132390893.+	UBA5	SUN
chr17:74387894-74387990.-	UBE2O	SUN
chr17:74391942-74392208.-	UBE2O	SUN
chrX:118972014-118972329.-	UPF3B	SUN
chr19:30503438-30505793.+	URI1	SUN
chr14:97342457-97347513.+	VRK1	SUN
chr10:122630858-122633350.+	WDR11	SUN
chr2:203748464-203748920.-	WDR12	SUN
chr6:43535091-43536447.-	XPO5	SUN
chr11:130108502-130109706.-	ZBTB44	SUN
chr9:37349449-37354706.+	ZCCHC7	SUN
chr1:35884173-35885070.+	ZMYM4	SUN
chr19:19825296-19843764.-	ZNF14	SUN
chr19:9529307-9529441.-	ZNF266	SUN
chr17:15604554-15609700.+	ZNF286A	SUN
chr19:35169718-35173681.+	ZNF302	SUN
chr19:56905810-56909249.+	ZNF582-AS1	SUN
chr7:149248037-149248664.-	ZNF767	SUN

chr7:5889147-5893737.+	ZNF815P	SUN
chr1:202914323-202915566.-		SUN
chr1:226109776-226109903.-		SUN
chr11:118223202-118223838.+		SUN
chr14:22959541-23016446.+		SUN
chr14:22968732-23016446.+		SUN
chr14:22978390-23016446.+		SUN
chr14:22984666-23016446.+		SUN
chr14:22994685-23016446.+		SUN
chr14:22998641-23016446.+		SUN
chr14:23005151-23016446.+		SUN
chr14:23008077-23016446.+		SUN
chr15:45002412-45003068.-		SUN
chr19:1221339-1221664.+		SUN
chr3:52009220-52011886.+	ABHD14A;ACY1;ABHD14A-ACY1	MRC
chr2:208527246-208531404.+	AC079767.4	MRC
chr17:43215355-43216387.+	ACBD4	MRC
chr19:36032486-36032652.-	AD000090.2	MRC
chr10:76074503-76153898.+	ADK	MRC
chr10:76430027-76468078.+	ADK	MRC
chr19:3054038-3054117.-	AES	MRC
chr19:3054192-3055661.-	AES	MRC
chr19:3055724-3056309.-	AES	MRC
chr19:3056354-3057676.-	AES	MRC
chr19:3057740-3061157.-	AES	MRC
chr7:100151123-100151715.+	AGFG2	MRC
chr11:67256926-67257508.+	AIP	MRC
chr2:112550132-112551654.-	ANAPC1	MRC
chr19:7535201-7535422.+	ARHGEF18	MRC
chr1:110029839-110030139.+	ATXN7L2	MRC
chr16:1396956-1397298.+	BAIAP3	MRC
chr4:102839346-102942670.+	BANK1	MRC
chr4:102942749-102946357.+	BANK1	MRC
chr4:102951422-102964995.+	BANK1	MRC
chr4:102981546-102984231.+	BANK1	MRC
chr4:102984295-102992431.+	BANK1	MRC
chr4:102993557-102994840.+	BANK1	MRC
chr20:49446917-49458302.+	BCAS4	MRC
chr20:49458437-49493022.+	BCAS4	MRC
chr2:127815177-127816586.-	BIN1	MRC
chr8:11352100-11400732.+	BLK	MRC
chr8:11400856-11403560.+	BLK	MRC
chr8:11403612-11405540.+	BLK	MRC
chr8:11405634-11406532.+	BLK	MRC
chr8:11406631-11407667.+	BLK	MRC
chr8:11407771-11412251.+	BLK	MRC
chr8:11412398-11412840.+	BLK	MRC
chr8:11412993-11414166.+	BLK	MRC
chr8:11414346-11415470.+	BLK	MRC
chr8:11415547-11418810.+	BLK	MRC
chr8:11418961-11420487.+	BLK	MRC
chr16:58149361-58149944.-	C16orf80	MRC
chr17:54869713-54872404.-	C17orf67	MRC
chr6:31802977-31803187.+	C6orf48	MRC
chr6:31804294-31805012.+	C6orf48	MRC
chr9:131585112-131586025.-	C9orf114	MRC
chr9:131587328-131588300.-	C9orf114	MRC
chr22:40073424-40073991.+	CACNA1I	MRC
chr3:50404350-50404441.-	CACNA2D2	MRC
chr12:120428101-120436324.+	CCDC64	MRC

