Supplemental data

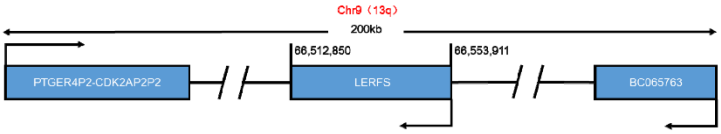

Fig S1. A schematic graphic of the genomic locus of LERFS.

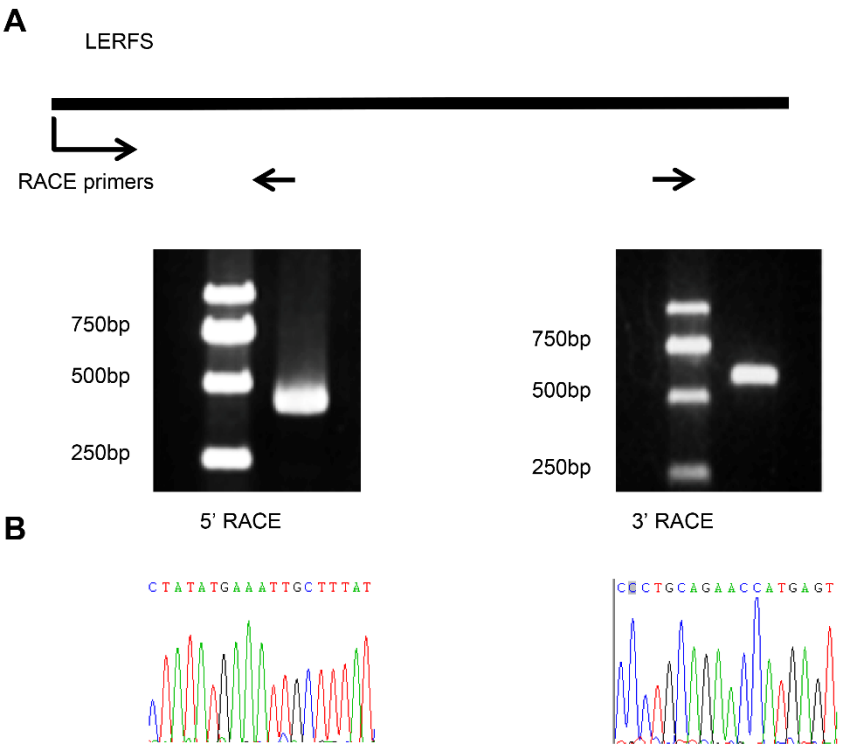

Fig. S2. RACE assay of LERFS. (A) Amplification products of 5' and 3' ends of LERFS. **(B)** Representative pictures of sequencing results of RACE products.

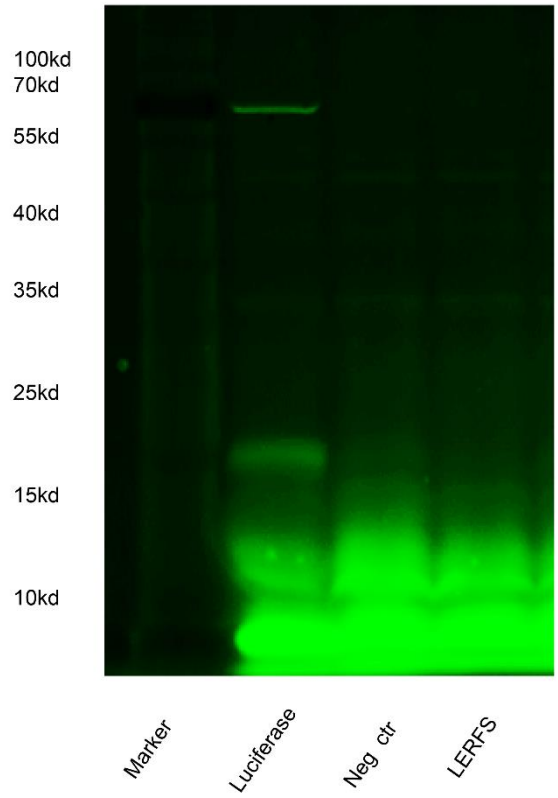

Fig.S3. Analysis of coding capacity of LERFS. Full-length LERFS was cloned into pcDNA3.1 downstream of the T7 promoter and translated *in vitro* using fluorescently labeled transfer RNA (tRNA). Luciferase mRNA was used as a positive translation control, and a mock-translated sample (no RNA template) was used as NC. The fluorescent translation product was resolved by SDS-PAGE and then visualized.

