

ONLINE SUPPLEMENTARY DATA

Supplementary Table 1. The micro-RNA included in the study.

hsa-miRNA	Relevance	Reference
<i>miR-1-3p</i>	Regulate Toll-like receptor 4 (TLR4)	(1)
<i>miR-7-5p</i>		
<i>let-7a-5p</i>	Directly Inhibits Expression of interleukin-6 (IL-6) ^{a b c}	(2)
<i>let-7b-5p</i>		
<i>let-7c</i>	Regulates dendritic cell activation	(3)
<i>let-7d-5p</i>		
<i>let-7e-5p</i>	Down-regulates Toll-like receptor 4 (TLR4) ^{a b}	(4)
<i>let-7i-5p</i>	Regulates TLR4 expression in cholangiocytes ^{a b c}	(5)
<i>miR-10a-5p</i>		(6)
<i>miR-10b-5p</i>		
<i>miR-15a</i>	Down in arthritic synovial tissue, apoptosis regulator. Regulates expression of inhibitor of nuclear factor κ -B kinase subunit α ^{a b c} (<i>CHUK</i>) and IFN- γ (<i>IFNG</i>).	(7-9)
<i>miR-15b-5p</i>	<i>miR-15/16</i> family specifically targets the IFN- γ 3'UTR ^{a b}	(9)
<i>miR-16</i>	Increased in PBMC from RA patients. Regulates expression of <i>CHUK</i> ^{a b c} and <i>IFNG</i> .	(7-12)
<i>miR-17-5p</i>	Part of the polycistronic <i>miR-17-92</i> family involved in monocytopoiesis. Down in SLE PBMCs	(11-13)
<i>miR-18a-5p</i>		
<i>miR-19a-3p</i>	<i>miR-19a</i> and <i>miR-19b</i> regulate IL-6 and MMP3 release by controlling TLR2 expression ^{a b c} . Down in RA FLS.	(14)
<i>miR-19b-3p</i>	See above	(14)
<i>miR-20a</i>	Part of the polycistronic <i>miR-17-92</i> family involved in monocytopoiesis. Down in EBV-transformed B-cell lines from SLE patients.	(13;15;16)
<i>miR-21</i>	Upregulated in SLE PBMCs, targets <i>PDCD4</i> and thereby negatively regulating TLR4 signaling	(7;13;17)
<i>miR-22-3p</i>	Down in RA synovial tissue. Regulates RA FLS proliferation and IL-6 production. Suggested as predictor of anti-TNF response in RA patients.	(18;19)
<i>miR-23a-3p</i>	Suggested as predictor of anti-TNF response in RA patients	(20)
<i>miR-23b-3p</i>	Represses autoimmune inflammation by targeting TGF- β -activated kinase 1/MAP3K7 binding protein 2 (<i>TAB2</i>), <i>TAB3</i> and inhibitor of nuclear factor κ -B kinase subunit α (<i>IKK-α /CHUK</i>) ^b	(21)
<i>miR-24</i>	Down in EBV-transformed B-cell lines from SLE patients	(15)
<i>miR-26a-5p</i>		
<i>miR-26b-5p</i>	Associated with etanercept response in psoriasis patients. Regulates <i>IFNG</i> , <i>TNFAIP3</i> and <i>TLR1</i> .	(22;23)
<i>miR-27a-3p</i>	Attenuates NK-cell cytotoxicity. Down-regulates TNF- α , IL-1b, IL-6, IL-12 and IL-23 through MAPK signaling pathway.	(24;25)
<i>miR-27b-3p</i>		
<i>miR-28-3p</i>		

miR-29a	Epigenetic regulation. Decreases DNA-methylation, decreases IFN- α receptor expression	(13;26)
miR-29b-3p	In a regulatory feedback loop with IFN- γ . Regulates IFN- γ via a direct interaction with the 3' UTR, and IFN- γ itself enhances miR-29b expression ^b . Regulate progranulin (GRN) ^{abcf} . Interacts with TLR.	(27-29)
miR-29c-3p	Interacts with TLR	(29)
<i>miR-31-5p</i>		
miR-34a	Expressed by DCs and B cells, promotes DC differentiation	(13;30)
miR-92a	Part of the polycistronic miR-17 -92 family involved in monocytopoiesis. Down in SLE and SSc plasma.	(16;31)
<i>miR-92b-5p</i>		
miR-98-5p		(32)
miR-100-5p	Predicted interaction with <i>NLRP3</i>	(33)
miR-101	Degradation of mRNA by Roquin (a protein that acts as a post-transcriptional repressor of mRNAs containing conserved stem loop motifs (constitutive decay elements (CDE)))	(12;34)
miR-103a-3p		
<i>miR-105-5p</i>	Modulator of TLR-2 protein translation in human gingival keratinocytes ^{abc}	(35)
miR-106a-5p	Part of the polycistronic miR-17 -92 family involved in monocytopoiesis. Down in SLE and SSc plasma.	(16;31)
miR-106b-5p	Regulate TLR2 expression ^e . Associated with etanercept response in psoriasis patients.	(22;36)
miR-107	Regulates progranulin (GRN) expression ^{bce}	(37)
<i>miR-122-5p</i>		
miR-125a-3p	Upregulated in SLE PBMCs. Regulate <i>TNFAIP3</i> expression ^{ac} .	(15;38)
miR-125b	Targets TNF- α , TLR signaling. Regulate <i>TNFAIP3</i> expression ^{ac} .	(12;38-40)
miR-126-3p	Associated with etanercept response in psoriasis patients.	(22)
<i>miR-126-5p</i>		
miR-128-3p	Target <i>PDE3A</i> ^e , which have been associated with anti-TNF response.	(41;42)
miR-132-3p	Upregulated in RA PBMCs	(7;10-12)
miR-133a-3p	Controls inflammasome activation	(43)
miR-142-3p	Up in SLE PBMCs and plasma, down in SSc, up in RA FLS. Associated with etanercept response in psoriasis patients.	(7;11;13;15;22;44)
miR-145-5p	Target Toll-interleukin-1 receptor domain-containing adaptor protein (<i>TIRAP</i>). Decreased in SLE T-cells	(45;46)
miR-146a	Down in SLE PBMCs. Target TLR4 ^{abcef} and <i>TIRAP</i> ^c . Inflammatory responses to TLR4, TLR2, and TLR5 ligands were reduced due to knockdown of miR-146a targets IL-1R-associated kinase 1 or TNFR-associated factor 6	(7;10-13;45;47;48)
miR-146b	Down in SLE PBMCs	(11;13)
<i>miR-147b</i>	Regulates murine macrophage inflammatory responses	(49)
miR-150	Represses MYB and blocks B-cell development	(12;13;15)
miR-155	TLR signaling, IgG class switch, germinal center response, expressed in lymphocytes, macrophages, and DCs. Regulator of myeloid differentiation primary response gene 88 (MyD88) ^c . Target <i>PDE3A</i> ^e , which have been associated with anti-TNF response.	(7;10-13;39;41;42;50)
miR-181a	Expressed by T cells, involved in T cell development, enhances TCR signaling.	(11-13;15;51)

