

Supplementary Table S1. MicroRNA 17-92a cluster is involved in hair follicle related gene ontology (GO) terms

Go term	ID	Rank	microRNA	# genes	Target genes	Method	P value
Hair cycle process	GO: 00224405	6	miR-20a-3p	2	SOX18	HITS-CLIP	1.21E-07
					CTNNB1	HITS-CLIP	
		9	miR-17-3P	2	ERCC2	HITS-CLIP	1.21E-07
					CTNNB1	Multiple	
		132	miR-92a-3p	6	DICER1	Multiple	5.24E-04
					CELSR1		
					FZD6	HITS-CLIP	
					TP63		
					VANGL2		
					AARS	Multiple	
Hair follicle development	GO: 0001942	43	miR-92a-3p	6	DICER1	Multiple	2.86E-11
					CELSR1		
					FZD6	HITS-CLIP	
					TP63		
					VANGL2		
					AARS	Multiple	
		60	miR-19a-3p	6	DICER1	Multiple	2.86E-11
					CELSR1	HITS-CLIP	
					FZD6	HITS-CLIP	
					INHBA	PAR-CLIP	
					EDARADD	Multiple	
					DKK1	HITS-CLIP	
		127	miR-19b-3p	4	DICER1	Multiple	3.25E-07
					CELSR1	HITS-CLIP	
					INHBA	PAR-CLIP	
					EDARADD	Multiple	
		117	miR-20a-5p	4	DICER1	HITS-CLIP	3.25E-07
					ACVR1B	Multiple	
					FZD6	PAR-CLIP	
					CD109	HITS-CLIP	
		154	miR-18a-3p	3	DICER1	Multiple	2.49E-05
					FZD3	PAR-CLIP	
					EDARADD		
		174	miR-17-5p	3	DICER1	Multiple	2.49E-05
					FZD6	Multiple	
					TFAP2C	Multiple	
Hair follicle morphogenesis	GO: 0031069	11	miR-17-3p	6	IGFBP5	HITS-CLIP	2.98E-13
					DICER1	Multiple	
					BCL2	PAR-CLIP	
					NOTCH1	HITS-CLIP	
					CTNNB1	Multiple	
					CDC42	HITS-CLIP	
		48	miR-17-5p	5	IGFBP5	PAR-CLIP	
					DICER1	Multiple	
					RUNX1	Multiple	
					BCL2	Multiple	
					RUNX3	Multiple	

