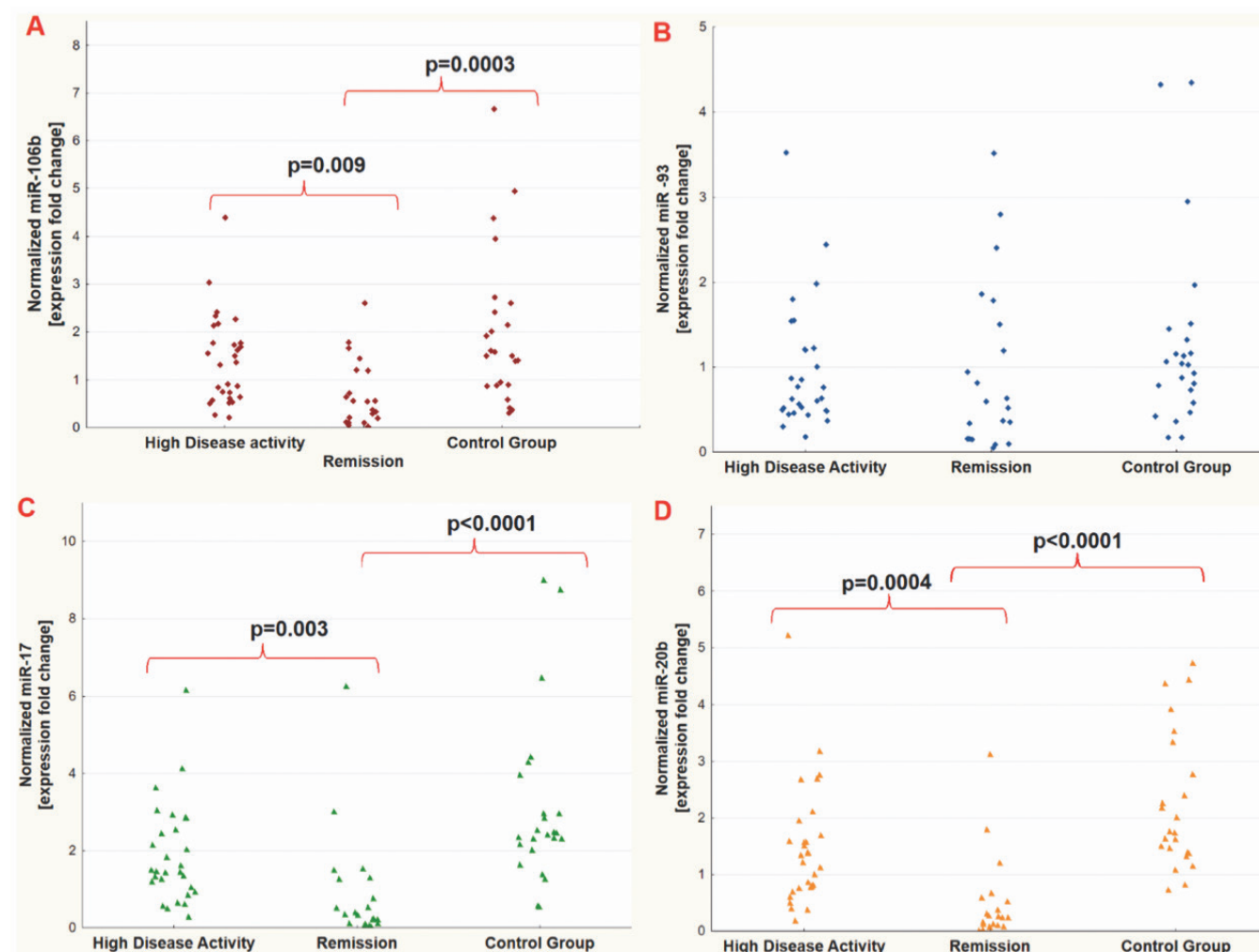


Supplementary Table S1. Differences in micro-RNAs concentration levels between patients with rheumatoid arthritis and healthy controls.

