

Supplementary Table S1 Basic demographic information of study participants and number of collected samples

	Healthy donors (n = 35)	SjD (n = 111)	RA (n = 40)	SLE (n = 40)	<i>P</i> -value
Age (years)	47.7 ± 10.2	47.8 ± 11.8	51.5 ± 12.7	46.4 ± 12.0	0.302*
Women	35 (100)	106 (95.5)	37 (92.5)	40 (100)	0.292†
Body mass index (kg/m ²)	22.4 ± 2.9	22.2 ± 2.9	22.8 ± 4.3	22.7 ± 4.7	0.805*
	(n = 17)	(n = 95)	(n = 37)		
Disease activity at the time of sampling	–	ESSDAI 3.7 ± 3.1	DAS28 5.03 ± 1.40	SLEDAI 3.9 ± 4.4	
Active disease		ESSDAI ≥ 5: 25 (22.5)	DAS 28 ≥ 3.2: 34 (85.0)	SLEDAI > 4: 29 (72.5)	
Number of collected samples					
Unstimulated whole saliva	35 (100)	65 (56.8)	–	–	
Plasma	35 (100)	79 (71.2)	40 (100)	40 (100)	
PBMCs	35 (100)	103 (92.8)	–	–	

Values are presented as mean ± standard deviation or number (%).

SjD, Sjögren disease; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; ESSDAI, EULAR Sjögren's Syndrome Disease Activity, Index; DAS28, Disease Activity Score 28; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; PBMCs, peripheral blood mononuclear cells.

*, p-values using ANOVA; †, p-values using chi-square test.

Supplementary Table S2 Primer sequences for RT-qPCR

Gene	Forward Primer (5'-3')	Reverse Primer (3'-5')
<i>CO1</i> (heavy strand)	GCCATAACCCAATACCAAACG	CGCAAATGGGCGGTAGGCGTG
<i>CO2</i> (heavy strand)	CTAGTCCTGTATGCCCTTTTCC	CGCAAATGGGCGGTAGGCGTG
<i>CYTB</i> (heavy strand)	CAATTATACCCTAGCCAACCCC	CGCAAATGGGCGGTAGGCGTG
<i>ND1</i> (light strand)	GTTGTGATAAGGGTGGAGAGG	CGCAAATGGGCGGTAGGCGTG
<i>ND4</i> (heavy strand)	CTCACACTCATTCTCAACCCC	CGCAAATGGGCGGTAGGCGTG
<i>ND5</i> (heavy strand)	CTAGGCCTTCTTACGAGCC	CGCAAATGGGCGGTAGGCGTG
<i>ND6</i> (heavy strand)	TCATACTCTTTCACCCACAGC	CGCAAATGGGCGGTAGGCGTG
<i>IFIT1</i>	CAGAATGAGGAAGCCCTGAA	CGCAAATGGGCGGTAGGCGTG
<i>IFIT3</i>	GTTCTCTTGGGCCTGAAACT	CGCAAATGGGCGGTAGGCGTG
<i>IFI44</i>	GGTCATTGAGCTCAGGAAGAG	CGCAAATGGGCGGTAGGCGTG
<i>IFI44L</i>	CAGGACTGTGCATGGATGA	CGCAAATGGGCGGTAGGCGTG
<i>LY6E</i>	TCCGACCAGGACAACACT	CGCAAATGGGCGGTAGGCGTG
<i>OAS1</i>	TGTGTGTCCAAGGTGGTAAAG	CGCAAATGGGCGGTAGGCGTG
<i>MX1</i>	CTGCATCCCACCCTCTATTAC	CGCAAATGGGCGGTAGGCGTG
<i>ISG15</i>	CTCATCTTTGCCAGTACAGGAG	CGCAAATGGGCGGTAGGCGTG
<i>GAPDH</i>	CTCTCTGCTCCTCCTGTTTCGAC	CGCAAATGGGCGGTAGGCGTG

