

A group of novel serum diagnostic biomarkers for multidrug-resistant tuberculosis by
iTRAQ-2D LC-MS/MS and Solexa sequencing

Table S1. Characteristics of healthy controls and pulmonary tuberculosis patients.

	MDR-TB (N = 42)	DS-TB (N = 60)	Controls (N = 60)	<i>P</i>
Age, years range (mean ± SD)	23-76 (44.88±14.56)	18-65 (40.48±16.46)	24-73 (42.57±13.17)	0.250 ^a
Gender: male, no. (%)	33 (78.57)	39 (65.00)	42 (70.00)	0.335 ^b
Body mass index (mean ± SD)	20.33 ± 2.98	21.32 ± 3.29	23.21± 4.38	0.210 ^a
Presence of TB history of relatives, no. (%)	9 (21.43)	8 (13.33)	6 (10.00)	0.258 ^b
BCG vaccination, no. (%)	16 (38.10)	25 (41.67)	33 (55.00)	0.177 ^b

MDR-TB: multidrug-resistant tuberculosis; DS-TB: drug-sensitive tuberculosis; N:
number of subjects. ^a*P* value among three groups, for Kruskal-Wallis test. ^b*P* value
among three groups, for chi-square test.

Table S2. Differentially expressed proteins and their expression levels quantified by iTRAQ analysis.

Protein ID	Alternative name	Gene name	Protein name	iTRAQ ratio		
				MDR-TB/ DS-TB	MDR-TB/ Control	DS-TB/ Control
Increased in MDR-TB/DS-TB						
P08519	APOA	LPA	Apolipoprotein(a)	9.94	3.73	0.38
P81605	DCD	DCD	Dermcidin	3.13	14.04	4.49
P0CG05	LAC2	IGLL5	Ig lambda-2 chain C regions	3.07	2.34	-
P04208	LV106	LV106	Ig lambda chain V-I region WAH	2.72	2.27	-
P06314	KV404	KV404	Ig kappa chain V-IV region B17	2.48	1.67	-
Q15063	POSTN	POSTN	Periostin	2.43	2.89	-
P01860	IGHG3	IGHG3	Ig gamma-3 chain C region	2.26	9.26	4.09
P01591	IGJ	IGJ	Immunoglobulin J chain	2.24	3.33	-
P00738	HPT	HP	Haptoglobin	2.17	17.72	8.17
P20742	PZP	PZP	Pregnancy zone protein	2.07	3.49	1.69
P02671	FIBA	FGA	Fibrinogen alpha chain	2.04	2.44	-
P01766	HV305	HV305	Ig heavy chain V-III region BRO	1.91	2.15	-
Q15149	PLEC	PLEC	Plectin	1.75	2.68	1.53
P0DJ18	SAA1	SAA1	Serum amyloid A-1 protein	1.67	11.40	6.84
P01767	HV306	HV306	Ig heavy chain V-III region BUT	1.55	2.03	-
A6NJ16	IV4F8	IV4F8	Putative V-set and immunoglobulin domain-containing-like protein IGHV4OR15-8	1.51	1.61	-
Decreased in MDR-TB/DS-TB						
P08697	A2AP	SERPINF2	Alpha-2-antiplasmin	0.24	0.20	-
P03951	FA11	F11	Coagulation factor XI	0.25	0.26	-

P01019	ANGT	AGT	Angiotensinogen	0.26	0.28	-
P02787	TRFE	TF	Serotransferrin	0.27	0.09	0.34
P02654	APOC1	APOC1	Apolipoprotein C-I	0.28	0.20	-
P00748	FA12	F12	Coagulation factor XII	0.30	0.37	-
O75636	FCN3	FCN3	Ficolin-3	0.31	0.23	-
O95810	SDPR	SDPR	Serum deprivation-response protein	0.32	0.46	-
P06727	APOA4	APOA4	Apolipoprotein A-IV	0.34	0.27	-
P19652	A1AG2	ORM2	Alpha-1-acid glycoprotein 2	0.34	2.60	7.59
P10909	CLUS	CLU	Clusterin	0.35	0.18	0.52
P01042	KNG1	KNG1	Kininogen-1	0.35	0.29	-
P35579	MYH9	MYH9	Myosin-9	0.35	0.41	-
P16070	CD44	CD44	CD44 antigen	0.38	0.44	-
P25311	ZA2G	AZGP1	Zinc-alpha-2-glycoprotein	0.39	0.30	-
P02656	APOC3	APOC3	Apolipoprotein C-III	0.39	0.25	-
P04275	VWF	VWF	von Willebrand factor	0.39	0.39	-
P02655	APOC2	APOC2	Apolipoprotein C-II	0.41	0.32	-
P02749	APOH	APOH	Beta-2-glycoprotein 1	0.41	0.56	-
P02652	APOA2	APOA2	Apolipoprotein A-II	0.42	0.18	0.43
P02745	C1QA	C1QA	Complement C1q subcomponent subunit A	0.43	0.32	-
P05155	IC1	SERPING1	Plasma protease C1 inhibitor	0.43	0.37	-
P43652	AFAM	AFM	Afamin	0.44	0.27	-
P01009	A1AT	SERPINA1	Alpha-1-antitrypsin	0.44	2.07	4.68
P04004	VTNC	VTN	Vitronectin	0.45	0.36	-
P06396	GELS	GSN	Gelsolin	0.48	0.20	0.42
Q16610	ECM1	ECM1	Extracellular matrix protein 1	0.50	0.36	-
P29622	KAIN	SERPINA4	Kallistatin	0.51	0.22	0.44