miR-181b	Regulates Ig class switch recombination in activated B cells, downregulates activation-induced cytidine deaminase (AID). Increased in SSc plasma, especially in dcSSc	(12;52)
miR-184	Down in SLE PBMCs	(7;11)
miR-192-5p	Pro-apoptotic	(53)
miR-193b-3p		
miR-199a-3p	regulator of IKK β (<i>IKBKB</i>) expression ^{a b c}	(54)
miR-200a-3p	Promotes Th17 differentiation	(55)
<i>miR-200b-3p</i>	Inhibits TLR4 pathway factors	(56)
miR-203	Downregulated by EBV, upregulated in RA synovium. Down in SLE plasma. Down-regulating MyD88 by targeting the 3'UTR ^{a b c} .	(7;11;31;57;58)
miR-206	Inversely correlated with number of circulating Th17 cells in dermatomyositis	(59)
miR-208a		
miR-208b-3p		
miR-218-5p	Down-regulating IKK β expression by directly targeting the 3'-UTR ^{a b c}	(60)
miR-221	Expressed in hematopoietic stem cells, targets expression of the KIT genes. Directs TNF- α mRNA degradation	(7;13;61)
miR-223	Upregulated in T-lymphocytes from RA patients, targets E2F1 and CEBPa. Regulator of NLRP3 inflammasome by targeting the 3'-UTR. Regulate IKK α (<i>CHUK</i>). Suggested as biomarker and predictor of anti-TNF response in psoriasis and RA patients, respectively	(7;8;10;12;15;20;22;62)
miR-224-5p	Increased in SLE circulating T-cells	(46)
miR-335-5p	Targets <i>IL17A</i> , <i>TLR1</i> , <i>TLR2</i> , <i>TLR4</i> , <i>IKBKB</i> ^e .	(63).
miR-342-3p	Upregulated/downregulated in SLE PBMCs. Decreased in SSc plasma, especially in dcSSc.	(7;11;15;52)
<i>miR-346</i>	Targets TNF-a, TLR signaling. Regulate IL-18 release in LPS-activated RA FLS ^{b c d} .	(7;40;64)
miR-363	Downregulated in RA T cells	(7;65)
<i>miR-369-3p</i>		(61)
miR-375	Up-regulates caspase recruitment domain family, member 8 (<i>CARD8</i>) ^e (cancer cell line)	(66)
miR-378a-5p		
miR-383	Down in SLE PBMCs	(7;11)
<i>miR-409-3p</i>	Down in SLE PBMCs. Targets <i>IFNG</i> (interferon- γ) ^b	(7;11;67)
miR-423-5p	Upregulated in SLE PBMCs, targets genes activated in IFN signaling	(7;15)
miR-451a	Down-regulates neutrophil chemotaxis via p38 MAPK. Down in RA plasma. Correlated with RA disease activity.	(68-70)
<i>miR-498</i>	Down in RA synovium	(7)
<i>miR-499-5p</i>		
mir-579-3p	Inhibit translation of TNF- α mRNA	(61)
miR-590-5p	Regulates TGF- β and TGF- β RII expression	(71)
miR-638	Up in SLE peripheral blood cells	(7;15;72)
miR-659-3p	A common loss-of-function genetic variant (rs5848) in progranulin (GRN) is located in binding site for miR-659	(73)
<i>Cel-miR-238</i>	<i>Synthetic spike control</i>	
<i>Cel-miR-54</i>	<i>Synthetic spike control</i>	

Micro-RNA target interaction assessed by: ^a qRT-PCR, ^b Luciferase reporter assay, ^c Western blot, ^d Northern blot, ^e Microarray, ^f ELISA. MicroRNAs in italic were not analyzable in our study.

Supplementary Table 2. The 93 TaqMan micro-RNA Assays

miRBase ID	Assay Name	Assay ID	Mature miRNA sequence
hsa-miR-1	hsa-miR-1	002222	UGGAAUGUAAAGAAGUAUGUAU
hsa-miR-7-5p	dme-miR-7	000268	UGGAAGACUAGUGAUUUUGUUGU
hsa-let-7a-5p	hsa-let-7a-5p	000377	UGAGGUAGUAGGUUGUAUAGUU
hsa-let-7b-5p	hsa-let-7b	002619	UGAGGUAGUAGGUUGUGUGGUU
hsa-let-7c	hsa-let-7c	000379	UGAGGUAGUAGGUUGUAUGGUU
hsa-let-7d-5p	hsa-let-7d	002283	AGAGGUAGUAGGUUGCAUAGUU
hsa-let-7e-5p	hsa-let-7e	002406	UGAGGUAGGAGGUUGUAUAGUU
hsa-let-7i-5p	hsa-let-7i	002221	UGAGGUAGUAGUUUGUGCUGUU
hsa-miR-10a-5p	hsa-miR-10a	000387	UACCCUGUAGAUCCGAAUUUGUG
hsa-miR-10b-5p	hsa-miR-10b	002218	UACCCUGUAGAACCGAAUUUGUG
hsa-miR-15a	hsa-miR-15a	000389	UAGCAGCACAUAAUGGUUUGUG
hsa-miR-15b-5p	hsa-miR-15b-5p	000390	UAGCAGCACAUCAUGGUUUACA
hsa-miR-16	hsa-miR-16	000391	UAGCAGCACGUAAAUAUUGGCG
hsa-miR-17-5p	hsa-miR-17	002308	CAAAGUGCUUACAGUGCAGGUAG
hsa-miR-18a-5p	hsa-miR-18a-5p	002422	UAAGGUGCAUCUAGUGCAGAUAG
hsa-miR-19a-3p	hsa-miR-19a	000395	UGUGCAAUUCUAUGCAAACUGA
hsa-miR-19b-3p	hsa-miR-19b	000396	UGUGCAAUCCAUGCAAACUGA
hsa-miR-20a	hsa-miR-20a	000580	UAAAGUGCUUAUAGUGCAGGUAG
hsa-miR-21	hsa-miR-21	000397	UAGCUUAUCAGACUGAUGUUGA
hsa-miR-22-3p	hsa-miR-22	000398	AAGCUGCCAGUUGAAGAACUGU
hsa-miR-23a-3p	hsa-miR-23a	000399	AUCACAUUGCCAGGGAUUUCC
hsa-miR-23b-3p	hsa-miR-23b	000400	AUCACAUUGCCAGGGAUUACC
hsa-miR-24	hsa-miR-24	000402	UGGCUCAGUUCAGCAGGAACAG
hsa-miR-26a-5p	hsa-miR-26a	000405	UUCAAGUAAUCCAGGAUAGGCU
hsa-miR-26b-5p	hsa-miR-26b	000407	UUCAAGUAAUUCAGGAUAGGU
hsa-miR-27a-3p	hsa-miR-27a-3p	000408	UUCACAGUGGCUAAGUUCGCG
hsa-miR-27b-3p	hsa-miR-27b	000409	UUCACAGUGGCUAAGUUCUGC
hsa-miR-28-3p	hsa-miR-28-3p	002446	CACUAGAUUGUGAGCUCCUGGA
hsa-miR-29a	hsa-miR-29a	002112	UAGCACCAUCUGAAAUCGGUUA
hsa-miR-29b-3p	hsa-miR-29b-3p	000413	UAGCACCAUUUGAAAUCAGUGUU
hsa-miR-29c-3p	hsa-miR-29c-3p	000587	UAGCACCAUUUGAAAUCGGUUA
hsa-miR-31-5p	hsa-miR-31-5p	002279	AGGCAAGAUGCUGGCAUAGCU
hsa-miR-34a	hsa-miR-34a	000426	UGGCAGUGUCUUAGCUGGUUGU
hsa-miR-92a	hsa-miR-92a	000431	UAUUGCACUUGUCCGGCCUGU
hsa-miR-92b-5p	hsa-miR-92b*	002343	AGGGACGGGACGCGGUGCAGUG
hsa-miR-98-5p	hsa-miR-98	000577	UGAGGUAGUAAGUUGUAUUGUU
hsa-miR-100-5p	hsa-miR-100	000437	AACCCGUAGAUCCGAACUUGUG

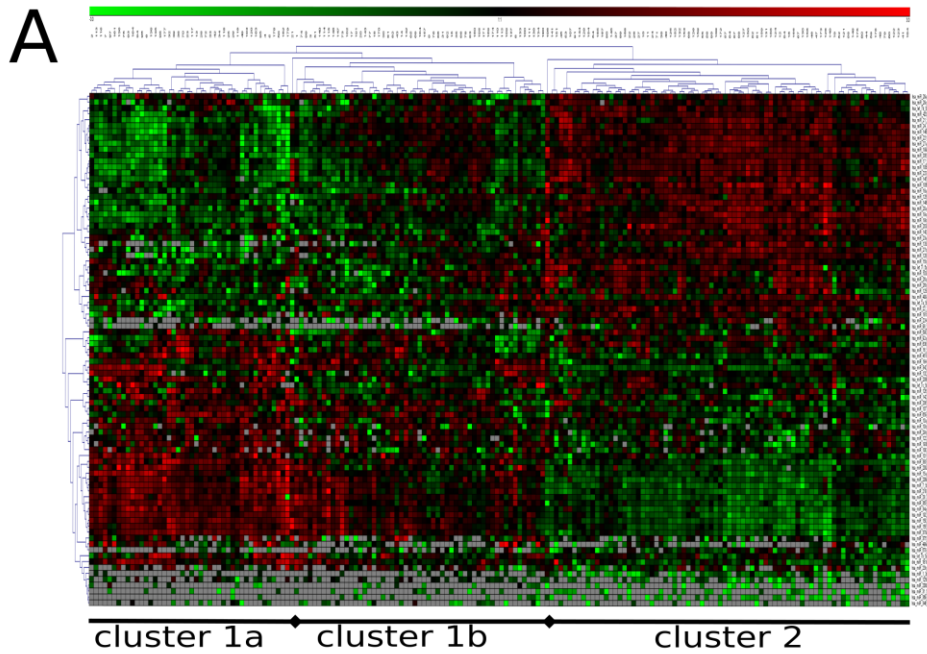
Online supplement to: Plasma MicroRNA Profiles in Patients with Early Rheumatoid Arthritis Responding to Adalimumab plus Methotrexate vs Methotrexate Alone: A Placebo-controlled Clinical Trial. *The Journal of Rheumatology*. doi:10.3899/jrheum.170266