Supplementary Table S3 Drugs prescribed within 3 months prior to enrollment

Drugs	SjD (n=111)	SLE (n=40)	RA (n=40)
Pilocarpine	19 (17.1)	1 (2.5)	0 (0.0)
NSAIDs	14 (12.6)	4 (10.0)	23 (57.5)
Glucocorticoids	9 (8.1)	25 (62.5)	14 (35.0)
PD equivalent dose (mg/day)	3.8 ± 2.3	10.9 ± 19.7	4.0 ± 1.4
Hydroxychloroquine (HCQ)	22 (19.8)	31 (77.5)	5 (12.5)
HCQ dose (mg/day)	284 ± 81	265 ± 61	260 ± 55
Other anti-rheumatic drugs			
Methotrexate	1 (0.9)	5 (12.5)	15 (37.5)
Sulfasalazine	1 (0.9)	0 (0.0)	2 (5.0)
Bucillamine	1 (0.9)	0 (0.0)	1 (2.5)
Mycophenolate	1 (0.9)	8 (20.0)	0 (0.0)
Azathioprine	1 (0.9)	6 (15.0)	0 (0.0)
Leflunomide	0 (0.0)	0 (0.0)	1 (2.5)
Cyclosporine A	0 (0.0)	3 (7.5)	0 (0.0)
Tacrolimus	0 (0.0)	7 (17.5)	1 (2.5)
Cyclophosphamide	0 (0.0)	2 (5.0)	0 (0.0)
Belimumab	0 (0.0)	1 (2.5)	0 (0.0)

Values are presented as mean ± standard deviation or number (%).

SjD, Sjögren disease; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; NSAIDs, non-steroidal anti-inflammatory drugs; PD, prednisolone.

Supplementary Table S4 Comparisons of mt-RNA or interferon-stimulated genes (ISG) scores according to clinical features of Sjögren disease

	Clinical variable	Yes	No	<i>p</i> -value
Saliva mt-RNA score	Highest quartile of ESSDAI or	3.298 ± 1.506	2.386 ± 1.424	0.032
	ClinESSDAI	(n=16)	(n=49)	
	Raynaud phenomenon	3.819 ± 1.893	2.416 ± 1.331	0.008
		(n=9)	(n=56)	
PBMC ISG score	Oral dryness	2.582 ± 1.775	1.787 ± 2.042	0.041
		(n=65)	(n=38)	
	ClinESSDAI >5	3.305 ± 2.093	2.087 ± 1.815	0.015
		(n=24)	(n=79)	
	Highest quartile of ClinESSDAI	3.139 ± 2.207	2.030 ± 1.741	0.012
		(n=17)	(n=86)	

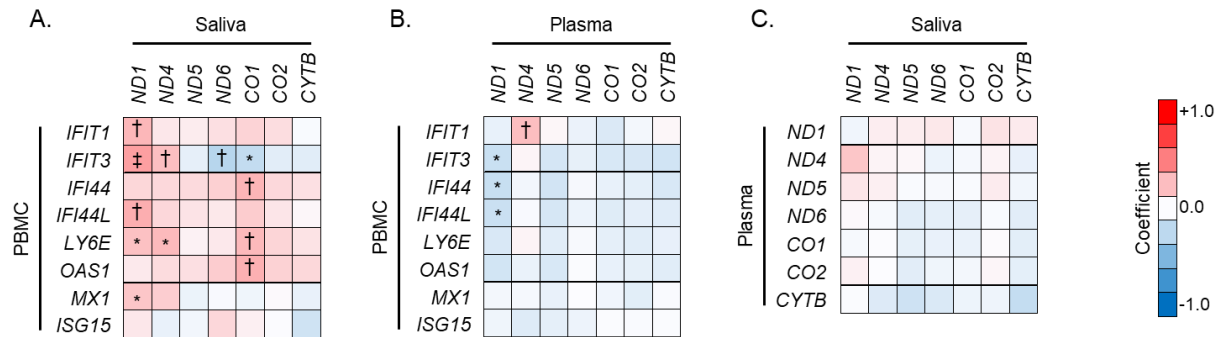
ISG, IFN-stimulated gene; ESSDAI, EULAR Sjögren's Syndrome Disease Activity; ClinESSDAI, Clinical ESSDAI; PBMC, peripheral blood mononuclear cell.