micro-RNA name	RA overall, n=50	Control Group, n=24	<i>p</i> -value*
hsa-miR-22-3p	1.35 [0.67-1.95]	0.8 [0.55-0.99]	0.005
hsa-miR-221-3p	0.6 [0.44-1.09]	0.6 [0.42-0.87]	0.64
hsa-miR-26a-5p	0.87 [0.09-2.49]	3.97 [2.98-5.91]	<0.0001
hsa-miR-125b-5p	1.02 [0.16-2.07]	2.47 [1.73-4.26]	<0.0001
hsa-miR-20b-5p	0.77 [0.26-1.57]	1.75 [1.38-3.05]	<0.0001
hsa-miR-17-5p	1.26 [0.41-2.04]	2.44 [2.09-3.47]	0.0001
hsa-miR-93-5p	0.62 [0.44-1.22]	1.03 [0.65-1.38]	0.13
hsa-miR-106b-5p	0.79 [0.49-1.68]	1.54 [0.88-2.51]	0.008

*A *p*-value was estimated by Mann-Whitney U-test. Statistically significant differences are given in bold. Micro-RNA expression data are given by median [interquartile range]. Hsa-miR: human micro-RNA; RA: patients with rheumatoid arthritis.

**Supplementary Fig. S1.** Diagrams from **A** to **D** show the concentration levels of miR-106b, miR-93, miR-17 and miR-20b, respectively.

A: the differences were found between high disease activity and remission ($p=0.009$) as well as between controls and remission ($p=0.0003$).

B: no differences were found between studied groups.

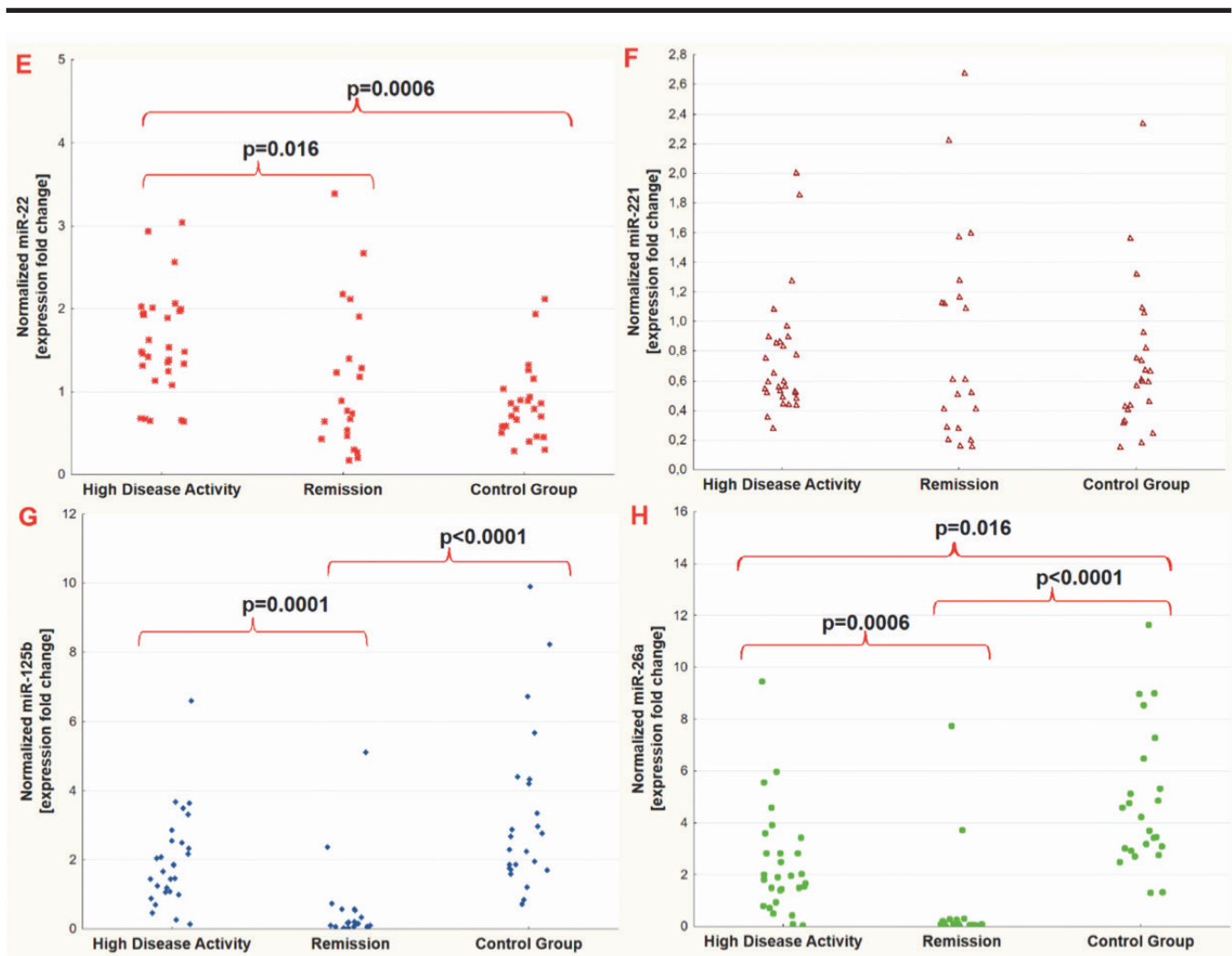
C: the differences were found between high disease activity and remission ($p=0.003$) as well as between controls and remission ($p<0.0001$).