hsa-miR-101	hsa-miR-101	002253	UACAGUACUGUGUAACUGAA
hsa-miR-103a-3p	hsa-miR-103a-3p	000439	AGCAGCAUUGUACAGGGCUAUGA
hsa-miR-105-5p	hsa-miR-105	002167	UCAAUUGCUCAGACUCCUGUGGU
hsa-miR-106a-5p	hsa-miR-106a	002169	AAAAGUGCUACAGUGCAGGUAG
hsa-miR-106b-5p	hsa-miR-106b	000442	UAAAGUGCUGACAGUGCAGAU
hsa-miR-107	hsa-miR-107	000443	AGCAGCAUUGUACAGGGCUAUCA
hsa-miR-122-5p	hsa-miR-122-5p	002245	UGGAGUGUGACAAUGGUGUUUG
hsa-miR-125a-5p	hsa-miR-125a-5p	002198	UCCCUGAGACCCUUUAACCUGUGA
hsa-miR-125b	hsa-miR-125b	000449	UCCCUGAGACCCUAAACUUGUGA
hsa-miR-126-3p	hsa-miR-126-3p	002228	UCGUACCGUGAGUAAUAAUGCG
hsa-miR-126-5p	hsa-miR-126*	000451	CAUUAUUACUUUUGGUACGCG
hsa-miR-128-3p	hsa-miR-128a	002216	UCACAGUGAACCGGUCUCUUU
hsa-miR-132-3p	hsa-miR-132	000457	UAACAGUCUACAGCCAUGGUCG
hsa-miR-133a-3p	hsa-miR-133a	002246	UUUGGUCCCCUUAACCAGCUG
hsa-miR-142-3p	hsa-miR-142-3p	000464	UGUAGUGUUCCUACUUUAUGGA
hsa-miR-145-5p	hsa-miR-145-5p	002278	GUCCAGUUUCCCAGGAAUCCCU
hsa-miR-146a	hsa-miR-146a	000468	UGAGAACUGAAUCCAUGGGUU
hsa-miR-146b-5p	hsa-miR-146b	001097	UGAGAACUGAAUCCAUAGGCU
hsa-miR-147b	hsa-miR-147b	002262	GUGUGCGGAAAUGCUUCUGCUA
hsa-miR-150	hsa-miR-150	000473	UCUCCCAACCCUUGUACCAGUG
hsa-miR-155	hsa-miR-155	002623	UUAAUGCUGAAUCGUGAUAGGGGU
hsa-miR-181a-5p	hsa-miR-181a	000480	AACAUUCAACGCUGUCGGUGAGU
dre-miR-181b	hsa-miR-181b	001098	AACAUUCAUUGCUGUCGGUGGG
hsa-miR-184	hsa-miR-184	000485	UGGACGGAGAACUGAUAAAGGGU
hsa-miR-192-5p	hsa-miR-192-5p	000491	CUGACCUAUGAAUUGACAGCC
hsa-miR-193b-3p	hsa-miR-193b	002367	AACUGGCCUCUCAAAGUCCCGCU
hsa-miR-199a-3p	hsa-miR-199a-3p	002304	ACAGUAGUCUGCACAUUGGUUA
hsa-miR-200a-3p	hsa-miR-200a	000502	UAACACUGUCUGGUAACGAUGU
hsa-miR-200b-3p	hsa-miR-200b	002251	UAAUACUGCCUGGUAUUGAUGA
hsa-miR-203	hsa-miR-203	000507	GUGAAAUGUUUAGGACCACUAG
hsa-miR-206	hsa-miR-206	000510	UGGAAUGUAAGGAAGUGUGUGG
hsa-miR-208a	hsa-miR-208a	000511	AUAAGACGAGCAAAAAGCUUGU
hsa-miR-208b-3p	hsa-miR-208b	002290	AUAAGACGAACAAAAGGUUUGU
hsa-miR-218-5p	hsa-miR-218	000521	UUGUGCUUGAUCUAACCAUGU
hsa-miR-221	hsa-miR-221	000524	AGCUACAUUGUCUGCUGGGUUUC
hsa-miR-223	hsa-miR-223	002295	UGUCAGUUUGUCAAAUACCCCA
hsa-miR-224-5p	hsa-miR-224	002099	CAAGUCACUAGUGGUUCCGUU
hsa-miR-335-5p	hsa-miR-335	000546	UCAAGAGCAAUACGAAAAAUGU
hsa-miR-342-3p	hsa-miR-342-3p	002260	UCUCACACAGAAAUCGCACCCGU

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hsa-miR-346	hsa-miR-346	000553	UGUCUGCCCCGCAUGCCUGCCUCU
hsa-miR-363-3p	hsa-miR-363	001271	AAUUGCACGGUAUCCAUCUGUA
hsa-miR-369-3p	hsa-miR-369-3p	000557	AAUAAUACAUGGUUGAUCUUU
hsa-miR-375	hsa-miR-375	000564	UUUGUUCGUUCGGCUCGCGUGA
hsa-miR-378a-5p	hsa-miR-378	000567	CUCCUGACUCCAGGUCCUGUGU
hsa-miR-383	hsa-miR-383	000573	AGAUCAGAAGGUGAUUGUGGCU
hsa-miR-409-3p	hsa-miR-409-3p	002332	GAAUGUUGCUCGGUGAACCCCU
hsa-miR-423-5p	hsa-miR-423-5p	002340	UGAGGGGCAGAGAGCGAGACUUU
hsa-miR-451a	hsa-miR-451a	001141	AAACCGUUACCAUUACUGAGUU
hsa-miR-498	hsa-miR-498	001044	UUUCAAGCCAGGGGGCGUUUUUC
hsa-miR-499-5p	mmu-miR-499	001352	UUAAGACUUGCAGUGAUGUUU
hsa-miR-579-3p	hsa-miR-579	002398	UUCAUUUGUAUAAACCGCGAUU
hsa-miR-590-5p	hsa-miR-590-5p	001984	GAGCUUAUUCAUAAAAGUGCAG
hsa-miR-638	hsa-miR-638	001582	AGGGAUCGCGGGCGGGUGGCGGCCU
hsa-miR-659-3p	hsa-miR-659	001514	CUUGGUUCAGGGAGGGUCCCA
cel-miR-238-3p	cel-miR-238	000248	UUUGUACUCCGAUGCCAUUCAGA
cel-miR-54-3p	cel-miR-54	001361	UACCCGUAAUCUUCAUAAUCCGAG

Supplementary Figure 1. Unsupervised hierarchical clustering plot based on all patients and miRNAs



B

Hospital	cluster 1a	cluster 1b	cluster 2	Total
A	0	4	14	18
B	0	0	1	1
C	3	5	4	12
D	21	9	0	30
E	0	0	1	1
F	0	1	7	8
G	0	1	25	26
H	0	3	8	11
I	0	1	0	1
J	15	5	8	28
K	0	1	0	1
L	1	7	2	10
M	0	0	2	2
N	1	10	8	19
O	3	9	0	12
Total	44	56	80	180

Supplementary Table 3. Adalimumab group univariate analyses of association between pre-treatment micro-RNA and ACR/EULAR Boolean remission