chr14:20779911-20781626.-	CCNB1IP1	MRC
chr1:1323890-1324005.-	CCNL2	MRC
chr16:28943409-28943666.+	CD19	MRC
chr16:28949001-28949089.+	CD19	MRC
chr16:28950089-28950192.+	CD19	MRC
chr16:28950299-28950461.+	CD19	MRC
chr1:158262155-158262385.+	CD1C	MRC
chr1:158262664-158263001.+	CD1C	MRC
chr12:6554397-6554589.+	CD27	MRC
chr12:6554721-6559338.+	CD27	MRC
chr12:6559518-6559706.+	CD27	MRC
chr11:60783307-60784950.+	CD6	MRC
chr11:60785485-60785760.+	CD6	MRC
chr11:60785865-60786725.+	CD6	MRC
chr17:62008745-62009554.-	CD79B	MRC
chr12:58145519-58145957.-	CDK4	MRC
chr16:845356-845684.+	CHTF18	MRC
chr7:100876001-100876113.-	CLDN15	MRC
chr19:42891394-42891491.-	CNFN	MRC
chr14:74428273-74428439.+	COQ6	MRC
chr14:105953309-105953549.+	CRIP1	MRC
chr1:17295835-17296279.+	CROCC	MRC
chr11:118754701-118764304.+	CXCR5	MRC
chr4:53579126-53579660.+	DANCR	MRC
chr16:11023416-11035425.-	DEXI	MRC
chr6:43193881-43194064.-	DNPH1	MRC
chr9:140459058-140459344.-	DPH7	MRC
chr9:140459606-140468659.-	DPH7	MRC
chr1:1271895-1273356.-	DVL1	MRC
chr1:1274033-1274666.-	DVL1	MRC
chr16:2285002-2285081.+	E4F1	MRC
chr11:831032-831223.+	EFCAB4A	MRC
chr17:7155915-7156088.+	ELP5	MRC
chr12:7031565-7031893.+	ENO2	MRC
chr17:4855209-4856089.+	ENO3	MRC
chr17:4856636-4857006.+	ENO3	MRC
chr17:4859438-4859867.+	ENO3	MRC
chr17:4860184-4860272.+	ENO3	MRC
chr12:112451413-112459953.+	ERP29	MRC
chr3:45049067-45052726.+	EXOSC7	MRC
chr11:61646981-61647512.-	FADS3	MRC
chr1:207078492-207082806.-	FAIM3	MRC
chr1:207083213-207083554.-	FAIM3	MRC
chr1:207085297-207086273.-	FAIM3	MRC
chr1:207086387-207087206.-	FAIM3	MRC
chr1:207086387-207095162.-	FAIM3	MRC
chr3:122103146-122121606.+	FAM162A	MRC
chr3:122121729-122123104.+	FAM162A	MRC
chr3:122126236-122128585.+	FAM162A	MRC
chrX:152853852-152857963.-	FAM58A	MRC
chr6:35427231-35427458.+	FANCE	MRC
chr19:17865490-17865926.+	FCHO1	MRC
chr19:17875258-17877477.+	FCHO1	MRC
chr19:17877619-17881233.+	FCHO1	MRC
chr19:17883364-17883453.+	FCHO1	MRC
chr19:17883550-17885047.+	FCHO1	MRC
chr1:157716564-157716660.-	FCRL2	MRC
chr1:157716689-157718342.-	FCRL2	MRC
chr1:157718750-157719439.-	FCRL2	MRC
chr1:157719467-157736644.-	FCRL2	MRC