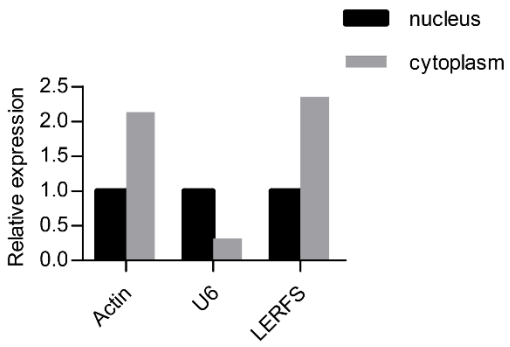

Fig. S4. Localization of LERFS by nuclear/cytoplasm fractionation. RT-qPCR analysis of cytoplasmic and nuclear fraction of HC FLSs revealed that LERFS expression was enriched in cytoplasm. Values are expressed relative to expression level of nucleus. Actin served as a cytoplasmic marker; U6 served as a nuclear marker.

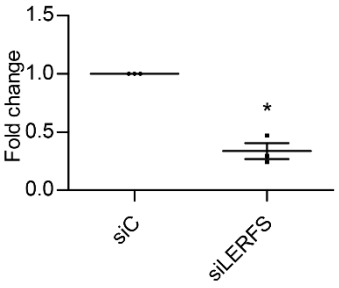

Fig. S5. Efficiency of LERFS knockdown. RA FLSs were transfected with LncRNA Smart Silencer for 48h, and silencing efficiency was determined by RT-qPCR. Data show the Silencing efficiency of LERFS siRNA from 3 independent experiments. Ct values are normalized to GAPDH. *P < 0.05 vs. control Smart Silencer (siC) by Student's t test.

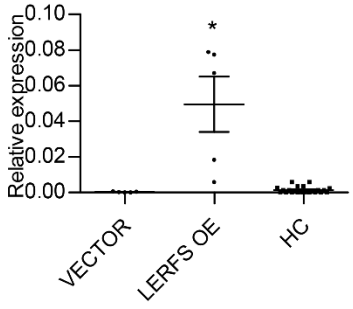

Fig. S6. Infected efficiency of LERFS overexpression lentivirus in RA FLSs. RA FLSs infected with control lentivirus (VECTOR) or LERFS OE for 5 days were analyzed for LERFS expression by RT-qPCR assay. Ct values are normalized to GAPDH. * *P* < 0.05 vs. VECTOR by Student's t test.

