

Figure S1. CD19⁺ B cell proportion is significantly different ($P=0.012$) among DICERAA (mean $\pm$ SD, 12.17 ± 5.48), AG (mean $\pm$ SD, 9.69 ± 3.00) and GG (mean $\pm$ SD, 13.62 ± 5.01). DICER, dicer 1, ribonuclease III.

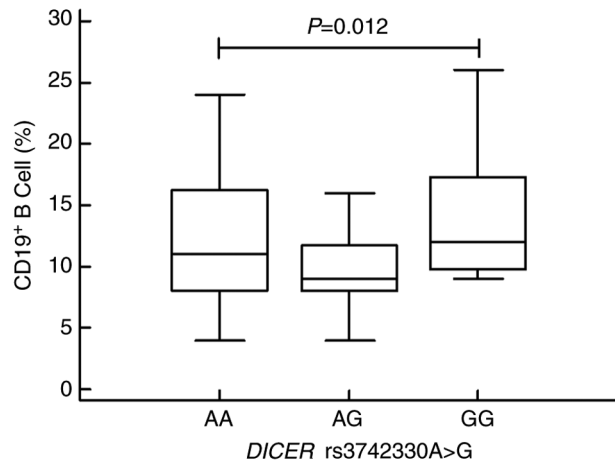


Figure S2. Blood urea nitrogen levels are significantly different ($P=0.037$) among XPO5AA (mean $\pm$ SD, 10.10 ± 2.89), AC (mean $\pm$ SD, 10.62 ± 2.12) and CC (mean $\pm$ SD, 5.10 ± 0.71). XPO5, exportin 5.

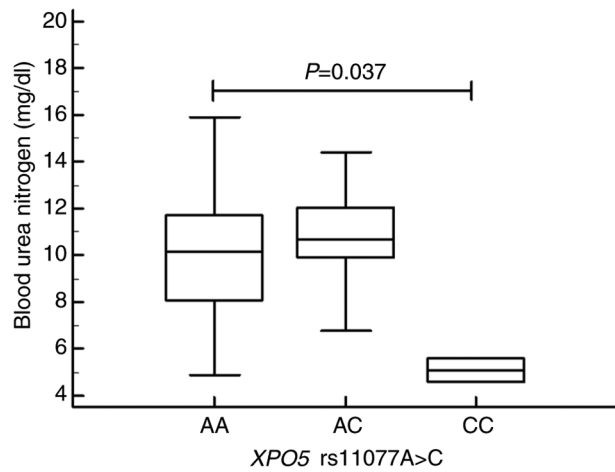


Table S1. Genotype frequency of miRNA machinery gene polymorphisms between subgroups of RIF patients and controls.