chr1:157650560-157650770.-	FCRL3	MRC
chr1:161677133-161680264.+	FCRLA	MRC
chr1:161680282-161680549.+	FCRLA	MRC
chr1:161681264-161681723.+	FCRLA	MRC
chr6:112041265-112080036.-	FYN	MRC
chr19:1399025-1399126.-	GAMT	MRC
chr15:52420441-52425574.-	GNB5	MRC
chr19:2515145-2520605.-	GNG7	MRC
chr19:2646278-2702643.-	GNG7	MRC
chr12:100551223-100551305.-	GOLGA2B	MRC
chr17:18927696-18939270.-	GRAP	MRC
chr11:45948422-45948865.+	GYLTL1B	MRC
chr11:45949620-45949727.+	GYLTL1B	MRC
chr9:99233376-99246743.+	HABP4	MRC
chr9:99246915-99250370.+	HABP4	MRC
chr4:108935744-108940695.+	HADH	MRC
chr4:108944719-108948843.+	HADH	MRC
chr4:108954448-108955394.+	HADH	MRC
chr16:779088-779287.+	HAGHL	MRC
chr5:140053913-140054263.-	HARS	MRC
chr19:36103794-36104631.+	HAUS5	MRC
chr19:36104694-36104769.+	HAUS5	MRC
chr19:36113635-36113777.+	HAUS5	MRC
chr1:32797843-32798301.+	HDAC1	MRC
chr3:50617370-50617546.+	HEMK1	MRC
chr12:123339509-123339599.+	HIP1R	MRC
chr12:123339952-123340097.+	HIP1R	MRC
chr12:123344083-123344318.+	HIP1R	MRC
chr12:123344624-123344694.+	HIP1R	MRC
chr12:123344757-123344969.+	HIP1R	MRC
chr12:123345331-123345462.+	HIP1R	MRC
chr12:123346061-123346252.+	HIP1R	MRC
chr6:32781028-32781216.-	HLA-DOB	MRC
chr12:54678101-54680445.+	HNRNPA1	MRC
chr11:532755-533276.-	HRAS	MRC
chr19:5684916-5684999.+	HSD11B1L	MRC
chr12:111126513-111127530.-	HVCN1	MRC
chr1:23884906-23885425.-	ID3	MRC
chr1:23885510-23885617.-	ID3	MRC
chr14:106206530-106207817.-	IGHG1	MRC
chr12:56732990-56733209.+	IL23A	MRC
chr19:14161695-14162418.+	IL27RA	MRC
chr7:110526751-110603555.-	IMMP2L	MRC
chr3:49065755-49065863.-	IMPDH2	MRC
chr9:139325569-139326275.-	INPP5E	MRC
chr8:145169378-145169456.+	KIAA1875	MRC
chr11:66032543-66032638.+	KLC2	MRC
chr12:53345429-53345514.+	KRT18	MRC
chr9:139634500-139636332.-	LCN10	MRC
chr9:139634005-139634401.-	LCN10;LCN6	MRC
chr12:21788643-21790004.-	LDHB	MRC
chr12:21795059-21796868.-	LDHB	MRC
chr12:21797042-21799832.-	LDHB	MRC
chr12:21799950-21807476.-	LDHB	MRC
chr12:21807611-21810684.-	LDHB	MRC
chr21:35304046-35318113.+	LINC00649	MRC
chr15:57599266-57599739.+	LINC00926	MRC
chr3:195435139-195435617.+	LINC00969	MRC
chr15:34651946-34652311.-	LPCAT4	MRC
chr15:34652410-34653600.-	LPCAT4	MRC