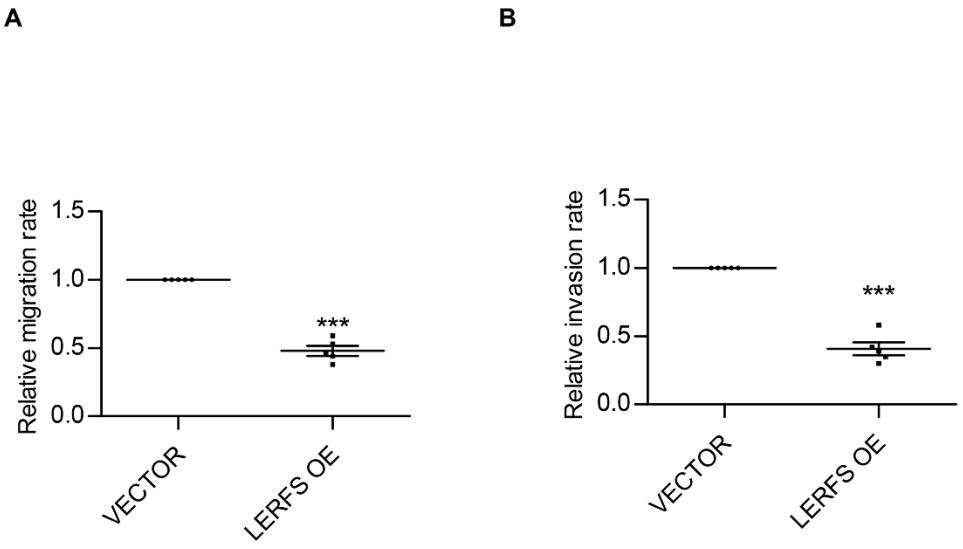

Fig. S7. Inhibitory effect of LERFS overexpression on migration and invasion of RA FLSs induced by monocyte chemoattractant protein-1 (MCP-1). (A) Chemotaxis migration of RA FLSs was evaluated using a Transwell assay. MCP-1 (50 ng/ml) was used as a chemoattractant in the lower wells. (B) In vitro invasion was determined using inserts coated with Matrigel Basement Membrane Matrix. Relative invasion rate was calculated by counting invaded cells and normalized to VECTOR. Data are shown as mean ± SEM from 5 independent experiments of 5 different RA patients. *** $P < 0.001$ vs. VECTOR by Student's t test.

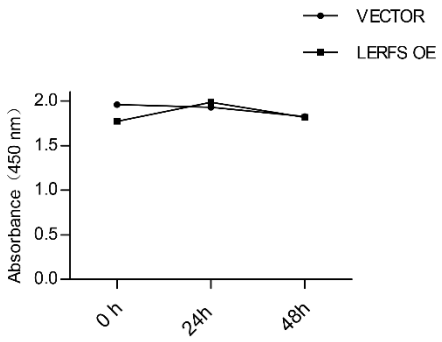

Fig. S8. Growth rate of RA FLSs in serum-free medium at 0, 24 and 48 hours. Cell number was evaluated by absorbance at 490 nm using an MTT assay at the indicated time points after lentivirus infection (D0 indicates day of infection). Values are expressed relative to D0 as mean ± SEM from 3 independent experiments of 3 different patients with RA.