hsa-miRNA	3m				12m			
	Rank	Regr. Coeff. ± SE	p-value	q-value	Rank	Regr. Coeff. ± SE	p-value	q-value
miR-27a-3p	10	0.29±0.16	0.08	0.64	1	0.55±0.16	0.001	0.06
miR-10b-5p	15	-0.71±0.47	0.14	0.67	2	-1.38±0.46	0.004	0.12
miR-423-5p	73	-0.03±0.15	0.87	0.95	3	0.44±0.15	0.01	0.12
miR-142-3p	16	-0.18±0.12	0.15	0.67	4	-0.33±0.12	0.01	0.12
miR-24-3p	22	0.21±0.16	0.19	0.69	5	0.44±0.16	0.01	0.12
miR-27b-3p	4	0.48±0.23	0.04	0.56	6	0.62±0.24	0.01	0.12
miR-23a-3p	12	0.61±0.37	0.10	0.64	7	0.95±0.37	0.01	0.12
miR-342-3p	69	-0.04±0.20	0.84	0.95	8	-0.50±0.20	0.01	0.12
miR-101-3p	39	-0.23±0.26	0.37	0.75	9	-0.65±0.26	0.01	0.12
miR-17-5p	25	0.14±0.11	0.23	0.73	10	0.28±0.11	0.02	0.14
miR-223-3p	11	0.21±0.12	0.10	0.64	11	0.30±0.13	0.02	0.16
miR-19b-3p	1	0.41±0.16	0.01	0.56	12	0.36±0.16	0.03	0.16
miR-221-3p	42	0.15±0.18	0.42	0.8	13	0.42±0.18	0.03	0.16
miR-19a-3p	2	0.56±0.22	0.01	0.56	14	0.52±0.23	0.03	0.16
miR-106a-5p	45	0.09±0.12	0.46	0.8	15	0.26±0.12	0.03	0.18
miR-128-3p	24	0.28±0.23	0.23	0.73	16	0.49±0.24	0.04	0.21
miR-10a-5p	5	-0.97±0.48	0.04	0.56	17	-0.96±0.49	0.05	0.22
miR-16-5p	61	0.07±0.16	0.65	0.86	18	0.30±0.15	0.05	0.22
miR-199a-b-3p	8	0.40±0.21	0.06	0.56	19	0.41±0.21	0.05	0.22
miR-146b-5p	33	-0.11±0.11	0.32	0.75	20	-0.22±0.11	0.06	0.22
miR-29b-3p	6	-0.85±0.43	0.05	0.56	21	-0.83±0.44	0.06	0.22
miR-146a-5p	18	0.18±0.13	0.16	0.67	22	0.25±0.13	0.06	0.22
let-7a-5p	17	-0.49±0.34	0.16	0.67	23	-0.66±0.35	0.06	0.22
miR-184	23	-0.23±0.18	0.20	0.69	24	-0.33±0.18	0.08	0.26
miR-21-5p	72	0.02±0.12	0.86	0.95	25	0.21±0.12	0.09	0.28
miR-140-3p	67	-0.07±0.25	0.79	0.94	26	0.42±0.25	0.10	0.31
miR-29c-3p	27	-0.29±0.26	0.26	0.75	27	-0.43±0.26	0.11	0.31
miR-18a-5p	57	0.19±0.35	0.59	0.83	28	0.56±0.36	0.12	0.33
miR-579-3p	30	0.28±0.27	0.30	0.75	29	0.39±0.25	0.13	0.33
miR-7-5p	59	-0.07±0.15	0.63	0.86	30	-0.24±0.15	0.13	0.33
miR-92a-3p	62	0.04±0.11	0.70	0.91	31	0.15±0.10	0.14	0.33
miR-26a-5p	36	-0.10±0.11	0.35	0.75	32	-0.17±0.11	0.14	0.33
let-7i-5p	20	-0.15±0.10	0.17	0.67	33	-0.15±0.10	0.14	0.33
miR-659-3p	40	-0.22±0.25	0.38	0.77	34	-0.37±0.25	0.14	0.33
miR-218-5p	53	-0.08±0.14	0.55	0.82	35	-0.21±0.14	0.14	0.33
miR-106b-5p	47	-0.10±0.14	0.49	0.8	36	0.21±0.15	0.15	0.34
miR-335-5p	70	0.04±0.22	0.85	0.95	37	0.31±0.22	0.17	0.36
miR-208a-3p	19	-0.20±0.15	0.16	0.67	38	-0.20±0.15	0.18	0.37
miR-208b-3p	13	-0.35±0.22	0.11	0.64	39	-0.30±0.23	0.19	0.39
miR-363-3p	60	-0.09±0.19	0.65	0.86	40	-0.25±0.19	0.20	0.39
miR-103a-3p	44	-0.26±0.33	0.44	0.8	41	-0.43±0.34	0.20	0.39
miR-107	77	-0.02±0.23	0.94	0.97	42	-0.28±0.23	0.22	0.42

miR-98-5p	52	-0.31±0.51	0.54	0.82	43	-0.59±0.50	0.25	0.44
miR-15a-5p	74	-0.03±0.22	0.88	0.95	44	-0.27±0.23	0.25	0.44
miR-193b-3p	3	-0.77±0.36	0.03	0.56	45	-0.44±0.37	0.25	0.44
miR-122-5p	26	-0.68±0.57	0.24	0.73	46	-0.66±0.58	0.26	0.44
miR-22-3p	54	-0.12±0.21	0.56	0.82	47	-0.23±0.20	0.26	0.44
miR-133a-3p	63	-0.11±0.32	0.74	0.92	48	0.35±0.33	0.29	0.48
miR-20a-5p	65	0.04±0.12	0.75	0.92	49	0.12±0.12	0.32	0.51
let-7d-5p	21	-0.28±0.21	0.19	0.69	50	-0.21±0.21	0.32	0.51
miR-126-3p	43	-0.07±0.09	0.43	0.8	51	-0.09±0.09	0.33	0.51
miR-29a-3p	48	0.12±0.17	0.49	0.8	52	0.15±0.17	0.38	0.57
miR-378a-3p	34	-0.18±0.18	0.32	0.75	53	-0.17±0.19	0.38	0.57
miR-28-3p	46	-0.12±0.18	0.49	0.8	54	-0.15±0.18	0.41	0.59
miR-181a-5p	29	-0.34±0.31	0.27	0.75	55	-0.25±0.31	0.42	0.59
miR-590-5p	32	-0.14±0.14	0.31	0.75	56	-0.11±0.14	0.43	0.59
miR-145-5p	56	0.16±0.29	0.59	0.83	57	0.24±0.30	0.43	0.59
miR-125a-5p	38	0.17±0.18	0.36	0.75	58	0.15±0.19	0.43	0.59
let-7c-5p	66	-0.08±0.26	0.77	0.93	59	-0.21±0.27	0.44	0.60
miR-150-5p	37	-0.16±0.17	0.36	0.75	60	-0.13±0.17	0.45	0.60
miR-126-5p	41	-0.16±0.19	0.40	0.78	61	0.14±0.20	0.48	0.62
miR-383-5p	58	0.09±0.20	0.63	0.86	62	-0.14±0.20	0.50	0.64
miR-638	51	-0.06±0.10	0.51	0.8	63	-0.06±0.10	0.52	0.66
miR-132-3p	76	-0.05±0.57	0.93	0.97	64	-0.38±0.59	0.53	0.66
miR-192-5p	7	-0.35±0.18	0.06	0.56	65	-0.12±0.19	0.54	0.66
let-7b-5p	49	0.10±0.15	0.50	0.8	66	0.09±0.15	0.58	0.70
miR-203a-3p	14	0.32±0.20	0.11	0.64	67	-0.11±0.20	0.58	0.70
miR-200a-3p	55	0.15±0.27	0.58	0.83	68	-0.13±0.28	0.63	0.75
miR-23b-3p	35	0.54±0.55	0.33	0.75	69	0.23±0.53	0.67	0.77
miR-206	79	-0.01±0.25	0.96	0.97	70	-0.11±0.25	0.68	0.77
miR-451a	80	0.01±0.23	0.97	0.97	71	-0.09±0.22	0.68	0.77
miR-155-5p	71	0.04±0.20	0.86	0.95	72	-0.06±0.21	0.77	0.85
miR-100-5p	68	-0.14±0.58	0.81	0.95	73	-0.17±0.58	0.78	0.85
miR-15b-5p	78	0.02±0.31	0.95	0.97	74	-0.07±0.32	0.82	0.88
miR-375	28	0.39±0.35	0.27	0.75	75	0.04±0.36	0.91	0.97
miR-224-5p	75	0.06±0.50	0.91	0.97	76	0.04±0.52	0.93	0.97
miR-34a-5p	9	-0.30±0.17	0.08	0.64	77	0.01±0.17	0.93	0.97
miR-181b-5p	64	-0.07±0.20	0.74	0.92	78	0.01±0.21	0.94	0.97
miR-26b-5p	31	-0.18±0.17	0.30	0.75	79	-0.01±0.17	0.97	0.98
miR-125b-5p	50	-0.17±0.26	0.51	0.8	80	0.00±0.27	0.99	0.99

Linear mixed effects model (hospital=random effect). A negative regression coefficient corresponds to a lower level of pre-treatment miRNA predictive of remission and vice versa. False discovery rate corrections for multiple testing (q-values) are based on the total number miRNAs analyzed per hypothesis (N=80). Feature-selected miRNAs (p<0.1) in bold. Abbreviations: hsa, homo sapiens; Regr. Coeff., β regression coefficient; SE, standard error;