chr15:34653733-34654396.-	LPCAT4	MRC
chr15:34654522-34654773.-	LPCAT4	MRC
chr15:34655037-34655622.-	LPCAT4	MRC
chr22:25747869-25750562.-	LRP5L	MRC
chr22:25750779-25753221.-	LRP5L	MRC
chr8:145749193-145749307.+	LRRC14	MRC
chr19:35757641-35757738.+	LSR	MRC
chr16:249237-256002.-	LUC7L	MRC
chr16:258663-270647.-	LUC7L	MRC
chr1:160784551-160788007.+	LY9	MRC
chr1:160793586-160793970.+	LY9	MRC
chr1:160794039-160797537.+	LY9	MRC
chr6:5187214-5216850.-	LYRM4	MRC
chr16:29819614-29819890.+	MAZ	MRC
chr22:20905453-20905722.+	MED15	MRC
chr22:20905774-20906825.+	MED15	MRC
chr1:3410463-3410559.-	MEGF6	MRC
chr11:60223418-60229831.+	MS4A1	MRC
chr11:60229771-60229890.+	MS4A1	MRC
chr19:1369339-1369594.+	MUM1	MRC
chr1:45797758-45797837.-	MUTYH	MRC
chr1:45797982-45798062.-	MUTYH	MRC
chr12:57486978-57487189.+	NAB2	MRC
chr12:57118307-57119046.-	NACA	MRC
chr22:50960277-50960414.+	NCAPH2	MRC
chr10:15148697-15151700.-	NMT2	MRC
chr7:72718033-72718226.-	NSUN5	MRC
chr7:72420500-72420596.-	NSUN5P2	MRC
chr1:233092189-233105654.+	NTPCR	MRC
chr16:1837832-1837941.+	NUBP2	MRC
chr1:224418998-224420902.-	NVL	MRC
chr1:224424284-224437913.-	NVL	MRC
chr1:224468887-224473727.-	NVL	MRC
chr1:224475695-224477185.-	NVL	MRC
chr4:48906628-48908674.-	OCIAD2	MRC
chr3:31705724-31710133.-	OSBPL10	MRC
chr3:31710316-31712288.-	OSBPL10	MRC
chr3:31725606-31743850.-	OSBPL10	MRC
chr3:31774903-31789401.-	OSBPL10	MRC
chr3:31789612-31871531.-	OSBPL10	MRC
chrX:78200992-78216004.+	P2RY10	MRC
chr3:49028043-49028265.+	P4HTM	MRC
chr3:49043620-49044119.+	P4HTM	MRC
chr14:23792275-23792585.+	PABPN1;BCL2L2-PABPN1	MRC
chr2:242063548-242065610.-	PASK	MRC
chr21:47863861-47864606.+	PCNT	MRC
chr11:117077876-117078369.-	PCSK7	MRC
chr11:117078451-117078685.-	PCSK7	MRC
chr6:33378992-33380024.+	PHF1	MRC
chr6:33380199-33380284.+	PHF1	MRC
chr6:33380366-33380474.+	PHF1	MRC
chr6:33380570-33380972.+	PHF1	MRC
chr6:33381073-33381185.+	PHF1	MRC
chr6:33381334-33381512.+	PHF1	MRC
chr6:33381886-33382019.+	PHF1	MRC
chr6:33382921-33383011.+	PHF1	MRC
chr6:33383106-33383366.+	PHF1	MRC
chr6:33383447-33383586.+	PHF1	MRC
chr22:21832983-21834047.-	PI4KAP2	MRC
chr20:43243348-43246925.+	PKIG	MRC