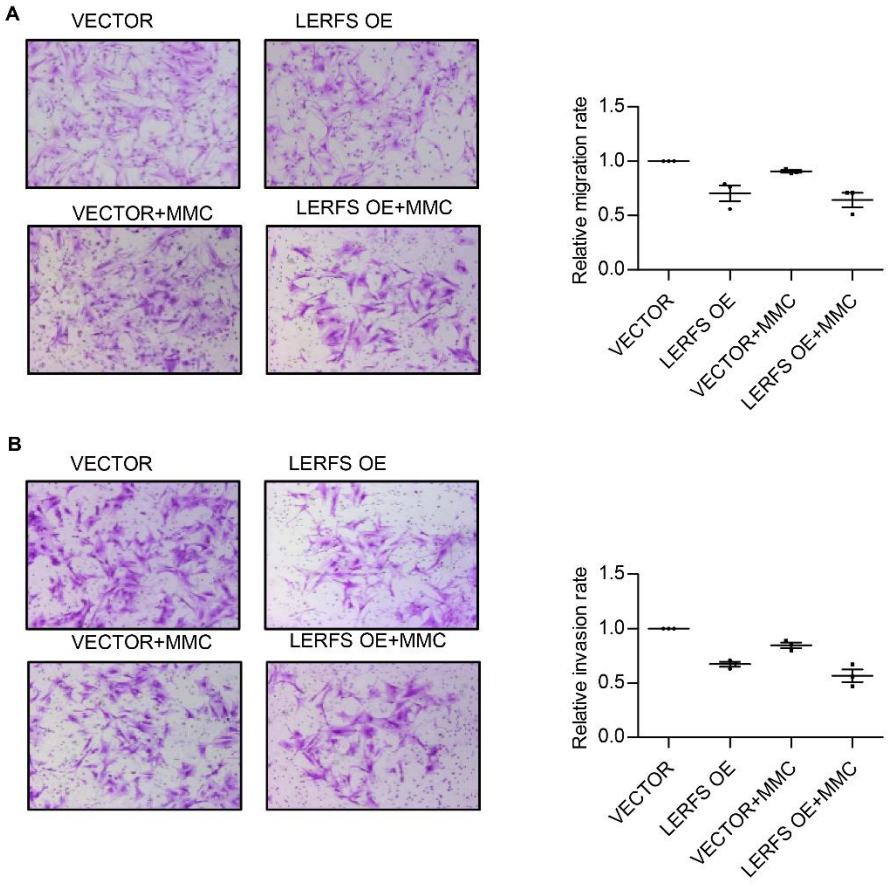

Fig. S9. Effect of a proliferation inhibitor mitomycin on the migration and invasion of RA FLSs. Cells were pretreated with or without mitomycin (MMC，10 μg/ml) for 6 hours. (A) Chemotaxis migration of RA FLSs was evaluated using a Transwell assay. (B) In vitro invasion was determined using inserts coated with Matrigel Basement Membrane Matrix. Relative invasion rate was calculated by counting invaded cells and normalized to VECTOR. Data are shown as mean ± SEM from 3 independent experiments of 3 different RA patients.

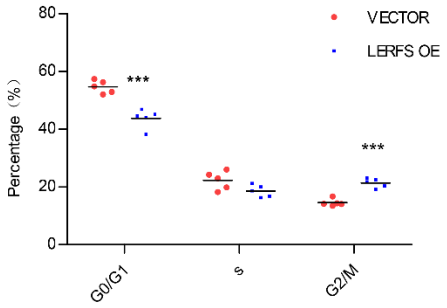

Fig. S10. Effect of LERFS overexpression on cell cycle by RA FLS cell line MH7A. Cells were stained with DAPI and detected by flow cytometry to analyze the cell cycle. Percentages of cells in the different phases of the cell cycle were calculated, and data are shown as mean ± SEM from 5 independent experiments. *** $P < 0.001$ vs. VECTOR by Student's t test.

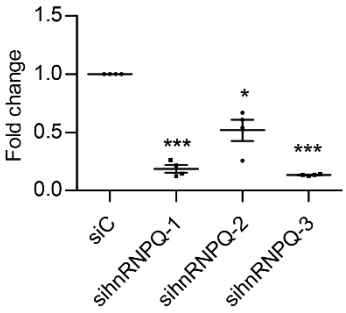

Fig.S11. Silencing efficiency of hnRNP Q siRNA. RA FLSs were transfected with hnRNP Q siRNA Q1–3 for 48 hours and subjected to RT-qPCR analysis. Data shown are mean ± SEM from 3 independent experiments. **P* < 0.05, ***P* < 0.01, ****P* < 0.001 vs. control siRNA (siC) by 1-way ANOVA.

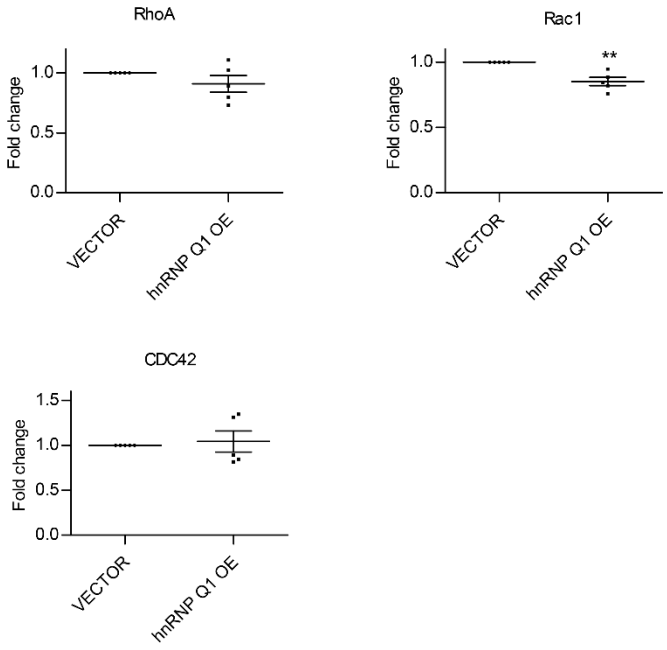

Fig.S12. Effect of hnRNP Q1 on mRNA expression of RhoA, Rac1 and CDC42 in RA FLSs. RA FLSs were infected with control lentivirus (VECTOR) or hnRNP Q1 OE, and mRNA expression of indicated targets was analyzed by RT-qPCR. Ct values are normalized to GAPDH. ** *P* < 0.01 vs. VECTOR by Student's t test.