P02760	AMBP	AMBP	Protein AMBP	0.51	0.30	0.58
P02751	FINC	FN1	Fibronectin	0.52	0.13	0.25
P19823	ITIH2	ITIH2	Inter-alpha-trypsin inhibitor heavy chain H2	0.53	0.19	0.35
P02763	A1AG1	ORM1	Alpha-1-acid glycoprotein 1	0.53	8.17	15.32
P36955	PEDF	SERPINF1	Pigment epithelium-derived factor	0.56	0.30	0.55
P01880	IGHD	IGHD	Ig delta chain C region	0.57	3.63	6.43

MDR-TB: multidrug-resistant tuberculosis; DS-TB: drug-sensitive tuberculosis; -: ratio between 0.60 and 1.50.

Table S3. Overview of reads from raw data to cleaned sequences.

Classification	MDR-TB	DS-TB	Controls
Raw reads	832,178	886,704	464,603
3ADT&length filter	577,094	582,154	334,564
Junk reads	1,754	2,145	909
Rfam	35,851	45,507	14,950
mRNA	19,171	23,114	14,821
Repeats	2,126	2,623	1,307
valid reads	202,848	239,654	102,624
rRNA	20,678	25,924	6,947
tRNA	8,344	11,105	3,780
snoRNA	1,144	1,516	570
snRNA	2,009	2,439	1,104
other Rfam RNA	3,676	4,523	2,549

MDR-TB: multidrug-resistant tuberculosis; DS-TB: drug-sensitive tuberculosis;

3ADT&length filter: reads removed due to 3ADT not found and length with <18

and >26 were removed; Junk reads: Junk: $\geq 2N$, $\geq 7A$, $\geq 8C$, $\geq 6G$, $\geq 7T$, ≥ 10 Dimer,

≥ 6 Trimer, or ≥ 5 Tetramer; Rfam: Collection of many common non-coding RNA

families except micro RNA, <http://rfam.janelia.org>; Repeats: Prototypic sequences

representing repetitive DNA from different eukaryotic species.

<http://www.girinst.org/replib>.

Table S4. Differentially expressed miRNAs and their expression levels quantified by Solexa sequencing.

miR name	miR ID	miR sequence	Solexa sequencing ratio		
			MDR-TB/ DS-TB	MDR-TB/ Control	DS-TB/ Control
Increased in MDR-TB/DS-TB					
hsa-miR-628-3p_L+1R-1	hsa-miR-628-3p	TCTAGTAAGAGTGGCAGTCGA	7.96	0.23	0.03
hsa-miR-664a-5p_R-1	hsa-miR-664a-5p	ACTGGCTAGGGAAAATGATTGGAT	5.40	2.21	0.41
hsa-miR-582-5p_R-1	hsa-miR-582-5p	TTACAGTTGTTCAACCAGTTACT	3.66	3.78	-
hsa-miR-132-5p	hsa-miR-132-5p	ACCGTGGCTTTCGATTGTTACT	2.73	11.39	4.17
hsa-miR-744-5p_R-2	hsa-miR-744-5p	TGCGGGGCTAGGGCTAACAGCA	2.62	1.77	-
hsa-miR-331-5p_R-2	hsa-miR-331-5p	CTAGGTATGGTCCCAGGGATCC	2.56	2.21	-
hsa-miR-296-5p	hsa-miR-296-5p	AGGGCCCCCCTCAATCCTGT	2.48	1.93	-
hsa-miR-27b-5p	hsa-miR-27b-5p	AGAGCTTAGCTGATTGGTGAAC	2.48	3.59	-
hsa-miR-16-2-3p_R-3	hsa-miR-16-2-3p	CCAATATTACTGTGCTGCTTTA	2.22	2.60	-
hsa-miR-501-3p	hsa-miR-501-3p	AATGCACCCGGGCAAGGATTCT	2.18	0.25	0.11
hsa-miR-3120-3p_R+1	hsa-miR-3120-3p	CACAGCAAGTGTAGACAGGCA	2.16	1.80	-
hsa-miR-548e-5p	hsa-miR-548e-5p	CAAAAGCAATCGCGGTTTTTGC	2.15	16.65	7.74
hsa-miR-550a-3p_R-1	hsa-miR-550a-3p	TGTCTTACTCCCTCAGGCACAT	1.91	0.26	0.14
hsa-miR-590-3p	hsa-miR-590-3p	TAATTTTATGTATAAGCTAGT	1.87	5.85	3.12
hsa-miR-1260b_1ss9AG	hsa-miR-1260b	ATCCCACCACTGCCACCAT	1.85	0.31	0.16
hsa-miR-99b-5p_R-1	hsa-miR-99b-5p	CACCCGTAGAACCGACCTTGCG	1.84	0.13	0.07
hsa-miR-424-5p_R-1	hsa-miR-424-5p	CAGCAGCAATTCATGTTTTGAA	1.82	4.24	2.33
hsa-miR-450b-5p_R-1	hsa-miR-450b-5p	TTTTGCAATATGTTTCCTGAATA	1.76	1.56	-
hsa-miR-199b-5p_R-1	hsa-miR-199b-5p	CCCAGTGTTTAGACTATCTGTTC	1.71	7.97	4.67
hsa-miR-151a-5p	hsa-miR-151a-5p	TCGAGGAGCTCACAGTCTAGT	1.68	0.19	0.11