Supplementary Table 4. Placebo group univariate analyses of association between pre-treatment micro-RNA and ACR/EULAR Boolean remission

miRNA	3m				12m			
	Rank	Regr. Coeff. ± SE	p-value	q-value	Rank	Regr. Coeff. ± SE	p-value	q-value
miR-28-3p	37	0.23±0.32	0.48	0.89	1	0.7±0.3	0.02	0.75
miR-106a-5p	70	-0.02±0.14	0.87	0.97	2	-0.28±0.13	0.03	0.75
miR-19a-3p	7	-0.55±0.27	0.05	0.55	3	-0.53±0.25	0.04	0.75
miR-181b-5p	59	0.08±0.24	0.73	0.97	4	0.44±0.21	0.04	0.75
miR-29c-3p	78	0.00±0.26	0.99	1.00	5	-0.49±0.24	0.05	0.75
miR-19b-3p	2	-0.56±0.23	0.02	0.48	6	-0.39±0.22	0.09	0.75
miR-590-5p	26	-0.15±0.15	0.32	0.89	7	-0.24±0.14	0.09	0.75
let-7c-5p	71	0.04±0.24	0.87	0.97	8	-0.38±0.22	0.09	0.75
miR-20a-5p	33	-0.12±0.14	0.40	0.89	9	-0.22±0.13	0.09	0.75
miR-145-5p	29	0.32±0.35	0.37	0.89	10	-0.58±0.34	0.09	0.75
miR-133a-3p	22	-0.48±0.43	0.27	0.89	11	-0.63±0.41	0.13	0.75
miR-126-5p	5	-0.40±0.20	0.04	0.55	12	-0.28±0.19	0.13	0.75
miR-223-3p	18	-0.19±0.15	0.20	0.89	13	-0.21±0.15	0.16	0.75
miR-378a-3p	48	0.15±0.26	0.56	0.89	14	0.34±0.24	0.16	0.75
miR-199a-b-3p	9	-0.54±0.30	0.08	0.68	15	-0.41±0.29	0.17	0.75
miR-17-5p	60	-0.04±0.13	0.75	0.97	16	-0.16±0.12	0.17	0.75
miR-140-3p	16	-0.44±0.33	0.18	0.87	17	-0.43±0.31	0.17	0.75
miR-7-5p	39	-0.12±0.18	0.49	0.89	18	0.23±0.17	0.18	0.75
miR-23a-3p	12	-0.55±0.40	0.17	0.87	19	-0.49±0.39	0.21	0.75
miR-16-5p	30	-0.14±0.16	0.38	0.89	20	-0.2±0.16	0.21	0.75
miR-125a-5p	25	0.28±0.28	0.32	0.89	21	0.34±0.27	0.22	0.75
miR-218-5p	74	-0.03±0.19	0.90	0.97	22	0.22±0.18	0.23	0.75
miR-155-5p	79	0.00±0.29	0.99	1.00	23	0.33±0.27	0.23	0.75
miR-579-3p	32	-0.26±0.31	0.40	0.89	24	0.34±0.29	0.24	0.75
miR-29b-3p	51	0.29±0.51	0.57	0.89	25	-0.56±0.49	0.26	0.75
miR-107	20	0.45±0.37	0.23	0.89	26	0.4±0.36	0.26	0.75
miR-375	80	0.00±0.40	1.00	1.00	27	-0.45±0.4	0.27	0.75
miR-24-3p	8	-0.36±0.19	0.06	0.64	28	-0.19±0.19	0.31	0.75
miR-150-5p	72	0.04±0.24	0.88	0.97	29	0.22±0.22	0.33	0.75
miR-224-5p	63	0.14±0.64	0.82	0.97	30	-0.6±0.62	0.34	0.75
miR-208a-3p	56	0.09±0.22	0.67	0.95	31	0.19±0.21	0.35	0.75
miR-15b-5p	44	-0.21±0.32	0.52	0.89	32	-0.3±0.31	0.35	0.75
miR-34a-5p	65	-0.05±0.22	0.83	0.97	33	0.19±0.21	0.35	0.75
miR-100-5p	19	-0.78±0.63	0.22	0.89	34	0.56±0.6	0.36	0.75
miR-184	76	0.01±0.17	0.95	0.99	35	-0.16±0.17	0.36	0.75
miR-208b-3p	11	0.44±0.30	0.14	0.87	36	-0.26±0.29	0.37	0.75
miR-363-3p	42	0.23±0.36	0.52	0.89	37	0.31±0.35	0.37	0.75
miR-26a-5p	17	0.18±0.14	0.19	0.87	38	-0.11±0.13	0.39	0.75
miR-106b-5p	62	-0.06±0.20	0.76	0.97	39	-0.16±0.19	0.40	0.75
miR-122-5p	64	0.13±0.58	0.83	0.97	40	-0.45±0.57	0.42	0.75
miR-128-3p	1	-0.93±0.35	0.01	0.48	41	-0.27±0.34	0.43	0.75
miR-200a-3p	46	0.17±0.29	0.55	0.89	42	-0.22±0.27	0.43	0.75

miR-101-3p	21	0.39±0.33	0.25	0.89	43	-0.25±0.32	0.44	0.75
miR-423-5p	52	-0.10±0.18	0.58	0.89	44	-0.14±0.18	0.44	0.75
miR-451a	61	0.08±0.27	0.75	0.97	45	0.2±0.26	0.45	0.75
miR-192-5p	77	0.01±0.23	0.95	0.99	46	0.16±0.22	0.46	0.75
miR-126-3p	66	-0.02±0.10	0.84	0.97	47	-0.08±0.1	0.46	0.75
miR-10b-5p	58	-0.23±0.67	0.73	0.97	48	-0.47±0.64	0.46	0.75
miR-27b-3p	3	-0.66±0.28	0.02	0.48	49	-0.19±0.26	0.48	0.75
miR-193b-3p	67	0.09±0.48	0.85	0.97	50	-0.33±0.47	0.49	0.75
miR-23b-3p	53	0.34±0.66	0.60	0.90	51	0.39±0.57	0.50	0.75
miR-125b-5p	28	0.47±0.52	0.37	0.89	52	0.34±0.5	0.50	0.75
let-7b-5p	35	0.13±0.17	0.46	0.89	53	-0.11±0.17	0.51	0.75
let-7i-5p	41	0.10±0.15	0.51	0.89	54	-0.1±0.15	0.52	0.75
miR-203a-3p	6	-0.41±0.20	0.05	0.55	55	-0.12±0.18	0.52	0.75
miR-29a-3p	68	0.04±0.25	0.87	0.97	56	0.15±0.24	0.53	0.75
miR-206	15	0.45±0.33	0.18	0.87	57	-0.2±0.32	0.53	0.75
miR-10a-5p	4	-0.98±0.43	0.02	0.48	58	0.25±0.43	0.56	0.77
miR-92a-3p	47	-0.07±0.11	0.55	0.89	59	0.06±0.1	0.58	0.79
miR-146b-5p	57	-0.05±0.13	0.71	0.97	60	0.07±0.13	0.60	0.8
miR-342-3p	43	0.14±0.22	0.52	0.89	61	0.11±0.22	0.62	0.81
miR-132-3p	69	-0.13±0.80	0.87	0.97	62	-0.35±0.74	0.63	0.81
miR-659-3p	27	0.38±0.42	0.37	0.89	63	0.19±0.41	0.64	0.81
miR-26b-5p	10	0.38±0.22	0.09	0.70	64	0.1±0.22	0.65	0.82
miR-383-5p	13	0.32±0.23	0.17	0.87	65	0.08±0.21	0.71	0.87
miR-146a-5p	55	-0.08±0.17	0.63	0.91	66	0.06±0.16	0.72	0.87
miR-18a-5p	38	-0.34±0.49	0.49	0.89	67	-0.17±0.47	0.73	0.87
miR-21-5p	31	-0.12±0.14	0.38	0.89	68	0.04±0.13	0.75	0.88
let-7a-5p	75	0.05±0.44	0.91	0.97	69	0.11±0.43	0.79	0.92
miR-27a-3p	23	-0.22±0.20	0.27	0.89	70	-0.05±0.19	0.81	0.92
miR-335-5p	73	0.05±0.36	0.89	0.97	71	-0.08±0.35	0.82	0.92
miR-98-5p	50	0.29±0.50	0.57	0.89	72	0.09±0.49	0.85	0.93
miR-221-3p	36	-0.18±0.24	0.47	0.89	73	-0.04±0.23	0.86	0.93
miR-15a-5p	45	0.16±0.26	0.55	0.89	74	-0.04±0.25	0.86	0.93
miR-638	49	-0.05±0.09	0.57	0.89	75	0.01±0.09	0.90	0.95
miR-181a-5p	24	-0.38±0.35	0.28	0.89	76	0.04±0.35	0.91	0.95
miR-103a-3p	54	-0.21±0.41	0.61	0.90	77	0.04±0.39	0.92	0.95
miR-22-3p	34	-0.22±0.27	0.41	0.89	78	-0.02±0.26	0.93	0.95
miR-142-3p	14	0.20±0.15	0.17	0.87	79	-0.01±0.14	0.96	0.97
let-7d-5p	40	0.19±0.28	0.51	0.89	80	0.01±0.27	0.98	0.97

Linear mixed effects model (hospital=random effect). A negative regression coefficient corresponds to a lower level of pre-treatment miRNA predictive of remission and vice versa. False discovery rate corrections for multiple testing (q-values) are based on the total number miRNAs analyzed per hypothesis (N=80). Feature-selected miRNAs (p<0.1) in bold. Abbreviations: hsa, homo sapiens; Regr. Coeff., β regression coefficient; SE, standard error;