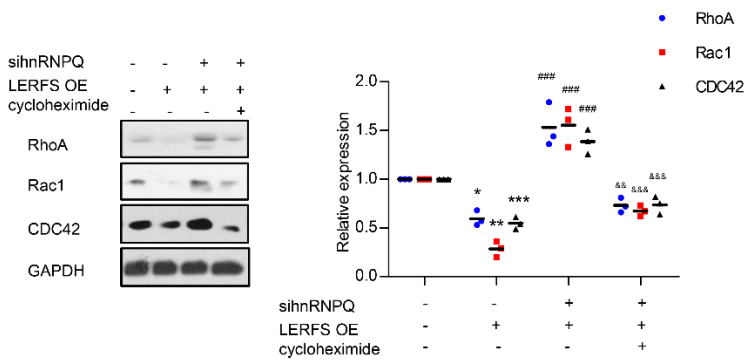

Fig.S13. Effect of translation inhibitor cycloheximide on hnRNP Q knockdown-induced increase of protein expression of CDC 42 and RhoA in LERFS overexpressed-RA FLSs. Cells were transfected with hnRNP Q siRNA or siC for 24 hours, followed by infection of control lentivirus (VECTOR) or LERFS OE for three days, and then treated with or without cycloheximide (10 μM) for 24 hours. Representative WB images are shown in left panel. The semi-quantification of protein levels (right panel) is expressed as mean ± SEM of 3 independent experiments from 3 different RA patients. **P*<0.05, ***P* < 0.01, ****P*<0.001 vs. VECTOR + siC, $^{###}$ *P* < 0.001 vs. LERFS OE + siC, $^{\&\&}$ *P* <0.01, $^{\&\&\&}$ *P* <0.001 vs. sihnRNPQ +LERFS OE by Student's t test