		63	miR-92a-3p	4	IGFBP5	HITS-CLIP	1.60E-08
					DICER1	Multiple	
					TP63		
					CTNNB1	Multiple	
		202	miR-18a	2	DICER1	Multiple	3.19E-04
					RUNX1	Multiple	
		269	miR-19a-3p	2	DICER1	Multiple	3.19E-04
					FGF7	HITS-CLIP	
		372	miR-18a-3p	1	DICER1	Multiple	2.54E-02
		506	miR-92a-1-5p	1	DICER1	PAR-CLIP	2.54E-02
Hair follicle cell proliferation	GO: 0071335	54	miR-92a-1-5p	1	DICER1	Multiple	3.28E-05
		95	miR-19b-3p	1	DICER1	Multiple	3.28E-05
		98	miR-18a-3p	1	DICER1	Multiple	3.28E-05
		120	miR-19a-3p	1	DICER1	Multiple	3.28E-05
		148	miR-17-5p	1	DICER1	Multiple	3.28E-05
		206	miR-17-3p	1	DICER1	Multiple	3.28E-05
		208	miR-20a-5p	1	DICER1	Multiple	3.28E-05
Hair follicle placode formation	GO: 0060789	1	miR-17-3p	5	GNAS	Multiple	2.99E-18
					HDAC1	PAR-CLIP	
					CTNNB1	Multiple	
					HDAC2	HITS-CLIP	
					CDC42	HITS-CLIP	
		6	miR-92a-3p	3	HDAC1	PAR-CLIP	1.22E-10
					CTNNB1	Multiple	
					HDAC2	PAR-CLIP	
		139	miR-18a-3p	1			9.91E-04
		225	miR-17-5p	1			9.91E-04
		228	20a-3p	1	CTNNB1	HITS-CLIP	9.91E-04
Hair follicle maturation	GO: 0048820	1	miR-17-5p	2	ERCC2	HITS-CLIP	1.89E-09
					RBPJ	Multiple	
		14	miR-92a-3p	1	RBPJ	Multiple	7.37E-05
		31	miR-92a-1-5p	1	RBPJ	Multiple	7.37E-05
		33	miR-18a-3p	1	RBPJ	HITS-CLIP	7.37E-05
		68	miR-18a-5p	1	RBPJ	HITS-CLIP	7.37E-05
		117	miR-19b-3p	1	RBPJ	HITS-CLIP	7.37E-05
		126	miR-17-3p	1	ERCC2	HITS-CLIP	7.37E-05
		128	miR-20a-5p	1	RBPJ	HITS-CLIP	7.37E-05
Hair cell differentiation	GO: 0035315	13	miR-17-3p	2	ERCC2	HITS-CLIP	1.55E-07
					CTNNB1	Multiple	
		23	miR-19b-1-5p	1	ERCC3	Multiple	5.92E-04
		36	miR-92a-3p	1	ERCC3	Multiple	5.92E-04
		100	miR-17-5p	1	ERCC2	Multiple	5.92E-04
		122	miR-19a-5p	1	ERCC3	PAR-CLIP	5.92E-04
Hair cycle	GO: 0042633	25	miR-92a-3p	1	SNRPE	HITS-CLIP	2.23E-03
		87	miR-17-5p	1	PPP1R13L	HITS-CLIP	2.23E-03

Supplementary Table S2. Functional enrichment analysis of the microRNAs 17-92a cluster

KEGG pathway	p-value	#genes	#miRNAs
Proteoglycans in cancer	1.0e-325	97	6
TGF-beta signaling pathway	4.55E-15	43	7
Chronic myeloid leukemia	7.54E-13	46	6
Hepatitis B	7.83E-13	68	4
Glioma	1.22E-11	32	4
Hippo signaling pathway	1.95E-11	72	7
Adherens junction	4.48E-11	38	5
Viral carcinogenesis	1.08E-10	75	5
Pathways in cancer	1.09E-10	139	4
Cell cycle	7.91E-10	52	6
FoxO signaling pathway	3.96E-09	63	4
Thyroid hormone signaling pathway	6.66E-09	63	4
Bladder cancer	1.37E-08	27	6
p53 signaling pathway	1.79E-08	37	5
Bacterial invasion of epithelial cells	2.03E-08	39	4
ECM-receptor interaction	2.26E-08	18	2
Fatty acid biosynthesis	2.95E-08	1	1
Prion diseases	3.80E-08	6	1
Colorectal cancer	5.34E-07	35	4
Prostate cancer	1.42E-06	41	3
Focal adhesion	2.19E-06	90	5
Regulation of actin cytoskeleton	3.13E-06	86	5
Prolactin signaling pathway	3.95E-06	34	3
Pancreatic cancer	3.32E-05	31	3
Lysine degradation	4.76E-05	18	5
Signaling pathways regulating pluripotency of stem cells	4.99E-05	62	4
Protein processing in endoplasmic reticulum	5.92E-05	55	2
Sphingolipid signaling pathway	7.53E-05	49	3
RNA transport	0.000102	58	3
Melanoma	0.000134	25	3
RNA degradation	0.000135	30	5
mTOR signaling pathway	0.000213	28	3
Transcriptional misregulation in cancer	0.000319	55	3
mRNA surveillance pathway	0.00034	36	2
Sphingolipid metabolism	0.000607	8	2
Non-small cell lung cancer	0.000611	26	3
Fatty acid metabolism	0.002094	9	3
Insulin signaling pathway	0.002313	52	3
Renal cell carcinoma	0.002908	26	2
Estrogen signaling pathway	0.004091	40	3
Ubiquitin mediated proteolysis	0.004364	46	3
Endometrial cancer	0.005013	24	2
Circadian rhythm	0.005096	15	3
Thyroid cancer	0.006483	16	4
Small cell lung cancer	0.007543	26	2
Shigellosis	0.008276	19	1