Supplementary Table 5. Univariate analyses of association between 3-month micro-RNA and 12-month ACR/EULAR Boolean remission

hsa-miRNA	<u>Adalimumab</u> <u>group</u>				<u>Placebo</u> <u>group</u>			
	Rank	Regr. Coeff. ± SE	p-value	q-value	miRNA	Regr. Coeff. ± SE	p-value	q-value
miR-98-5p	1	-0.38±0.15	0.02	0.88	miR_208a_3p	0.34±0.17	0.05	0.95
miR-125b-5p	2	1.16±0.52	0.03	0.88	miR_98_5p	0.28±0.16	0.09	0.95
miR-184	3	-0.28±0.13	0.03	0.88	miR_106b_5p	-0.45±0.26	0.09	0.95
miR-106b-5p	4	0.51±0.27	0.06	0.89	miR_23a_3p	0.32±0.19	0.11	0.95
miR-29b-3p	5	1.33±0.7	0.06	0.89	miR_150_5p	-0.36±0.22	0.11	0.95
miR-181b-5p	6	-0.23±0.13	0.08	0.89	let_7a_5p	-0.49±0.31	0.12	0.95
miR-122-5p	7	-0.43±0.25	0.09	0.89	miR_140_3p	0.56±0.39	0.15	0.95
let-7a-5p	8	-0.54±0.31	0.09	0.89	miR_26a_5p	-0.20±0.15	0.19	0.95
miR-224-5p	9	0.44±0.27	0.11	0.89	miR_192_5p	0.27±0.20	0.19	0.95
miR-132-3p	10	-0.78±0.49	0.11	0.89	miR_103a_3p	0.22±0.17	0.20	0.95
miR-181a-5p	11	-0.43±0.27	0.12	0.89	miR_579_3p	0.55±0.43	0.20	0.95
let-7c-5p	12	0.21±0.17	0.21	0.99	miR_184	-0.20±0.16	0.24	0.95
miR-19b-3p	13	-0.17±0.14	0.23	0.99	miR_34a_5p	0.12±0.10	0.24	0.95
miR-20a-5p	14	-0.27±0.22	0.24	0.99	miR_142_3p	-0.16±0.13	0.24	0.95
miR-659-3p	15	0.63±0.56	0.26	0.99	miR_638	0.49±0.43	0.25	0.95
miR-378a-3p	16	-0.32±0.29	0.26	0.99	miR_132_3p	-0.70±0.62	0.26	0.95
miR-23a-3p	17	-0.27±0.25	0.27	0.99	miR_218_5p	0.30±0.26	0.26	0.95
miR-133a-3p	18	-0.31±0.29	0.28	0.99	miR_23b_3p	-0.21±0.18	0.27	0.95
miR-140-3p	19	0.44±0.41	0.29	0.99	miR_126_3p	-0.44±0.40	0.27	0.95
miR-10a-5p	20	-0.16±0.17	0.37	0.99	miR_208b_3p	0.24±0.22	0.27	0.95
miR-34a-5p	21	-0.1±0.12	0.39	0.99	miR_28_3p	0.22±0.20	0.28	0.95
let-7i-5p	22	0.11±0.13	0.41	0.99	miR_22_3p	0.24±0.22	0.28	0.95
miR-126-5p	23	-0.29±0.36	0.42	0.99	miR_125b_5p	-0.55±0.54	0.31	0.95
let-7d-5p	24	0.13±0.16	0.43	0.99	miR_20a_5p	0.17±0.17	0.32	0.95
miR-223-3p	25	0.2±0.25	0.44	0.99	miR_100_5p	0.41±0.41	0.32	0.95
miR-145-5p	26	-0.1±0.13	0.45	0.99	miR_342_3p	-0.45±0.47	0.34	0.95
miR-221-3p	27	0.28±0.37	0.45	0.99	miR_16_5p	0.09±0.10	0.35	0.95
miR-146a-5p	28	0.18±0.24	0.45	0.99	miR_101_3p	0.18±0.19	0.35	0.95
miR-18a-5p	29	-0.07±0.09	0.46	0.99	miR_125a_5p	-0.35±0.38	0.36	0.95
miR-22-3p	30	0.2±0.28	0.47	0.99	miR_10a_5p	0.12±0.13	0.37	0.95
miR-92a-3p	31	-0.32±0.44	0.47	0.99	miR_155_5p	-0.14±0.16	0.39	0.95
miR-200a-3p	32	-0.19±0.26	0.47	0.99	miR_146a_5p	0.23±0.27	0.41	0.95
miR-7-5p	33	-0.36±0.5	0.48	0.99	miR_193b_3p	-0.13±0.18	0.46	0.95
miR-579-3p	34	-0.26±0.37	0.48	0.99	miR_17_5p	-0.09±0.12	0.47	0.95
miR-142-3p	35	0.12±0.17	0.49	0.99	miR_27a_3p	0.15±0.21	0.48	0.95
miR-192-5p	36	0.17±0.27	0.54	0.99	miR_223_3p	0.14±0.21	0.49	0.95
miR-590-5p	37	0.18±0.3	0.55	0.99	miR_145_5p	0.09±0.14	0.50	0.95
miR-29a-3p	38	0.17±0.28	0.55	0.99	miR_92a_3p	-0.25±0.37	0.51	0.95
miR-27b-3p	39	0.13±0.21	0.56	0.99	miR_423_5p	-0.18±0.29	0.54	0.95
miR-17-5p	40	0.1±0.19	0.59	0.99	miR_590_5p	-0.18±0.31	0.56	0.95
miR-208b-3p	41	-0.11±0.21	0.61	0.99	miR_181b_5p	-0.08±0.13	0.56	0.95
miR-342-3p	42	0.2±0.38	0.61	0.99	miR_15a_5p	0.09±0.16	0.57	0.95

miR-101-3p	43	-0.12±0.23	0.61	0.99	miR_335_5p	-0.14±0.25	0.57	0.95
miR-126-3p	44	0.2±0.4	0.62	0.99	miR_106a_5p	-0.26±0.46	0.57	0.95
miR-100-5p	45	-0.21±0.42	0.62	0.99	miR_29b_3p	-0.41±0.72	0.57	0.95
miR-638	46	0.29±0.58	0.62	0.99	let_7d_5p	-0.06±0.11	0.60	0.95
miR-451a	47	-0.14±0.29	0.63	0.99	miR_24_3p	0.10±0.20	0.61	0.95
let-7b-5p	48	-0.16±0.34	0.65	0.99	let_7b_5p	0.13±0.27	0.63	0.95
miR-19a-3p	49	-0.1±0.24	0.68	0.99	miR_206	-0.16±0.32	0.63	0.95
miR-218-5p	50	-0.16±0.4	0.69	0.99	miR_378a_3p	-0.17±0.35	0.63	0.95
miR-203a-3p	51	0.14±0.35	0.69	0.99	miR_122_5p	0.12±0.26	0.63	0.95
miR-363-3p	52	-0.21±0.54	0.70	0.99	miR_21_5p	0.09±0.19	0.65	0.95
miR-103a-3p	53	-0.07±0.19	0.70	0.99	let_7i_5p	-0.05±0.12	0.66	0.95
miR-146b-5p	54	-0.16±0.41	0.71	0.99	miR_27b_3p	-0.07±0.17	0.67	0.95
miR-23b-3p	55	0.07±0.19	0.72	0.99	miR_133a_3p	-0.17±0.41	0.68	0.95
miR-26b-5p	56	0.08±0.23	0.73	0.99	miR_19b_3p	-0.06±0.16	0.69	0.95
miR-193b-3p	57	0.07±0.21	0.73	0.99	miR_18a_5p	-0.03±0.09	0.70	0.95
miR-106a-5p	58	-0.13±0.39	0.75	0.99	miR_146b_5p	-0.10±0.28	0.71	0.95
miR-128-3p	59	0.11±0.37	0.77	0.99	miR_363_3p	0.17±0.46	0.72	0.95
miR-28-3p	60	-0.16±0.56	0.77	0.99	miR_128_3p	0.15±0.42	0.72	0.95
miR-206	61	-0.07±0.27	0.81	0.99	miR_383_5p	-0.12±0.33	0.72	0.95
miR-155-5p	62	0.04±0.19	0.83	0.99	miR_221_3p	0.06±0.25	0.80	0.97
miR-16-5p	63	0.02±0.12	0.84	0.99	let_7c_5p	-0.04±0.16	0.81	0.97
miR-150-5p	64	0.07±0.32	0.84	0.99	miR_224_5p	-0.05±0.21	0.82	0.97
miR-15b-5p	65	-0.05±0.24	0.84	0.99	miR_26b_5p	-0.05±0.22	0.84	0.97
miR-24-3p	66	0.06±0.28	0.84	0.99	miR_199a_b_	-0.05±0.24	0.84	0.97
miR-29c-3p	67	-0.03±0.14	0.84	0.99	miR_15b_5p	-0.03±0.17	0.84	0.97
miR-26a-5p	68	0.04±0.22	0.85	0.99	miR_29c_3p	0.03±0.13	0.84	0.97
miR-199ab-3p	69	-0.03±0.24	0.89	0.99	miR_375	0.07±0.36	0.85	0.97
miR-335-5p	70	0.05±0.37	0.90	0.99	miR_181a_5p	-0.05±0.27	0.85	0.97
miR-423-5p	71	-0.04±0.31	0.91	0.99	miR_203a_3p	-0.04±0.27	0.88	0.98
miR-10b-5p	72	-0.02±0.23	0.95	0.99	miR_7_5p	0.06±0.46	0.89	0.98
miR-383-5p	73	-0.03±0.39	0.95	0.99	miR_107	-0.07±0.67	0.92	0.98
miR-375	74	-0.02±0.34	0.95	0.99	miR_10b_5p	-0.01±0.16	0.93	0.98
miR-15a-5p	75	-0.01±0.23	0.96	0.99	miR_451a	0.02±0.23	0.93	0.98
miR-21-5p	76	0.01±0.27	0.96	0.99	miR_19a_3p	0.01±0.17	0.94	0.98
miR-27a-3p	77	-0.01±0.34	0.97	0.99	miR_29a_3p	-0.02±0.22	0.95	0.98
miR-125a-5p	78	0.01±0.4	0.97	0.99	miR_200a_3p	0.01±0.28	0.97	1.00
miR-107	79	-0.01±0.58	0.98	0.99	miR_659_3p	0.00±0.50	1.00	1.00
miR-208a-3p	80	0±0.22	0.99	0.99	miR_126_5p	0.00±0.37	1.00	1.00