Supplementary Table S5 Comparisons of plasma mt-RNA score according to clinical features of RA or SLE

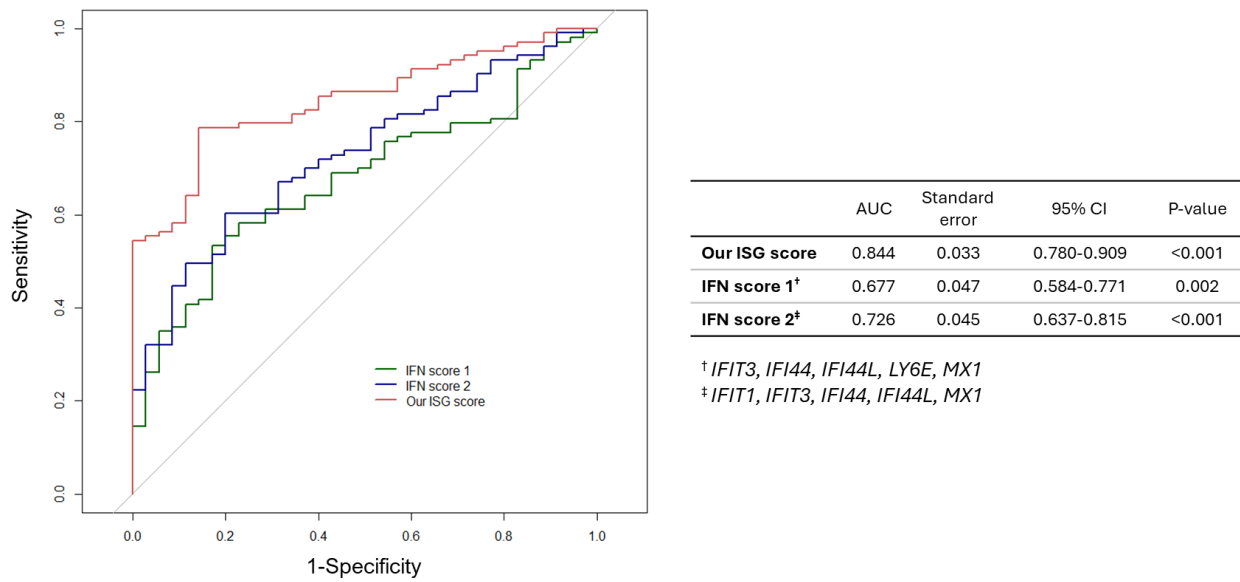
	Clinical variable	Yes	No	<i>p</i> -value
RA	Active disease (DAS28 $\geq$ 3.2)	2.021 $\pm$ 1.145	0.144 $\pm$ 1.764	0.007
		(n=34)	(n=6)	
	Anti-CCP positivity	1.663 $\pm$ 1.670	2.677 $\pm$ 0.154	0.001
		(n=37)	(n=3)	
	Use of hydroxychloroquine	2.646 $\pm$ 0.347	1.610 $\pm$ 1.700	0.003
		(n=5)	(n=35)	
SLE	Moderate-to-high disease activity (SLEDAI $\geq$ 6)	2.719 $\pm$ 1.708	0.966 $\pm$ 1.717	0.014
		(n=8)	(n=32)	
	High disease activity (SLEDAI $\geq$ 11)	3.330 $\pm$ 0.890	1.153 $\pm$ 1.801	0.047
		(n=3)	(n=37)	

RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; DAS28, Disease Activity Score 28; anti-CCP, anti-cyclic citrullinated peptide; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index.