chrX:153698127-153698319.+	PLXNA3	MRC
chrX:153698510-153698784.+	PLXNA3	MRC
chr6:43485115-43487070.+	POLR1C	MRC
chr12:42720031-42726461.+	PPHLN1	MRC
chr14:102298141-102302505.+	PPP2R5C	MRC
chr10:6622889-6625637.+	PRKCQ-AS1	MRC
chr16:68381197-68381533.+	PRMT7	MRC
chr19:10823304-10823433.+	QTRT1	MRC
chrX:129306294-129318258.+	RAB33A	MRC
chrX:154490514-154493358.-	RAB39B	MRC
chr11:64494603-64494767.-	RASGRP2	MRC
chr11:64494832-64496334.-	RASGRP2	MRC
chr11:64497270-64497524.-	RASGRP2	MRC
chr11:64497666-64502583.-	RASGRP2	MRC
chr11:64502699-64503013.-	RASGRP2	MRC
chr11:64503452-64504224.-	RASGRP2	MRC
chr11:64504506-64506831.-	RASGRP2	MRC
chr11:64506948-64507107.-	RASGRP2	MRC
chr11:64507281-64507484.-	RASGRP2	MRC
chr11:64507635-64508419.-	RASGRP2	MRC
chr11:64508551-64508910.-	RASGRP2	MRC
chr11:64508973-64509481.-	RASGRP2	MRC
chr11:64509584-64510265.-	RASGRP2	MRC
chr11:64510409-64511474.-	RASGRP2	MRC
chr11:64510409-64512213.-	RASGRP2	MRC
chr11:561892-562078.+	RASSF7	MRC
chr16:67684053-67685089.+	RLTPR	MRC
chr16:67685911-67686101.+	RLTPR	MRC
chr11:117153566-117153830.+	RNF214	MRC
chr17:7221993-7222368.-	RP11-542C16.2;NEURL4	MRC
chr1:2513089-2514808.+	RP3-395M20.9	MRC
chr1:2514934-2515563.+	RP3-395M20.9	MRC
chr1:81107086-81109909.+	RP5-887A10.1	MRC
chr17:5331531-5335861.+	RPAIN	MRC
chr22:42976365-42977934.-	RRP7B	MRC
chr10:102267808-102268763.-	SEC31B;NDUFB8	MRC
chr11:75280216-75282825.+	SERPINH1	MRC
chr10:99527617-99529424.-	SFRP5	MRC
chr10:99529502-99531061.-	SFRP5	MRC
chr2:219001-229965.-	SH3YL1	MRC
chr2:230044-231022.-	SH3YL1	MRC
chr2:233229-234159.-	SH3YL1	MRC
chr9:35650242-35650353.-	SIT1	MRC
chr9:35650412-35650498.-	SIT1	MRC
chr17:46239931-46247970.-	SKAP1	MRC
chr3:121646686-121647267.+	SLC15A2	MRC
chr14:23817880-23818480.-	SLC22A17	MRC
chr14:23821660-23821854.-	SLC22A17	MRC
chr17:78197136-78199635.+	SLC26A11	MRC
chr17:78215620-78218994.+	SLC26A11	MRC
chr17:78223086-78225127.+	SLC26A11	MRC
chr11:66136670-66136839.-	SLC29A2	MRC
chr3:125752521-125769785.-	SLC41A3	MRC
chr1:28905192-28906044.-	SNHG12	MRC
chr1:28906493-28907071.-	SNHG12	MRC
chr1:28907158-28907622.-	SNHG12	MRC
chr19:49606844-49607890.+	SNRNP70	MRC
chr15:25200209-25207260.+	SNURF;SNRPN	MRC
chr15:25207356-25213078.+	SNURF;SNRPN	MRC
chr15:25213229-25219457.+	SNURF;SNRPN	MRC