Genotypes	Controls, n (%) (n=210)	RIF ≥3, n (%) (n=107)	AOR (95% CI) ^a	P-value	RIF ≥4, n (%) (n=75)	AOR (95% CI) ^a	P-value
<i>DICER</i> rs3742330A>G							
AA	65 (31.0)	35 (32.7)	1.000 (reference)		29 (38.7)	1.000 (reference)	
AG	114 (54.3)	54 (50.5)	0.885 (0.524-1.495)	0.648	33 (44.0)	0.651 (0.362-1.171)	0.152
GG	31 (14.8)	18 (16.8)	1.091 (0.533-2.235)	0.811	13 (17.3)	0.960 (0.436-2.114)	0.920
Dominant (AA vs AG+GG)							
Recessive (AA+AG vs. GG)							
<i>DROSHA</i> rs10719T>C							
TT	95 (45.2)	63 (58.9)	1.000 (reference)		43 (57.3)	1.000 (reference)	
TC	99 (47.1)	36 (33.6)	0.547 (0.333-0.900)	0.018	27 (36.0)	0.601 (0.344-1.050)	0.074
CC	16 (7.6)	8 (7.5)	0.767 (0.309-1.902)	0.567	5 (6.7)	0.696 (0.239-2.025)	0.506
Dominant (TT vs TC+CC)							
Recessive (TT+TC vs. CC)							
<i>RAN3'UTR</i> rs14035C>T							
CC	112 (53.3)	67 (62.6)	1.000 (reference)		48 (64.0)	1.000 (reference)	
CT	89 (42.4)	35 (32.7)	0.637 (0.386-1.049)	0.077	22 (29.3)	0.551 (0.307-0.990)	0.046
TT	9 (4.3)	5 (4.7)	0.867 (0.268-2.810)	0.813	5 (6.7)	1.212 (0.373-3.935)	0.749
Dominant (CC vs CT+TT)							
Recessive (CC+CT vs. TT)							
<i>XPO5</i> rs11077A>C							
AA	176 (83.8)	87 (81.3)	1.000 (reference)		61 (81.3)	1.000 (reference)	
AC	32 (15.2)	18 (16.8)	1.112 (0.589-2.098)	0.744	13 (17.3)	1.143 (0.561-2.328)	0.713
CC	2 (1.0)	2 (1.9)	1.672 (0.215-12.987)	0.623	1 (1.3)	1.048 (0.081-13.640)	0.972
Dominant (AA vs AC+CC)							
Recessive (AA+AC vs. CC)							
<i>DGCR8</i> rs417309G>A							
GG	197 (93.8)	99 (92.5)	1.000 (reference)		67 (89.3)	1.000 (reference)	
GA	13 (6.2)	8 (7.5)	1.220 (0.489-3.041)	0.670	8 (10.7)	1.803 (0.716-4.541)	0.211
AA	0 (0.0)	0 (0.0)	NA	NA	0 (0.0)	NA	NA
Dominant (GG vs GA+AA)							
Recessive (GG+GA vs. AA)							
			1.220 (0.489-3.041)	0.670		1.803 (0.716-4.541)	0.211
			NA	NA		NA	NA

^a Adjusted by age. RIF, recurrent implantation failure; AOR, adjusted odds ratio; HWE, Hardy-Weinberg equilibrium; 95% CI, 95% confidence interval; NA, not applicable; FDR, false discovery rate.

Table SII. Clinical variables in recurrent implantation failure patients stratified by the miRNA machinery gene polymorphisms status.