Fatty acid elongation	0.008908	2	1
Central carbon metabolism in cancer	0.012451	23	2
Axon guidance	0.01594	42	3
Oocyte meiosis	0.016976	32	2
Adrenergic signaling in cardiomyocytes	0.017312	44	3
Neurotrophin signaling pathway	0.020944	38	2
Long-term depression	0.024704	19	3
Endocytosis	0.031641	62	3
Acute myeloid leukemia	0.042271	23	3
PI3K-Akt signaling pathway	0.046219	96	3

GO Category	p-value	#genes	#miRNAs
transforming growth factor beta receptor signaling pathway	0	80	4
cellular component disassembly involved in execution phase of apoptosis	0	30	5
platelet activation	0	70	5
innate immune response	0	199	5
phosphatidylinositol-mediated signaling	0	46	5
positive regulation of protein insertion into mitochondrial membrane	0	21	5
G2/M transition of mitotic cell cycle	0	65	6
Fc-gamma receptor signaling pathway involved in phagocytosis	0	41	6
immune system process	0	436	7
transcription initiation from RNA polymerase II promoter	0	92	7
fibroblast growth factor receptor signaling pathway	0	76	7
protein complex assembly	0	259	8
blood coagulation	0	174	8
intrinsic apoptotic signaling pathway	0	36	8
DNA metabolic process	0	282	9
transcription, DNA-templated	0	750	9
epidermal growth factor receptor signaling pathway	0	85	9
cellular component assembly	0	445	9
mitotic cell cycle	0	206	10
cellular protein modification process	0	925	10
response to stress	0	768	10
biological_process	0	4652	10
cell death	0	366	10
catabolic process	0	742	10
biosynthetic process	0	1441	10
gene expression	0	343	10
viral process	0	268	10
RNA metabolic process	0	122	10
mRNA metabolic process	0	114	10
cellular nitrogen compound metabolic process	0	1784	10
nucleobase-containing compound catabolic process	0	371	10
Fc-epsilon receptor signaling pathway	0	80	10
cellular protein metabolic process	0	214	10
small molecule metabolic process	0	799	10
symbiosis, encompassing mutualism through parasitism	0	296	10
neurotrophin TRK receptor signaling pathway	0	134	10
membrane organization	0	261	10
macromolecular complex assembly	0	330	10
cellular lipid metabolic process	1.11E-16	65	8
cell cycle	7.77E-16	282	6
toll-like receptor 10 signaling pathway	6.77E-15	31	6
mRNA processing	1.41E-14	183	9
viral life cycle	1.74E-13	50	8
nucleocytoplasmic transport	3.92E-13	113	5
toll-like receptor TLR1:TLR2 signaling pathway	6.69E-13	30	6
toll-like receptor TLR6:TLR2 signaling pathway	6.69E-13	30	6