chr15:25219603-25220504.+	SNURF;SNRPN	MRC
chr15:25222176-25222924.+	SNURF;SNRPN	MRC
chr15:25223063-25223339.+	SNURF;SNRPN	MRC
chr15:25223465-25223553.+	SNURF;SNRPN	MRC
chr21:33038831-33039570.+	SOD1	MRC
chr1:24301570-24304400.-	SRSF10	MRC
chr7:99956702-99956959.+	STAG3L5P-PVRIG2P-PILRB;PILRB	MRC
chr7:99709452-99709544.-	TAF6	MRC
chr11:67171825-67172555.+	TBC1D10C	MRC
chr11:67172655-67172869.+	TBC1D10C	MRC
chr11:67172977-67173065.+	TBC1D10C	MRC
chr11:67173172-67173373.+	TBC1D10C	MRC
chr11:67174487-67176449.+	TBC1D10C	MRC
chr19:36613075-36616352.+	TBCB	MRC
chr11:134119156-134119721.-	THYN1	MRC
chr11:134120237-134121023.-	THYN1	MRC
chr17:76115473-76117093.-	TMC6	MRC
chr11:118403922-118404134.+	TMEM25	MRC
chr1:226036255-226036597.-	TMEM63A	MRC
chr1:151142579-151142994.-	TMOD4;VPS72	MRC
chr1:6521822-6522053.-	TNFRSF25	MRC
chr1:6522726-6522922.-	TNFRSF25	MRC
chr1:6524513-6524611.-	TNFRSF25	MRC
chr1:6525620-6526128.-	TNFRSF25	MRC
chr17:76103921-76105131.-	TNRC6C-AS1	MRC
chr1:209948834-209948943.+	TRAF3IP3	MRC
chr1:209951518-209952659.+	TRAF3IP3	MRC
chr1:209952719-209953814.+	TRAF3IP3	MRC
chr1:209953951-209954689.+	TRAF3IP3	MRC
chr16:3713563-3714274.-	TRAP1	MRC
chr14:22386481-22386640.+	TRAV13-2	MRC
chr14:22616091-22616305.+	TRAV27	MRC
chr7:142499895-142500186.+	TRBC2	MRC
chr7:142197867-142197959.-	TRBV11-2	MRC
chr7:142326619-142326751.+	TRBV19	MRC
chr7:142448153-142448440.+	TRBV29-1	MRC
chr7:142149221-142149343.-	TRBV5-5	MRC
chr19:50247661-50248458.-	TSKS	MRC
chr15:77346621-77348130.-	TSPAN3	MRC
chr22:50657326-50657496.-	TUBGCP6	MRC
chr22:50661021-50662569.-	TUBGCP6	MRC
chr22:50664807-50665161.-	TUBGCP6	MRC
chr21:43833331-43836550.+	UBASH3A	MRC
chr21:43846929-43852211.+	UBASH3A	MRC
chr21:43852311-43854941.+	UBASH3A	MRC
chr21:43855064-43857597.+	UBASH3A	MRC
chr16:74919693-74920167.-	WDR59	MRC
chr19:36592219-36592565.+	WDR62	MRC
chr3:48302429-48309404.+	ZNF589	MRC
chr1:26688666-26689516.-	ZNF683	MRC
chr1:2509335-2512998.+		MRC
chr3:50617171-50617274.+		MRC
chr7:142493848-142498724.+		MRC
chr7:142495186-142498724.+		MRC
chr8:66628871-66630556.-		MRC
chr11:67173219-67173373.+		MRC
chr12:47599928-47604422.-		MRC
chr14:106387140-106388061.+		MRC
chr16:2820210-2820352.+		MRC
chr19:3054035-3054117.-		MRC

chr19:39097655-39098503.-		MRC
chr17:7249810-7250126.+	ACAP1	AHRI
chr17:7250250-7250349.+	ACAP1	AHRI
chr7:4820943-4821198.+	AP5Z1	AHRI
chr14:21544802-21544932.+	ARHGEF40	AHRI
chr16:1395891-1395986.+	BAIAP3	AHRI
chr16:1397626-1397701.+	BAIAP3	AHRI
chrX:49104771-49104867.+	CCDC22	AHRI
chr19:46506424-46506676.+	CCDC61	AHRI
chr17:7810806-7810918.+	CHD3	AHRI
chr16:4438069-4438545.-	CORO7;CORO7-PAM16	AHRI
chr15:64231560-64263621.-	DAPK2	AHRI
chr1:6727870-6738453.-	DNAJC11	AHRI
chr16:3706186-3706638.+	DNASE1	AHRI
chr6:30879046-30879207.+	GTF2H4;VARS2	AHRI
chr22:19373259-19375233.-	HIRA;C22orf39	AHRI
chr7:99697716-99697835.-	MCM7	AHRI
chr4:103517489-103518676.+	NFKB1	AHRI
chr16:56867318-56868039.+	NUP93	AHRI
chr15:40583688-40583806.-	PLCB2	AHRI
chr19:10433950-10434050.-	RAVER1	AHRI
chr22:50894011-50894644.-	SBF1	AHRI
chr6:31927177-31927786.+	SKIV2L	AHRI
chr17:34169463-34171080.+	TAF15	AHRI
chr22:40697337-40704515.+	TNRC6B	AHRI
chr10:104415070-104415862.+	TRIM8	AHRI

Supplementary Table 20: The ability of all pairs with AUC>0.75 in all three cohorts to complement the top pair (C1QC/TRAV27) was analyzed using logistic regression.