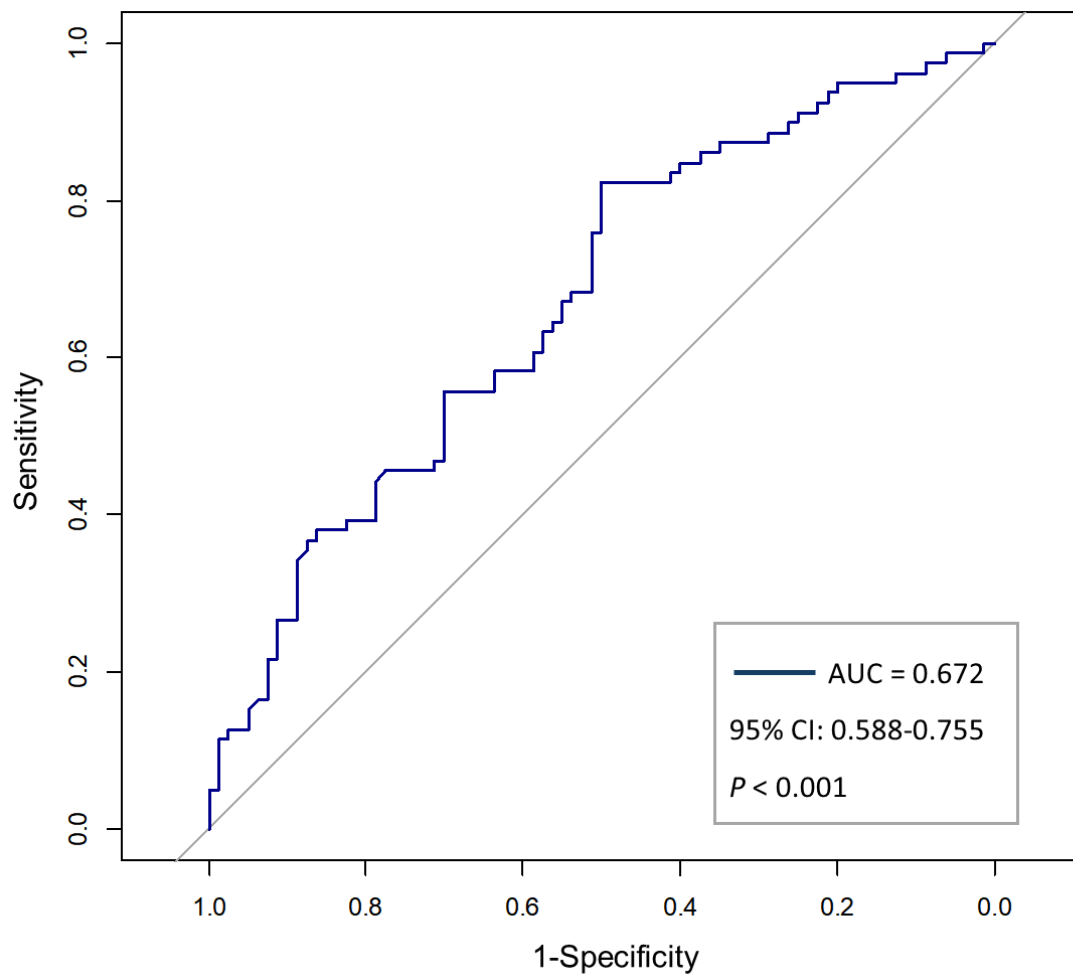
Supplementary Figure S1 Correlations among the expression of plasma mt-RNA, saliva mt-RNA, and PBMC IFN-stimulated genes in patients with Sjögren disease. * $p < 0.05$, † $p < 0.01$, ‡ $p < 0.001$.