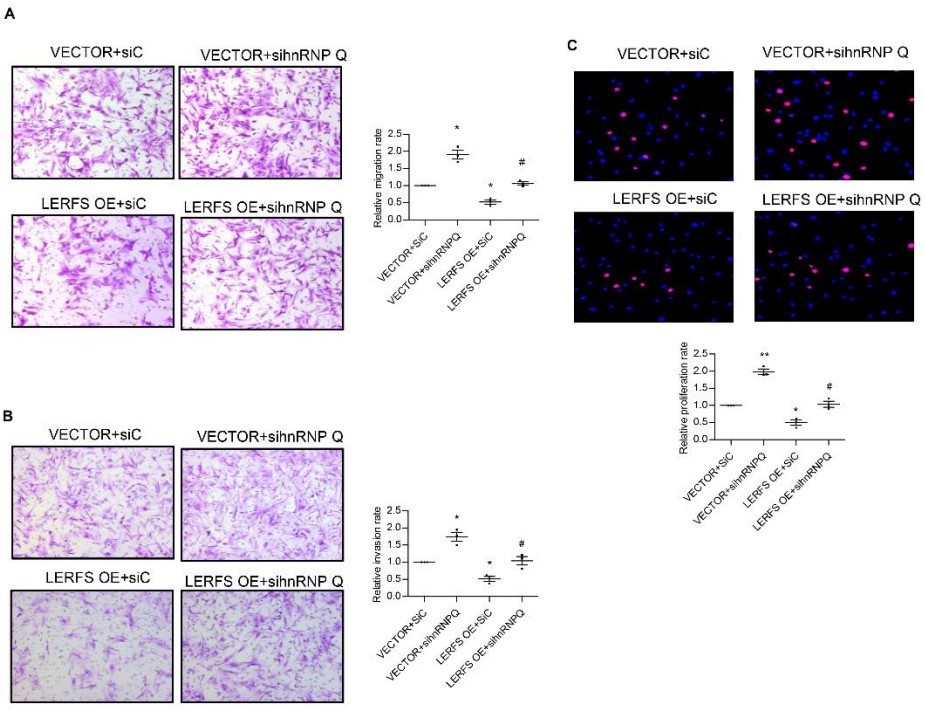

Fig.S14. Effect of hnRNP Q knockdown on migration, invasion and proliferation of LERFS-overexpressed RA FLSs. Cells were transfected with hnRNP Q siRNA or siC for 24 hours, followed by infection of control lentivirus (VECTOR) or LERFS OE for three days. (A) Chemotaxis migration of RA FLSs was evaluated using a Transwell assay. (B) In vitro invasion was determined using inserts coated with Matrigel Basement Membrane Matrix. Relative invasion rate was calculated by counting invaded cells and normalized to VECTOR. (C) An EdU incorporation assay was performed to evaluate cell proliferation. Proliferating RA FLSs were labeled with EdU (red), and nuclei were stained with Hoechst 33342 (blue). Representative images (left panel) are shown (original magnification 200×). Data (right panel) are expressed as mean ± SEM of 3 independent experiments from 3 different RA patients. **P* < 0.05, ***P*<0.01 vs. VECTOR + siC, $^{\#}$*P* < 0.05 vs. LERFS OE + siC by Student's t test.

Tables

Table S1. Demographic and clinical features of patients with active RA.

Age, yrs (mean±SD)	51.50±7.37
Female, n (%)	32 (34)
Disease duration, yrs (mean±SD)	4.00±1.86
Rheumatoid factor-positive, n (%)	26 (34)
Anti-CCP-positive, n (%)	22 (34)
DAS28 (CRP) (mean±SD)	5.69±2.26
Previous medications, n (%)	
Corticosteroids	12 (34)
Methotrexate	18 (34)
Leflunomide	10 (34)
Sulfasalazine	7 (34)
Hydroxychloroquine	15 (34)

Table S2. Comparison of RA patients and HC subjects in age and gender

Group	Number	Age (years) (mean±SD)	Gender (Number)	
			Female	Male
RA	34	51.50±7.37	32	2
HC	29	52.45±8.08	27	2

Table S3. Sequences of primers, siRNA and ASO.

RT-qPCR primers		
GAPDH	Forward	GCACCGTCAAGGCTGAGAAC
	Reverse	TGGTGAAGACGCCAGTGGA
LERFS	Forward	CGACTGGTGCTGAAGTGTTG
	Reverse	CCCTACTCCTGCCTGCTCTA
CDC42	Forward	CCATCGGAATATGTACCGACTG
	Reverse	CTCAGCGGTCGTAATCTGTCA
Rac1	Forward	ATGTCCGTGCAAAGTGGTATC
	Reverse	CTCGGATCGCTTCGTCAAACA
RhoA	Forward	GGAAAGCAGGTAGAGTTGGCT
	Reverse	GGCTGTCGATGGAAAAACACAT
hnRNP Q	Forward	CTGGTCTCAATAGAGGTTATGCG
	Reverse	TCCGGTTGGTGGTATAAAATGAC
MMP-1	Forward	CTCTGGAGTAATGTCACACCTCT
	Reverse	TGTTGGTCCACCTTTCATCTTC
MMP-3	Forward	CGGTTCCGCCTGTCTCAAG
	Reverse	CGCCAAAAGTGCCTGTCTT
MMP-13	Forward	TCCTGATGTGGGTGAATACAATG
	Reverse	GCCATCGTGAAGTCTGGTAAAAT
RACE primers		
LERFS 5' RACE	CGCAGGTAAAGTCCATCCGT	
LERFS 3' RACE	AAACCAAGATTACACAAAAGCG	
UPM	CTAATACGACTCACTATAGGGCAAGCAGTGGTATCAACGCAGAGT	
Clone primers		
LERFS	Forward	CTCTATTGAATGCTGGGTATCTTCCA
	Reverse	AGTGAGGTCGGCGCCC
RiboTM lncRNA Smart Silencer		
LERFS	siRNA-1	CTTCTGCCCTGAATTGAAA
	siRNA-2	CTGATTGCTTTGCCAGTTA
	siRNA-3	GCCAATGACCTGAAGTTAA
	ASO-1	AGGACACTGAGGACTGGGAC
	ASO-2	GACCTGCCAATGACCTGAAG
	ASO-3	AGAAGGCTGTAGAGGGATGA
siRNA		
hnRNP Q	siRNA-1	CCAAGAGATCTATTTGAGG
	siRNA-2	TCACTGGTCTCAATAGAGG
	siRNA-3	GTTGCCAACAATAGGCTTT