Genotypes	aPTT (sec)		Total cholesterol (mg/dl)		Creatinine (mg/dl)		BUN (mg/dl)		Uric Acid (mg/dl)		CD8 ⁺ suppressor T cell (%)		CD19 ⁺ B cell (%)	
	Mean ± SD	P-value ^a	Mean ± SD	P-value ^a	Mean ± SD	P-value ^a	Mean ± SD	P-value ^a	Mean ± SD	P-value ^a	Mean ± SD	P-value ^a	Mean ± SD	P-value ^a
<i>DICER</i>														
rs3742330A>G														
AA	30.75±3.60	0.440	185.39±31.94	0.556	0.80±0.08	0.103	10.42±2.89	0.762	3.51±0.92	0.064	27.03±7.71	0.234	12.17±5.48	0.012 ^b
AG	31.47±3.43		199.42±53.93		0.75±0.10		9.91±3.13		4.14±0.86		30.06±8.00		9.69±3.00	
GG	29.98±3.06		190.39±29.14		0.82±0.10		9.72±2.34		3.91±0.76		30.00±7.44		13.62±5.01	
A allele	31.05±3.50	0.676 ^c	191.27±42.54	0.652 ^c	0.78±0.09	0.732 ^c	10.21±2.96	0.457 ^c	3.82±1.00	0.146 ^c	28.45±7.92	0.175 ^c	11.01±4.62	0.995 ^c
G allele	30.78±3.29		194.90±42.97		0.78±0.10		9.81±2.72		4.08±0.88		30.04±7.72		11.01±4.17	
<i>DROSHA</i>														
rs10719T>C														
TT	30.90±3.31	0.531	188.36±41.79	0.282 ^b	0.78±0.10	0.025	10.32±3.08	0.119	3.89±0.90	0.992	29.44±7.88	0.763	11.37±4.79	0.276
TC	30.48±3.21		193.27±26.53		0.74±0.07		8.88±2.43		3.86±0.94		29.06±8.09		10.06±4.13	
CC	32.21±4.52		219.50±72.76		0.87±0.10		11.35±1.49		3.88±0.81		27.33±7.78		12.33±2.78	
T allele	30.82±3.26	0.533 ^c	189.21±39.24	0.652 ^c	0.77±0.09	0.290 ^c	10.06±2.99	0.841 ^c	3.89±0.90	0.369 ^c	29.35±7.87	0.484 ^c	11.06±4.64	0.808 ^c
C allele	31.26±3.80		204.93±50.91		0.80±0.10		9.94±2.38		4.08±1.12		28.44±7.87		10.88±3.81	
<i>RAN3'UTR</i>														
rs14035C>T														
CC	31.13±3.58	0.472	200.80±47.03	0.122	0.77±0.09	0.738	9.77±3.01	0.564	3.99±0.88	0.201	28.05±7.27	0.050	10.77±3.78	0.741
CT	30.09±3.12		175.27±26.85		0.79±0.12		10.69±1.98		3.55±0.84		30.06±8.59		11.49±5.50	
TT	32.30±1.87		179.00±17.78		0.80±0.10		10.30±4.89		4.27±1.05		38.67±3.06		10.33±4.04	
C allele	30.98±3.50	0.759 ^c	196.68±45.01	0.048 ^c	0.78±0.09	0.413 ^c	9.91±2.87	0.331 ^c	3.97±0.96	0.337 ^c	28.50±7.58	0.041 ^c	10.93±4.20	0.639 ^c
T allele	30.72±2.92		176.33±23.89		0.80±0.11		10.58±2.75		3.75±0.91		31.39±8.55		11.31±5.23	
<i>XPO5</i>														
rs11077A>C														
AA	30.25±3.07	0.009	195.27±45.30	0.159	0.78±0.10	0.147	10.10±2.89	0.037	3.85±0.94	0.469	29.14±8.03	0.975	10.74±4.39	0.257
AC	33.26±3.84		176.09±26.84		0.79±0.09		10.62±2.12		3.87±0.68		28.77±7.62		12.85±4.79	
CC	34.25±1.06		234.00±16.97		0.65±0.07		5.10±0.71		4.65±0.50		30.00±7.07		9.50±0.71	
A allele	30.56±3.26	0.001 ^c	193.14±43.71	0.892 ^c	0.78±0.09	0.256 ^c	10.16±2.80	0.200 ^c	3.91±0.98	0.524 ^c	29.11±7.95	0.979 ^c	10.91±4.43	0.307 ^c
C allele	33.53±3.30		191.53±35.47		0.75±0.11		9.15±3.11		4.08±0.70		29.06±7.08		12.06±4.41	
<i>DGCR8</i>														
rs417309G>A														
GG	31.07±3.41	0.356	192.20±43.66	0.709	0.78±0.10	0.730	9.95±2.94	0.540	3.85±0.88	0.414	28.81±7.51	0.267	10.89±4.36	0.437
GA	29.70±3.53		199.17±37.06		0.77±0.08		10.72±2.05		4.17±0.96		31.89±10.91		12.11±5.23	
AA	-		-		-		-		-		-		-	
G allele	31.00±3.39	0.364 ^c	192.58±42.99	0.714 ^c	0.78±0.10	0.734 ^c	9.99±2.89	0.547 ^c	3.92±0.95	0.539 ^c	28.97±7.69	0.278 ^c	10.96±4.39	0.446 ^c
A allele	29.70±3.53		199.17±37.06		0.77±0.08		10.72±2.05		4.17±0.96		31.89±10.91		12.11±5.23	

^aCalculated using the Turkey-Kramer test of ANOVA. ^bCalculated using the Kruskal-Wallis test. ^cCalculated using the ANOVA. ANOVA, analysis of variance; aPTT, activated partial thromboplastin time; BUN, blood urea nitrogen; SD, standard deviation.

Table SIII. Statistical power to detect various genetic associations in the present case-control study.

Characteristics	Table	AOR (95% CI)	Statistical power, %
<i>DROSHA</i> rs10719TC	Table II	0.550 (0.339-0.893)	65.3
<i>DROSHA</i> rs10719 Dominant model	Table II	0.620 (0.394-0.976)	50.8
<i>RAN3'UTR</i> rs14035CT	Table II	0.590 (0.363-0.958)	51.8
<i>RAN3'UTR</i> rs14035 Dominant model	Table II	0.616 (0.386-0.982)	50.6
<i>DROSHA</i> rs10719TC	Table SI	0.547 (0.333-0.900)	65.2
<i>DROSHA</i> rs10719 Dominant model	Table SI	0.577 (0.360-0.925)	61.2
<i>RAN3'UTR</i> rs14035CT	Table SI	0.551 (0.307-0.990)	37.4

AOR, adjust odds ratio; 95% CI, 95% confidence interval.