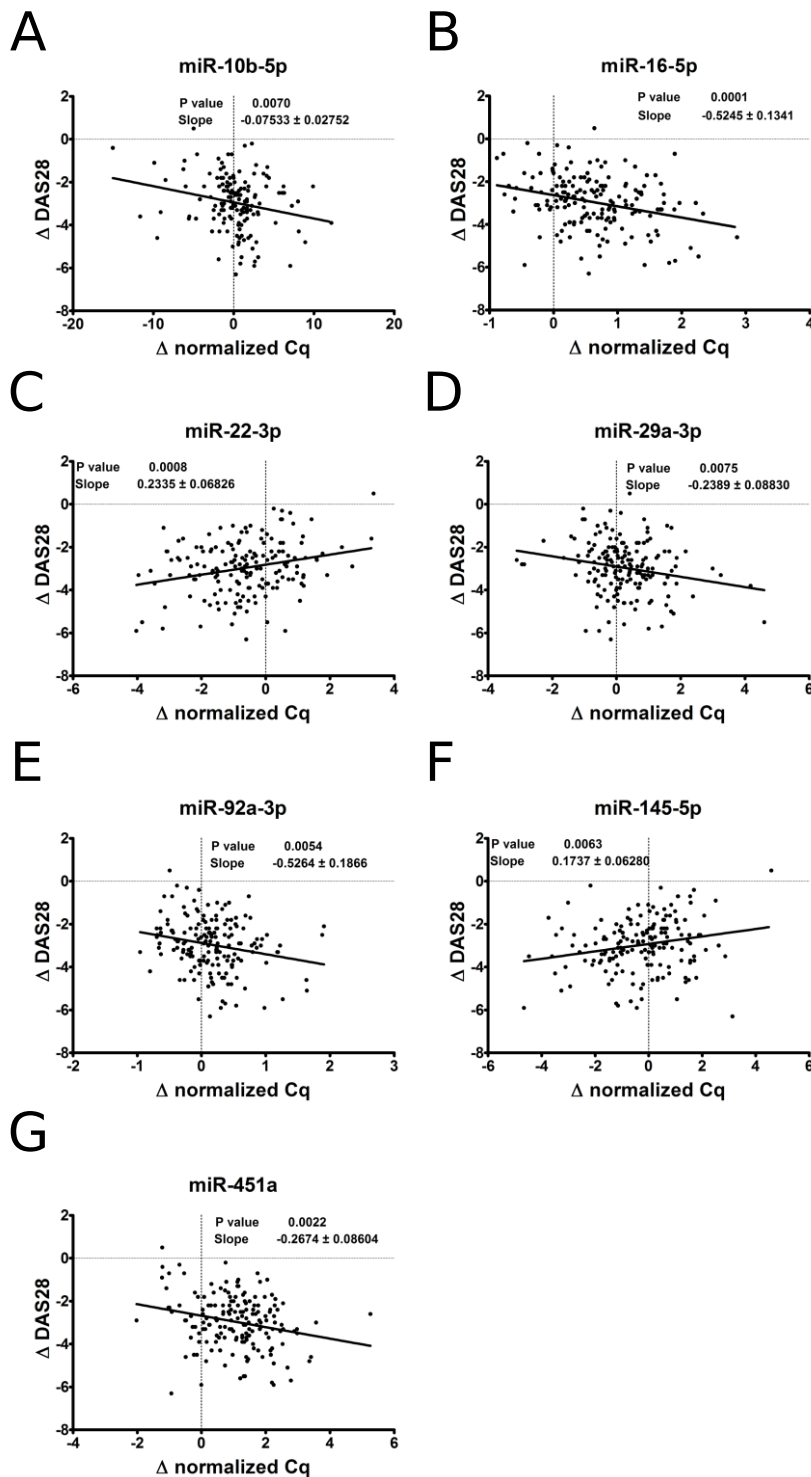
Supplementary Table 6. Univariate analyses of association between 3-month change in micro-RNA and 12-month ACR/EULAR Boolean remission

hsa-miRNA	Adalimumab group				Placebo group			
	Rank	Regr. Coeff. ± SE	p-value	q-value	Rank	Regr. Coeff. ± SE	p-value	q-value
miR-27a-3p	1	-0.56±0.14	0.0002	0.02	39	0.13±0.18	0.46	0.95
miR-423-5p	2	-0.51±0.19	0.01	0.31	4	0.35±0.19	0.07	0.94
miR-146a-5p	3	-0.43±0.17	0.01	0.31	77	0.01±0.19	0.95	0.96
miR-10a-5p	4	1.25±0.52	0.02	0.31	43	-0.3±0.47	0.52	0.96
miR-29b-3p	5	1.23±0.52	0.02	0.31	64	0.12±0.49	0.8	0.96
miR-21-5p	6	-0.29±0.13	0.03	0.36	33	0.09±0.11	0.43	0.94
miR-122-5p	7	1.46±0.67	0.03	0.36	59	0.2±0.66	0.76	0.96
miR-579-3p	8	-0.82±0.39	0.04	0.39	21	-0.36±0.34	0.3	0.94
miR-27b-3p	9	-0.55±0.27	0.05	0.41	67	0.07±0.35	0.84	0.96
miR-24-3p	10	-0.29±0.15	0.06	0.42	34	0.13±0.17	0.43	0.94
miR-23a-3p	11	-0.81±0.43	0.07	0.42	10	0.63±0.46	0.17	0.94
miR-19a-3p	12	-0.42±0.23	0.07	0.42	19	0.29±0.26	0.26	0.94
miR-145-5p	13	-0.58±0.32	0.08	0.42	24	0.37±0.38	0.34	0.94
miR-29c-3p	14	0.6±0.34	0.08	0.42	68	0.05±0.28	0.86	0.96
miR-363-3p	15	0.51±0.29	0.08	0.42	28	-0.34±0.37	0.36	0.94
miR-10b-5p	16	1.31±0.77	0.09	0.42	9	1.09±0.76	0.16	0.94
let-7c-5p	17	-0.55±0.32	0.1	0.42	70	-0.05±0.29	0.87	0.96
miR-140-3p	18	-0.51±0.31	0.1	0.42	25	0.26±0.28	0.35	0.94
miR-19b-3p	19	-0.26±0.16	0.1	0.42	6	0.31±0.18	0.09	0.94
miR-18a-5p	20	-0.82±0.51	0.11	0.42	18	0.7±0.6	0.25	0.94
miR-7-5p	21	0.39±0.24	0.11	0.42	63	-0.08±0.31	0.8	0.96
miR-221-3p	22	-0.36±0.25	0.15	0.52	56	0.09±0.25	0.73	0.96
miR-107	23	0.33±0.23	0.15	0.52	17	-0.45±0.38	0.24	0.94
miR-28-3p	24	0.28±0.2	0.16	0.52	11	-0.4±0.3	0.19	0.94
miR-184	25	0.28±0.21	0.19	0.57	55	-0.07±0.19	0.7	0.96
miR-126-5p	26	-0.23±0.18	0.19	0.57	15	0.23±0.18	0.2	0.94
miR-26b-5p	27	-0.25±0.2	0.21	0.6	2	-0.39±0.21	0.06	0.94
miR-133a-3p	28	-0.42±0.34	0.22	0.6	1	0.92±0.44	0.04	0.94
miR-199a-b-3p	29	-0.27±0.23	0.23	0.6	40	0.24±0.34	0.47	0.95
miR-378a-3p	30	0.26±0.22	0.23	0.6	27	-0.26±0.28	0.35	0.94
miR-335-5p	31	-0.37±0.3	0.23	0.6	16	0.41±0.33	0.22	0.94
miR-451a	32	0.28±0.24	0.24	0.6	26	-0.24±0.25	0.35	0.94
miR-125a-5p	33	-0.34±0.3	0.26	0.6	13	-0.37±0.29	0.2	0.94
miR-223-3p	34	-0.14±0.12	0.26	0.6	73	0.02±0.16	0.92	0.96
miR-16-5p	35	-0.18±0.16	0.28	0.6	35	0.12±0.15	0.43	0.94
miR-146b-5p	36	-0.14±0.13	0.28	0.6	20	0.19±0.18	0.29	0.94
miR-383-5p	37	0.22±0.2	0.28	0.6	38	-0.18±0.24	0.45	0.94
let-7d-5p	38	-0.37±0.35	0.29	0.6	71	-0.05±0.36	0.88	0.96
miR-208b-3p	39	0.28±0.26	0.3	0.6	29	0.29±0.32	0.37	0.94
miR-142-3p	40	0.16±0.15	0.3	0.6	45	-0.09±0.16	0.57	0.96
miR-181b-5p	41	-0.23±0.23	0.31	0.6	62	-0.07±0.24	0.78	0.96
miR-659-3p	42	0.31±0.31	0.32	0.6	5	-0.72±0.41	0.08	0.94