D: the differences were found between high disease activity and remission ($p=0.0004$) as well as between controls and remission ($p<0.0001$).

Supplementary Table S2. Differences between micro-RNAs concentration levels between patients divided into disease activity and healthy controls.

micro-RNA name	High Disease Activity, n=29	Remission, n=21	Control Group, n=24	p-value*
hsa-miR-22-3p	1.48 [1.25-1.97]	0.77 [0.47-1.4]	0.8 [0.55-0.99]	0.0004
hsa-miR-221-3p	0.59 [0.52-0.87]	0.61 [0.29-1.17]	0.6 [0.42-0.87]	0.88
hsa-miR-26a-5p	1.9 [1.41-2.84]	0.09 [0.03-0.23]	3.97 [2.98-5.91]	<0.0001
hsa-miR-125b-5p	1.66 [1.07-2.48]	0.15 [0.06-0.54]	2.47 [1.73-4.26]	<0.0001
hsa-miR-20b-5p	1.34 [0.78-1.69]	0.24 [0.1-0.52]	1.75 [1.38-3.05]	<0.0001
hsa-miR-17-5p	1.46 [1.05-2.54]	0.34 [0.11-1.26]	2.44 [2.09-3.47]	<0.0001
hsa-miR-93-5p	0.63 [0.49-1.21]	0.59 [0.15-1.5]	1.03 [0.65-1.38]	0.23
hsa-miR-106b-5p	1.36 [0.63-1.76]	0.54 [0.19-1.19]	1.54 [0.88-2.51]	0.0004

*A p-value was estimated by Kruskal-Wallis Anova. Statistically significant differences are given in bold. Micro-RNA expression data are given by median [interquartile range]. Abbreviations: please refer to Suppl. Table S1.



Supplementary Fig. S2. Diagrams from E to H show the concentration levels of miR-22, miR-221, miR-125b and miR-26a, respectively. E: the differences were found between high disease activity and remission ($p=0.016$) as well as between high disease activity and controls ($p=0.0006$). F: no differences between studied groups were found. G: the differences were found between high disease activity and remission ($p=0.0001$) as well as between remission and controls ($p<0.0001$). H: the differences were found between high disease activity and remission ($p=0.0006$), high disease activity and controls ($p=0.016$) as well as between remission and controls ($p<0.0001$).

Supplementary Table S3. The multilinear logistic regression analysis using presence of disease as outcome.