G1/S transition of mitotic cell cycle	9.76E-13	79	7
insulin receptor signaling pathway	1.16E-12	59	4
chromatin organization	2.01E-12	56	6
toll-like receptor 5 signaling pathway	2.73E-12	31	6
TRIF-dependent toll-like receptor signaling pathway	4.73E-12	34	6
activation of signaling protein activity involved in unfolded protein r	8.98E-12	32	5
toll-like receptor 9 signaling pathway	1.36E-11	32	6
nuclear-transcribed mRNA catabolic process, deadenylation-depend	1.66E-11	27	6
DNA damage response, signal transduction by p53 class mediator re	1.79E-11	38	6
apoptotic signaling pathway	1.93E-11	53	5
mitotic nuclear envelope disassembly	3.15E-11	20	5
platelet degranulation	8.75E-11	25	4
termination of RNA polymerase II transcription	3.09E-10	25	6
regulation of transcription from RNA polymerase II promoter in resp	3.24E-10	15	4
MyD88-independent toll-like receptor signaling pathway	5.36E-10	30	5
stress-activated MAPK cascade	6.26E-10	26	4
cytoskeleton organization	1.17E-09	155	4
cell junction organization	1.29E-09	48	3
ribonucleoprotein complex assembly	2.88E-09	43	4
in utero embryonic development	5.49E-09	108	4
RNA splicing	1.31E-08	101	6
toll-like receptor 3 signaling pathway	2.98E-08	28	4
toll-like receptor 2 signaling pathway	3.54E-08	26	4
toll-like receptor 4 signaling pathway	3.55E-08	38	6
apoptotic process	3.77E-08	195	3
toll-like receptor signaling pathway	4.15E-08	35	4
vesicle-mediated transport	6.81E-08	210	3
cellular component movement	7.09E-08	36	4
negative regulation of transcription from RNA polymerase II promot	1.11E-07	232	4
cell cycle arrest	1.18E-07	43	2
NLS-bearing protein import into nucleus	2.32E-07	11	7
transcription from RNA polymerase II promoter	4.43E-07	147	4
regulation of ubiquitin-protein ligase activity involved in mitotic cel	4.56E-07	31	5
protein polyubiquitination	4.81E-07	55	4
intracellular transport of virus	5.05E-07	11	5
mRNA 3'-end processing	6.36E-07	20	3
post-translational protein modification	1.03E-06	55	4
positive regulation of ubiquitin-protein ligase activity involved in m	2.02E-06	28	4
hexose transport	3.98E-06	22	6
generation of precursor metabolites and energy	7.36E-06	89	5
protein targeting	1.06E-05	70	4
regulation of glucose transport	1.14E-05	17	5
mRNA splicing, via spliceosome	1.19E-05	65	4
negative regulation of transcription, DNA-templated	1.29E-05	168	3
positive regulation of apoptotic process	1.39E-05	118	3
protein ubiquitination	2.27E-05	123	3
antigen processing and presentation of exogenous peptide antigen v	4.05E-05	37	4
cell proliferation	7.3E-05	135	3
JAK-STAT cascade involved in growth hormone signaling pathway	7.36E-05	13	3
nuclear-transcribed mRNA poly(A) tail shortening	8.5E-05	15	4