miR-342-3p	43	0.22±0.22	0.33	0.61	57	-0.08±0.23	0.73	0.96
miR-128-3p	44	-0.26±0.27	0.34	0.61	51	0.17±0.39	0.67	0.96
miR-100-5p	45	0.61±0.7	0.39	0.68	65	-0.17±0.77	0.82	0.96
miR-106a-5p	46	-0.11±0.13	0.4	0.68	12	0.16±0.13	0.2	0.94
miR-125b-5p	47	0.18±0.22	0.4	0.68	44	0.36±0.61	0.56	0.96
miR-92a-3p	48	-0.09±0.11	0.41	0.68	60	-0.03±0.11	0.77	0.96
miR-29a-3p	49	-0.2±0.24	0.41	0.68	58	0.09±0.25	0.73	0.96
miR-17-5p	50	-0.1±0.13	0.42	0.68	41	0.08±0.12	0.52	0.96
let-7a-5p	51	0.34±0.47	0.47	0.73	74	0.05±0.56	0.93	0.96
miR-98-5p	52	0.41±0.57	0.47	0.73	54	0.24±0.59	0.68	0.96
miR-206	53	0.2±0.28	0.48	0.73	32	0.24±0.3	0.42	0.94
miR-155-5p	54	0.16±0.26	0.54	0.78	22	-0.27±0.27	0.32	0.94
miR-208a-3p	55	0.12±0.2	0.54	0.78	48	0.12±0.24	0.61	0.96
miR-375	56	0.23±0.39	0.55	0.78	46	-0.24±0.44	0.58	0.96
let-7i-5p	57	0.08±0.14	0.56	0.78	42	0.12±0.18	0.52	0.96
miR-22-3p	58	-0.16±0.32	0.61	0.83	66	-0.07±0.32	0.84	0.96
miR-103a-3p	59	0.18±0.37	0.62	0.83	79	-0.03±0.51	0.96	0.96
miR-34a-5p	60	-0.1±0.2	0.63	0.83	3	-0.4±0.22	0.07	0.94
miR-23b-3p	61	0.32±0.68	0.64	0.83	23	0.71±0.73	0.33	0.94
miR-193b-3p	62	0.19±0.41	0.65	0.83	76	0.04±0.56	0.94	0.96
miR-106b-5p	63	-0.07±0.17	0.7	0.89	53	0.1±0.23	0.67	0.96
miR-638	64	-0.04±0.12	0.72	0.89	30	0.1±0.12	0.38	0.94
miR-101-3p	65	0.12±0.35	0.73	0.89	61	0.14±0.48	0.78	0.96
miR-132-3p	66	0.25±0.72	0.73	0.89	72	0.13±0.94	0.89	0.96
miR-224-5p	67	-0.13±0.47	0.78	0.93	47	0.3±0.57	0.6	0.96
miR-218-5p	68	0.04±0.18	0.82	0.94	78	-0.01±0.25	0.95	0.96
miR-203a-3p	69	0.05±0.22	0.83	0.94	52	-0.08±0.18	0.67	0.96
miR-15b-5p	70	-0.09±0.4	0.83	0.94	37	0.27±0.35	0.45	0.94
miR-15a-5p	71	0.04±0.21	0.84	0.94	69	0.05±0.31	0.86	0.96
miR-192-5p	72	0.04±0.21	0.85	0.94	36	-0.2±0.25	0.43	0.94
miR-26a-5p	73	-0.03±0.14	0.86	0.94	80	-0.01±0.17	0.96	0.96
miR-200a-3p	74	-0.06±0.36	0.87	0.94	7	0.74±0.46	0.11	0.94
miR-126-3p	75	0.01±0.11	0.91	0.97	75	-0.01±0.11	0.94	0.96
miR-150-5p	76	0.02±0.22	0.93	0.97	31	-0.22±0.26	0.39	0.94
let-7b-5p	77	-0.01±0.16	0.94	0.97	50	0.08±0.18	0.64	0.96
miR-590-5p	78	-0.01±0.13	0.96	0.98	8	0.23±0.15	0.13	0.94
miR-20a-5p	79	0.01±0.12	0.97	0.98	14	0.16±0.12	0.2	0.94
miR-181a-5p	80	-0.01±0.43	0.98	0.98	49	0.23±0.49	0.64	0.96

Linear mixed effects model (hospital=random effect). A negative regression coefficient corresponds to a lower level of pre-treatment miRNA predictive of remission and vice versa. False discovery rate corrections for multiple testing (q-values) are based on the total number miRNAs analyzed per hypothesis (N=80). Feature-selected miRNAs (p<0.1) in bold. Abbreviations: hsa, homo sapiens; Regr. Coeff., β regression coefficient; SE, standard error;

Supplementary Figure 2. Circulating miRNA levels and change in DAS28 in all RA patients after 3 months treatment. Significant correlations of 7 miRNAs.



Supplementary Table 7. Correlations between change in micro-RNA levels and change in DAS28

Δ miRNA	Δ DAS28				Δ CRP		Δ SJC		Δ TJC		Δ PG	
	Regr. Coeff.	95%CI	p-value	q-value	Corr.	p-value	Corr.	p-value	Corr.	p-value	Corr.	p-value
miR-16-5p	-0.52	-0.26 - -0.79	1*10⁻⁴	0.01	↓	0.001	↓	0.010	↓	0.005	↓	0.02
miR-22-3p	0.23	0.10 -0.10 -	8*10⁻⁴	0.03	↑	7*10⁻⁵	↑	0.007	↑	0.03	↑	0.05
miR-451a	-0.27	-0.44 -0.16 -	0.002	0.06	↓	0.001		0.26		0.22	↓	0.005
miR-92a-3p	-0.53	-0.89 0.30 -	0.005	0.09		0.31		0.13	↓	0.05		0.03
miR-145-5p	0.17	0.05 -0.02 -	0.006	0.09	↑	0.03		0.28		0.14		0.11
miR-10b-5p	-0.08	-0.13 -0.06 -	0.007	0.09	↓	0.006		0.74		0.37	↓	0.004
miR-29a-3p	-0.24	-0.41	0.008	0.09		0.31		0.30		0.05		0.05

Linear regression of Δ miRNA (baseline minus 3-months value) and Δ DAS28 (baseline minus 3-months value) – a positive coefficient represents a positive correlation between miRNA level and DAS28 score. Correlation between Δ miRNA level and Δ clinical variable: ↑ = positive correlation, ↓ = negative correlation. Abbreviations: DAS28, disease activity score across 28-joints; CRP, C-reactive protein; SJC, swollen joint count; TJC, tender joint count; PG, patient global VAS; Corr., correlation; Coeff., estimated coefficients; CI, confidence interval.

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