hsa-miR-106b-5p_R-1	hsa-miR-106b-5p	TAAAGTGCTGACAGTGCAGAT	1.67	1.73	-
hsa-miR-589-5p_R-1	hsa-miR-589-5p	TGAGAACCACGTCTGCTCTGAG	1.64	1.99	-
hsa-miR-17-3p_R-3	hsa-miR-17-3p	ACTGCAGTGAAGGCACTTGTAG	1.59	2.91	1.83
hsa-miR-29c-5p	hsa-miR-29c-5p	TGACCGATTTCTCCTGGTGTTC	1.59	3.23	2.03
hsa-miR-4433b-5p_R+1	hsa-miR-4433b-5p	ATGTCCCACCCCCACTCCTGT	1.59	0.24	0.15
hsa-miR-98-3p_1ss22CT	hsa-miR-98-3p	CTATACA ACTTACTACTTTCCC	1.58	6.14	3.90
hsa-miR-106a-5p_R-2	hsa-miR-106a-5p	AAAAGTGCTTACAGTGCAGGTAG	1.55	3.01	1.94
hsa-miR-194-5p	hsa-miR-194-5p	TGTAACAGCAACTCCATGTGGA	1.54	1.83	2.60
hsa-miR-199a-3p	hsa-miR-199a-3p	ACAGTAGTCTGCACATTGGTTA	1.52	1.74	7.67
Decreased in MDR-TB/DS-TB					
hsa-miR-34c-5p	hsa-miR-34c-5p	AGGCAGTGTAGTTAGCTGATTGC	0.30	0.02	0.05
hsa-miR-129-5p	hsa-miR-129-5p	CTTTTTGCGGTCTGGGCTTGC	0.33	0.12	0.37
hsa-miR-122-5p_R-1	hsa-miR-122-5p	TGGAGTGTGACAATGGTGTTTG	0.39	8.45	21.79
hsa-miR-1468-5p_R+1_1ss17CT	hsa-miR-1468-5p	CTCCGTTTGCCTGTTTCGCTG	0.41	9.93	24.27
hsa-miR-10a-5p_R-1_1ss12TA	hsa-miR-10a-5p	TACCCTGTAGATCCGAATTTGTG	0.41	0.21	0.51
hsa-miR-452-5p_1ss22AT	hsa-miR-452-5p	AACTGTTTGCAGAGGAAACTGA	0.47	3.83	8.13
hsa-miR-150-5p	hsa-miR-150-5p	TCTCCAACCCTTGTACCAGTG	0.48	0.45	-
hsa-miR-331-3p_R-1	hsa-miR-331-3p	GCCCCTGGGCCTATCCTAGAA	0.48	1.67	3.50
hsa-miR-320b_R-2	hsa-miR-320b	AAAAGCTGGGTTGAGAGGGCAA	0.53	2.88	5.42
hsa-miR-205-5p	hsa-miR-205-5p	TCCTTCATTCCACCGGAGTCTG	0.55	1.98	3.60
hsa-miR-125b-2-3p_L-2	hsa-miR-125b-2-3p	TCACAAGTCAGGCTCTTGGGAC	0.55	1.56	2.84
hsa-miR-122-3p_R-1	hsa-miR-122-3p	AACGCCATTATCACACTAAATA	0.56	10.89	19.44
hsa-miR-215-5p_L-1_1ss20AC	hsa-miR-215-5p	ATGACCTATGAATTGACAGAC	0.57	2.90	5.09
hsa-miR-381-3p	hsa-miR-381-3p	TATACAAGGGCAAGCTCTCTGT	0.59	0.44	-

miR name: the first known miR name in a cluster, a underscore, and a matching annotation; miR ID: representative known miR ID; miR

sequence: representative known miR sequence; MDR-TB: multidrug-resistant tuberculosis; DS-TB: drug-sensitive tuberculosis; -: ratio between 0.60 and 1.50.