The presence of disease (patients with rheumatoid arthritis vs. controls was used as dependent variable.
R = 0.68; R² = 0.46 and R² (adjusted) = 0.41

micro-RNA name	b*	Standard error from b*	b	Standard error from b	T	p-value
Intercept			0.641513	0.095450	6.72091	0.000000
hsa-miR-22-3p	0.420194	0.111460	0.272532	0.072292	3.76989	0.000348
hsa-miR-26a-5p	-0.661038	0.330027	-0.115087	0.057458	-2.00298	0.049228
hsa-miR-125b-5p	0.088602	0.329506	0.021240	0.078989	0.26889	0.788837
hsa-miR-20b-5p	0.246144	0.302611	0.094850	0.116609	0.81340	0.418870
hsa-miR-17-5p	-0.030249	0.347098	-0.007683	0.088163	-0.08715	0.930813
hsa-miR-106b-5p	-0.282954	0.192195	-0.108252	0.073529	-1.47222	0.145643

Statistically significant values are given in bold.

Supplementary Table S4. Spearman's rank correlation between micro-RNAs and the clinical variables.

micro-RNA\clinical variable	Age	Disease duration	ESR	CRP	no. of swelling joints	No. of painful joints	DAS-28	ACPA	RF
miR-22	0.09	-0.27	0.41	0.49	0.26	0.21	0.33	0.21	0.16
miR-26a	0.2	0.14	0.49	0.41	0.43	0.74	0.63	0.23	0.16
miR-106b	0.27	-0.01	0.38	0.35	0.25	0.54	0.48	0.2	0.21
miR-93	0.06	-0.09	0.15	0.16	0.05	0.24	0.19	0.18	0.08
miR-17	0.17	0.07	0.4	0.36	0.31	0.65	0.54	0.19	0.1
miR-221	0.06	-0.07	0.1	0.08	-0.03	0.1	0.09	0.2	0.12
miR-20b	0.31	0.13	0.49	0.41	0.39	0.71	0.6	0.24	0.24
miR-125b	0.25	0.18	0.5	0.45	0.44	0.74	0.64	0.21	0.16

The significant correlations are given in bold. ACPA: anti-citrullinated protein antibodies; CRP: C-reactive protein; DAS-28: disease activity score 28; ESR: erythrocyte sedimentation rate; RF: rheumatoid factor.

Supplementary Table S5. Differences between micro-RNA concentration levels in rheumatoid factor-positive and rheumatoid factor-negative patients.

micro-RNA name	RF-positive RA patients, n=35	RF-negative RA patients, n=15	p-value
hsa-miR-22-3p	1.35 [0.89-2.03]	0.77 [0.3-1.91]	0.04
hsa-miR-221-3p	0.61 [0.51-1.09]	0.52 [0.2-0.83]	0.09
hsa-miR-26a-5p	0.8 [0.11-2.0]	1.5 [0.03-3.43]	0.58
hsa-miR-125b-5p	1.05 [0.26-2.04]	0.99 [0.06-2.37]	0.51
hsa-miR-20b-5p	0.78 [0.37-1.58]	0.76 [0.07-1.51]	0.27
hsa-miR-17-5p	1.26 [0.54-1.83]	1.33 [0.1-2.87]	0.51
hsa-miR-93-5p	0.63 [0.45-1.5]	0.52 [0.14-1.19]	0.16
hsa-miR-106b-5p	0.86 [0.52-1.76]	0.63 [0.1-1.49]	0.14

A p-value was estimated by Mann-Whitney U-test. Statistically significant differences are given in bold. Micro-RNA expression data are given by median [interquartile range]. Abbreviations: please refer to Suppl. Tables S1 and S4.

Supplementary Table S6. The multilinear logistic regression analysis using disease activity score 28 as outcome.