androgen receptor signaling pathway	8.68E-05	25	4
endoplasmic reticulum unfolded protein response	9.74E-05	32	3
protein N-linked glycosylation via asparagine	0.000111	28	3
axon guidance	0.000131	106	3
positive regulation of transcription, DNA-templated	0.000179	214	4
MyD88-dependent toll-like receptor signaling pathway	0.000203	26	3
nucleotide-binding domain, leucine rich repeat containing receptor	0.000395	14	3
cell motility	0.000411	73	2
cell junction assembly	0.000486	20	2
regulation of defense response to virus by virus	0.00053	13	3
negative regulation of cell proliferation	0.000695	112	2
regulation of cell cycle	0.000855	52	3
regulation of nitric-oxide synthase activity	0.001055	5	2
negative regulation of transforming growth factor beta receptor signaling pathway	0.00129	35	3
positive regulation of nuclear-transcribed mRNA catabolic process, cytoplasmic	0.001311	8	2
anaphase-promoting complex-dependent proteasomal ubiquitin-dependent proteolysis	0.001314	22	2
regulation of cellular amino acid metabolic process	0.001463	16	2
Notch signaling pathway	0.001474	48	3
signal transduction	0.001648	774	2
extracellular matrix organization	0.001679	53	2
post-Golgi vesicle-mediated transport	0.001787	10	2
positive regulation of nuclear-transcribed mRNA poly(A) tail shortening	0.0018	8	4
nitric oxide metabolic process	0.002048	4	2
extracellular matrix disassembly	0.002346	29	3
activation of MAPKK activity	0.00252	27	3
glycerophospholipid biosynthetic process	0.002782	19	3
negative regulation of ubiquitin-protein ligase activity involved in morphogenesis	0.0029	14	2
COPII coating of Golgi vesicle	0.003121	6	2
nucleobase-containing small molecule metabolic process	0.003443	21	2
cellular response to hypoxia	0.003892	35	3
regulation of transcription involved in G1/S transition of mitotic cell cycle	0.004854	9	2
leukocyte migration	0.006869	25	2
nuclear-transcribed mRNA catabolic process, nonsense-mediated decay	0.010482	19	1
inositol phosphate metabolic process	0.012437	13	3
SRP-dependent cotranslational protein targeting to membrane	0.01485	11	2
viral transcription	0.016991	8	2
negative regulation of translation	0.01851	18	2
protein maturation	0.020399	32	2
anatomical structure morphogenesis	0.021381	29	2
stem cell maintenance	0.023488	13	1
positive regulation of viral transcription	0.024556	14	2
negative regulation of apoptotic process	0.025377	73	1
positive regulation of type I interferon production	0.026091	9	1
regulation of small GTPase mediated signal transduction	0.033218	54	3
virion assembly	0.036658	11	2
protein import into nucleus	0.048113	13	1
viral protein processing	0.049742	8	2

Supplementary Table S3. Association of MIR17 rs4284505 genotypes and MIR17 expression with clinical features

Characteristics		AA	AG	GG	<i>p</i> - value	MIR-17 expression	<i>p</i> - value
Number		38	136	74			
Demographic characteristics							
Age, year	≤30 years	17 (44.7)	72 (52.9)	36 (48.6)	<0.001	17.7 (1.16-343)	0.169
	>30 years	21 (55.3)	64 (47.1)	38 (51.4)		58.3 (5.34-1068)	
Sex	Male	35 (92.1)	118 (86.8)	63 (85.1)	0.69	35.8 (2.02-470.4)	0.357
	Female	3 (7.9)	18 (13.2)	11 (14.9)		6.15 (0.05-1906)	
Obesity	Absent	33 (86.8)	127 (93.4)	69 (93.2)	0.44	28.2 (1.68-476.3)	0.60
	Present	5 (13.2)	9 (6.6)	5 (6.8)		127 (11.4-568.9)	
Residence	Port-said	1 (2.6)	7 (5.1)	5 (6.8)	0.07	476.3 (373-2704)	0.052
	Suez	2 (5.3)	10 (7.4)	3 (4.1)		85.9 (15.1-1429)	
	Ismailia	12 (31.6)	42 (30.9)	23 (31.1)		6.9 (0.56-66.2)	
	Cairo	23 (60.5)	77 (56.6)	43 (58.1)		43.5 (1.95-809)	
Occupation	Student	18 (47.4)	62 (45.6)	27 (36.5)	0.005	22.5 (1.57-337.6)	0.553
	Unemployed	19 (50)	56 (41.2)	33 (44.6)		27.9 (2.02-578.1)	
	Employed	1 (2.6)	18 (13.2)	14 (18.9)		66.8 (3.1-2512)	
Family history	Alopecia	21 (55.3)	63 (46.3)	24 (32.4)	0.044	32.4 (1.68-1321)	0.534
	Autoimmune	20 (52.6)	60 (44.1)	25 (33.8)	0.13	85.9 (1.68-1370)	0.304
Prior episode of alopecia	No	8 (21.1)	40 (29.4)	35 (47.3)	0.007	36 (3.2-1784)	0.364
	Yes	30 (78.9)	96 (70.6)	39 (52.7)		22.6 (1.7-452.7)	
Duration of disease	≤ 12 months	32 (84.2)	113 (83.1)	65 (87.8)	0.65	29.4 (1.7-494.8)	0.801
	>12 months	6 (15.8)	23 (16.9)	9 (12.2)		39.9 (3.5-657.7)	
Age at onset	≤ 20 years	35 (92.1)	127 (93.4)	63 (85.1)	0.13	28.2 (1.8-452.7)	0.471
	>20 years	3 (7.9)	9 (6.6)	11 (14.9)		66.3 (0.4-3239.6)	
Disease characteristics							
Alopecia subtype	Patchy	35 (92.1)	118 (86.8)	56 (75.7)	0.038	13 (1.6-476.3)	0.165
	Others	3 (7.9)	18 (13.2)	18 (24.3)		66.9 (18.7-2299.6)	
Nail changes	Absent	27 (71.1)	89 (65.4)	47 (63.5)	0.72	35.7 (2.1-532.8)	0.93
	Present	11 (28.9)	47 (34.6)	27 (36.5)		27.8 (1.7-501.5)	
Itching	Absent	31 (81.6)	96 (70.6)	62 (83.8)	0.07	36 (4.3-531.9)	0.070
	Present	7 (18.4)	40 (29.4)	12 (16.2)		8 (0.1-532.8)	
Scalp infection	Absent	28 (73.7)	90 (66.2)	64 (86.5)	0.006	36 (1.7-452.7)	0.936