Table SIV. Statistical power to detect various genetic associations in the present case-control study.

Characteristics	Table	OR (95% CI)	Statistical power (%)
<i>DICER1</i> A>G/ <i>DROSHA</i> T>C/ <i>RAN</i> 3'UTR C>T/ <i>XPO5</i> A>C/ <i>DGCR8</i> G>A			
A-T-C-C-G	Table III	0.321 (0.116-0.888)	62.7
A-C-T-A-G	Table III	0.208 (0.070-0.618)	90.3
G-T-C-A-G	Table III	0.616 (0.381-0.998)	48.0
G-T-C-C-G	Table III	28.290 (1.634-490.000)	99.2
G-T-T-A-G	Table III	0.496 (0.269-0.913)	61.0
G-C-T-A-G	Table III	17.510 (0.972-315.500)	85.8
<i>DICER1</i> A>G/ <i>DROSHA</i> T>C/ <i>RAN</i> 3'UTR C>T/ <i>XPO5</i> A>C			
A-T-C-C	Table III	0.361 (0.148-0.879)	62.7
A-C-T-A	Table III	0.165 (0.056-0.487)	97.7
G-T-C-A	Table III	0.544 (0.340-0.871)	71.6
G-T-C-C	Table III	25.970 (1.499-450.000)	99.2
G-T-T-A	Table III	0.511 (0.279-0.938)	57.2
G-C-T-A	Table III	8.667 (1.045-71.880)	63.0
<i>DICER1</i> A>G/ <i>DROSHA</i> T>C/ <i>RAN</i> 3'UTR C>T/ <i>DGCR8</i> G>A			
A-C-T-G	Table III	0.302 (0.121-0.756)	78.5
G-C-T-G	Table III	16.590 (0.906-304.100)	74.3
<i>DICER1</i> A>G/ <i>RAN</i> 3'UTR C>T/ <i>XPO5</i> A>C/ <i>DGCR8</i> G>A			
G-C-C-G	Table III	3.434 (1.160-10.160)	59.6
<i>DICER1</i> A>G/ <i>DROSHA</i> T>C/ <i>RAN</i> 3'UTR C>T			
A-C-T	Table III	0.255 (0.103-0.633)	91.0
G-C-T	Table III	21.630 (1.219-383.800)	92.6
<i>DICER1</i> A>G/ <i>DROSHA</i> T>C/ <i>XPO5</i> A>C			
A-T-C	Table III	0.345 (0.144-0.829)	69.5
A-C-A	Table III	0.457 (0.281-0.744)	89.1
G-T-A	Table III	0.553 (0.369-0.827)	81.8
G-T-C	Table III	26.910 (1.557-465.100)	99.2
<i>DICER1</i> A>G/ <i>DROSHA</i> T>C/ <i>DGCR8</i> G>A			
A-C-G	Table III	0.590 (0.369-0.944)	58.3
<i>DICER1</i> A>G/ <i>RAN</i> 3'UTR C>T/ <i>XPO5</i> A>C			
A-T-C	Table III	0.090 (0.005-1.576)	69.2
<i>DICER1</i> A>G/ <i>XPO5</i> A>C/ <i>DGCR8</i> G>A			
G-C-G	Table III	3.672 (1.247-10.810)	64.9
<i>DICER1</i> A>G/ <i>DROSHA</i> T>C			
A-C	Table III	0.549 (0.345-0.875)	71.0
<i>DROSHA</i> T>C/ <i>RAN</i> 3'UTR C>T			
C-T	Table III	0.512 (0.264-0.991)	50.4
<i>RAN</i> 3'UTR C>T/ <i>XPO5</i> A>C			
T-C	Table III	0.089 (0.005-1.539)	54.6

OR, odds ratio; 95% CI, 95% confidence interval.