Disease activity score 28 was used as dependent variable.
R =0.98; R² =0.97 and R² (adjusted) =0.95

Variable	b*	Standard error from b*	b	Standard error from b	T	p-value
Intercept			1.041078	0.384040	2.710862	0.010841
Age, years	0.023632	0.043250	0.003916	0.007166	0.546404	0.588700
Disease duration, years	0.012391	0.044020	0.003211	0.011408	0.281486	0.780208
CRP	0.008679	0.048113	0.000510	0.002829	0.180392	0.858019
ESR	0.346180	0.072695	0.025073	0.005265	4.762095	0.000042
Number of painful joints	0.413107	0.059489	0.148209	0.021343	6.944220	0.000000
Number of swollen joints	0.128767	0.057090	0.062550	0.027732	2.255519	0.031304
VAS PGA	0.194515	0.100772	0.013555	0.007023	1.930236	0.062770
VAS PhGA	0.093728	0.092818	0.007131	0.007062	1.009809	0.320404
ACPA	-0.000738	0.039898	-0.000003	0.000135	-0.018509	0.985352
RF	0.026602	0.044254	0.001472	0.002449	0.601128	0.552125
hsa-miR-22-3p	0.041472	0.059384	0.113023	0.161839	0.698367	0.490154
hsa-miR-26a-5p	0.068315	0.165305	0.069775	0.168839	0.413264	0.682258
hsa-miR-125b-5p	-0.013910	0.199487	-0.020682	0.296602	-0.069731	0.944856
hsa-miR-20b-5p	-0.019999	0.221076	-0.041325	0.456821	-0.090463	0.928501
hsa-miR-17-5p	-0.041292	0.157846	-0.061932	0.236745	-0.261596	0.795363
hsa-miR-106b-5p	-0.030843	0.122082	-0.072377	0.286483	-0.252640	0.802215

Statistically significant values are given in bold.

VAS PhGA: visual analogue scale physician global assessments; VAS PGA: visual analogue scale patient global assessments; for other abbreviations, please refer to Suppl. Table S4.

Supplementary Table S7. Primers and micro-RNAs sequences.

micro-RNA name	Primer sense 5'→3'	Primer antisense 5'→3'	micro-RNA sequence 5'→3'	miRBase ID
cel-miR-39-3p	GCAGTCACCGGGTGTAATCAG	GGTCCAGTTTTTTTTTTTTTTTCAAG	UCACCGGGUGUAAAUCAGCUUG	MIMAT0000010
hsa-miR-22-3p	CGAGAAGCTGCCAGTTGAAGA	GGTCCAGTTTTTTTTTTTTTTTACAGT	AAGCUGCCAGUUGAAGAACUGU	MIMAT0000077
hsa-miR-221-3p	CGTGAGTGCTACATTGTCTGCTG	TCTTTTTTTTTTTTTTTTGAACCCA	AGCUACAUUGUCUGCGGGUUUC	MIMAT0000278
hsa-miR-26a-5p	CGAGCAGTTCAAGTAATCCAGG	CCAGTTTTTTTTTTTTTTTAGCCT	UUCAAGUAAUCCAGGAUAGGCU	MIMAT0000082
hsa-miR-125b-5p	ATAGTCCCTGAGACCCTTTAACCT	CCCTGAGACCCTTTAACCT	UCCUGAGACCCUAACUUGUGA	MIMAT0000423
hsa-miR-20b-5p	CTAATGGCAAAGTGCTCATAGTG	GGTCCAGTTTTTTTTTTTTTTTCTAC	CAAAGUGCUCAUAGUGCAGGUAG	MIMAT0001413
hsa-miR-17-5p	CAGGTTCAAAGTGCTTACAGTGC	GGTCCAGTTTTTTTTTTTTTTTCTAC	CAAAGUGCUUACAGUGCAGGUAG	MIMAT0000070
hsa-miR-93-5p	TTGGCAAAGTGCTGTTCTGTG	GTCCAGTTTTTTTTTTTTTTTCTACCT	CAAAGUGCUGUUCGUGCAGGUAG	MIMAT0000093
hsa-miR-106b-5p	CTAATGGCAAAGTGCTCATAGTG	GGTCCAGTTTTTTTTTTTTTTTCTAC	UAAAGUGCUGACAGUGCAGAU	MIMAT0000680