Complementation Chi-squared p-values

	C1QA/TBCB	C1QC/RP3-395M20.9	C1QC/PIK3C2B	C1QC/RPIA	C1QC/NELL2	C1QC/OSBPL10	ANKRD22/OSBPL10	RHBDF2/TUBGCP6
SUN	0.002	0.108	0.178	0.635	0.271	0.099	0.0004	0.035
MRC	0.245	0.011	0.594	0.807	0.806	0.143	0.006	0.027
AHRI	0.126	0.157	0.123	0.305	0.084	0.047	0.032	0.167

Supplementary Table 21: AUCs of C1QC/TRAV27, ANKRD22/OBSPL10 and the combination of the two on all three cohorts.

	AUC		
	SUN	**MRC**	**AHRI**
C1QC/TRAV27	0.761	0.771	0.769
ANKRD22/OBSPL10	0.757	0.754	0.777
C1QC/TRAV27 + ANKRD22/OBSPL10	0.801	0.796	0.795

Supplementary Table S22: Performance of RISK4 at different sensitivities

RISK4 Threshold	Sensitivity	Specificity: all sites	Specificity: SUN, South Africa	Specificity: MRC, Gambia	Specificity: AHRI, Ethiopia	Global RISK4 Positivity Rate	Incidence (Control event rate (CER))	Proportion of Incident cases detected by RISK4	Proportion of incidents not detected (Experimental event rate- EER)	Potential absolute risk reduction (ARR) by RISK4-guided preventative treatment	Number to harm (NTH) (number ideintified for RISK4-guided prevention
0.05	100%	1%	1%	22%	24%	98%	0.022	0.02200	0.00000	0.02200	45
0.35	90%	30%	28%	22%	24%	61%	0.022	0.01990	0.00210	0.01990	50
0.37	81%	34%	33%	23%	24%	54%	0.022	0.01781	0.00419	0.01781	56
0.49	71%	52%	63%	69%	53%	38%	0.022	0.01571	0.00629	0.01571	64
0.57	62%	63%	63%	69%	56%	29%	0.022	0.01362	0.00838	0.01362	73
0.67	50%	77%	96%	91%	80%	19%	0.022	0.01100	0.01100	0.01100	91
0.73	40%	81%	96%	92%	89%	17%	0.022	0.00890	0.01310	0.00890	112
0.85	31%	94%	99%	95%	93%	6%	0.022	0.00681	0.01519	0.00681	147
0.92	21%	98%	99%	95%	96%	2%	0.022	0.00471	0.01729	0.00471	212
0.94	12%	98%	99%	97%	98%	1%	0.022	0.00262	0.01938	0.00262	382

Supplementary Table S23: Estimated RISK4 positive and negative predictive values based on population TB prevalence of 2% in HHC

	Specificities					
Sensitivity	**All Test**	**SUN**	**MRC**	**AHRI**	**PPV***	**NPV****
10%	98%	99%	97%	98%	9.3%	98.2%
20%	98%	99%	95%	96%	16.9%	98.4%
30%	94%	99%	95%	93%	9.3%	98.5%
40%	81%	96%	92%	89%	4.1%	98.5%
50%	77%	96%	91%	80%	4.2%	98.7%
60%	63%	63%	69%	56%	3.2%	98.7%
70%	52%	63%	69%	53%	2.9%	98.8%
80%	34%	33%	23%	24%	2.4%	98.8%
90%	30%	28%	22%	24%	2.6%	99.3%
100%	1%	1%	22%	24%	2.0%	100.0%

*Positive predictive value (PPV)=Prevalence×Sensitivity/{(Prevalence×Sensitivity)+(1−Prevalence)×(1−Specificity)}
**Negative predictive value (NPV)=(1−Prevalence)×Specificity/{(1−Prevalence)×Specificity)}+{Prevalence×(1−Sensitivity)}