Atopy	Present	10 (26.3)	46 (33.8)	10 (13.5)		10.7 (1.9-810)	
	Absent	34 (89.5)	98 (72.1)	57 (77)	0.08	36 (1.9-810)	0.522
Hypertension	Present	4 (10.5)	38 (27.9)	17 (23)		22.6 (1.3-228.4)	
	Absent	30 (78.9)	127 (93.4)	70 (94.6)	0.010	27.8 (1.7-452.7)	0.262
Emotional stress	Present	8 (21.1)	9 (6.6)	4 (5.4)		123 (1.7-2234.1)	
	Absent	8 (21.1)	38 (27.9)	14 (18.9)	0.30	35.8 (1.9-1224.8)	0.580
Concomitant autoimmune disease	Present	30 (78.9)	98 (72.1)	60 (81.1)		29.4 (1.7-458.6)	
	Absent	22 (57.9)	98 (72.1)	53 (71.6)	0.22	9.7 (0.6-289.8)	0.049
Responded to treatment	Present	16 (42.1)	38 (27.9)	21 (28.4)		112.6 (4.1-1189.6)	
	No	5 (13.2)	44 (32.4)	16 (21.6)	0.033	66.9 (1.7-1465.8)	0.189
	Yes	33 (86.8)	92 (67.6)	58 (78.4)		11 (1.7-452.7)	

Data are shown as number (percentage) or as medians (upper-lower limits). Chi-square and Fisher's Exact tests were used for categorical variables, and Mann-Whitney U test was applied for quantitative variables. Bold values indicate statistical significance at p -value < 0.05.

Supplementary Table S4. Functional impact of MIR17HG polymorphism on regulatory regions.

Consequence type	Transcription factors	Motif position	Motif score change
TF binding site	FOXO1::ELF1, FOXJ2::ELF1, FOXJ3::ELF1	13 (out of 15)	Less like consensus sequence
TF binding site	ELF1, ELF4, ELF5, ELF3, ELF2, ETV7	3 (out of 12)	More like consensus sequence
TF binding site	ETV2::DLX3, HOXB2::ELF1, HOXB2::ELK3	9 (out of 18)	Less like consensus sequence
TF binding site	E2F1::ELK1	14 (out of 22)	Less like consensus sequence
TF binding site	ETV2::PAX5, ELK1::PAX1, ELK1::PAX5, ELK1::PAX9	1 (out of 20)	Less like consensus sequence
TF binding site	HOXB2::ELF1	8 (out of 17)	Less like consensus sequence
TF binding site	ETV2::HOXA2, FLI1::DLX2, HOXB2::ELF1, HOXB2::ELK3, ETV2::DRGX, ELK1::HOXA1, FLI1::DRGX, ETV5::DRGX, ETV5::HOXA2, HOXB2::ELK1	1 (out of 14)	Less like consensus sequence
TF binding site	HOXB2::ELF1	13 (out of 22)	More like consensus sequence
TF binding site	HOXA3::PAX5	14 (out of 20)	Less like consensus sequence

Motif position is the position of the variant within the motif, in base pair coordinates, from the start of the motif.

The motif scores are between 0 and 1. It indicates how strong a binding site it is for the transcription factor, with 1 the best and 0 the worst. The score change indicates whether the score increases or decreases and by how much as a result of the SNP. It indicates whether the SNP changes a base which is vital to the motif function or not.

Data source: ensembl.org

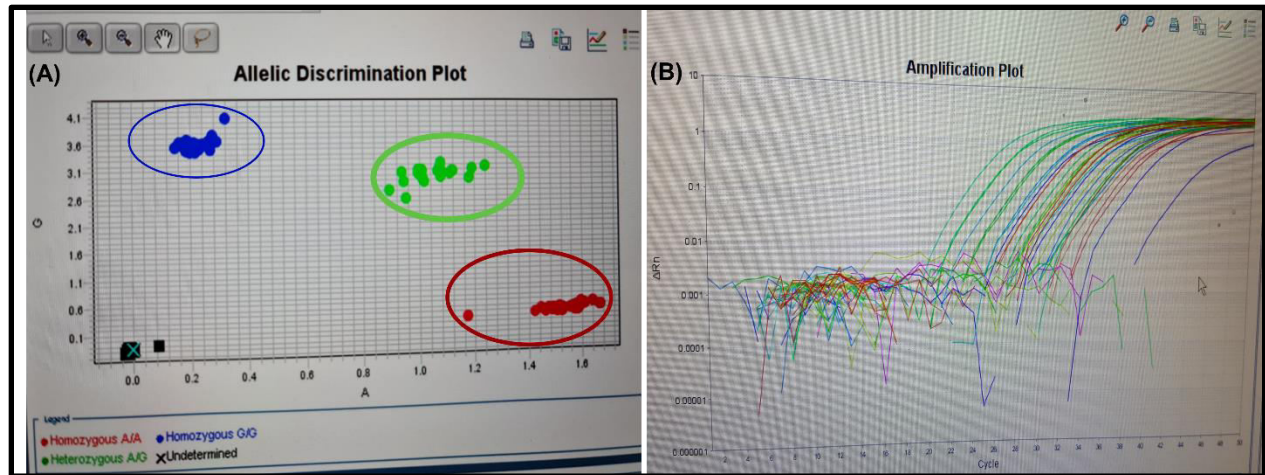


Figure S1. (A) Allele discrimination plot (single nucleotide polymorphism assay, rs4284505) using TaqMan genotyping polymerase chain reaction (StepOne Real-Time; Applied Biosystems, Thermo Fisher Scientific, Foster City, CA, USA). Alleles as homozygous A/A (lower right red cluster), heterozygous A/G (middle green cluster) and homozygous G/G (upper left blue cluster) were retrieved using allele calling software. The negative control samples were represented as black squares (x: undetermined) in the lower left corner of the plot. (B) Amplification plot for the quantification of MIR17HG by the Real-Time TaqMan® PCR assay shows log of change in gene expression plotted vs. PCR cycle number. This plot from the AB 7500HT instrument (Applied Biosystems, USA).