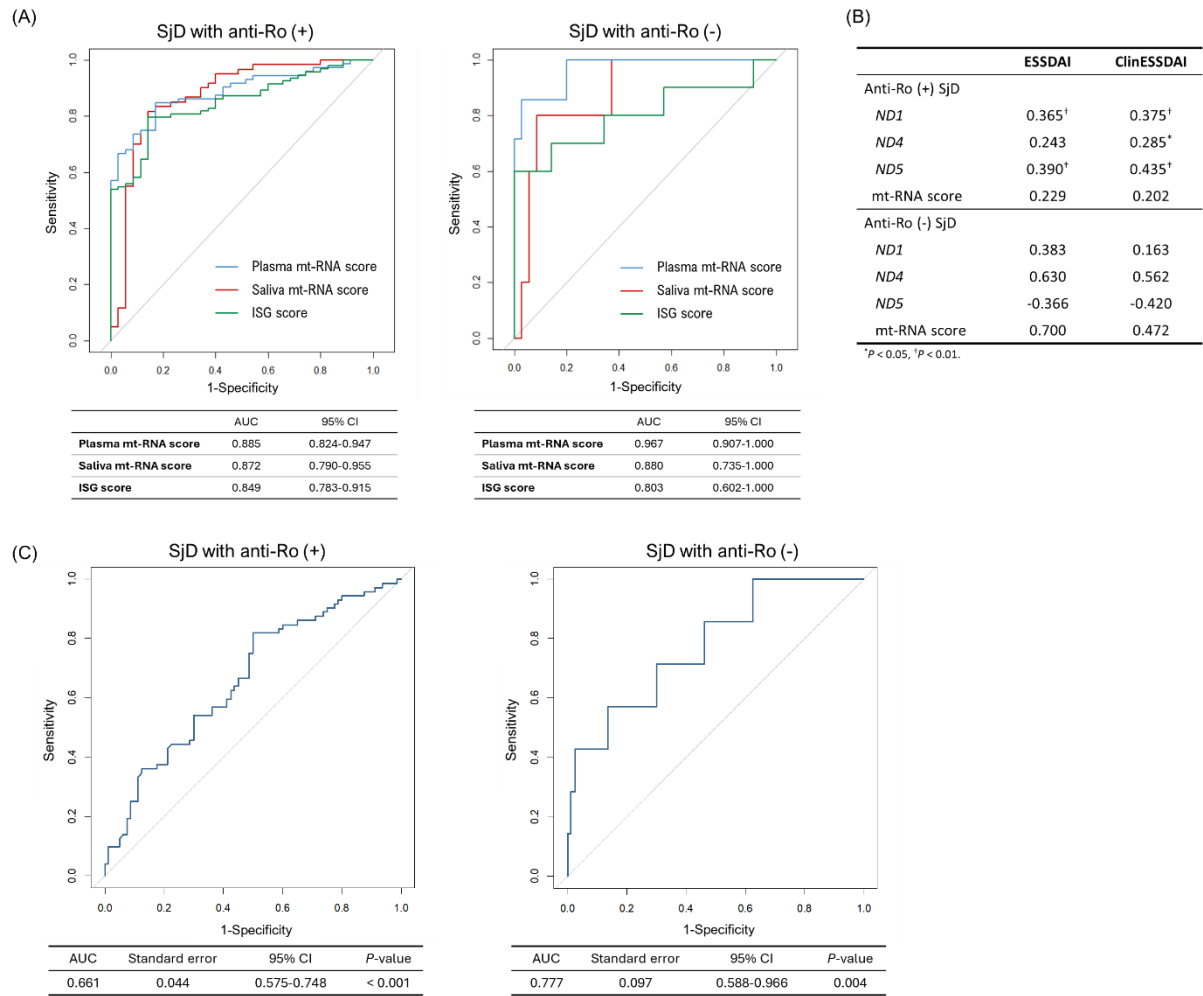
Supplementary Figure S2 Receiver operating characteristic curves of our interferon-stimulated gene (ISG) score and previously suggested interferon (IFN) scores to differentiate patients with Sjögren disease and healthy controls.



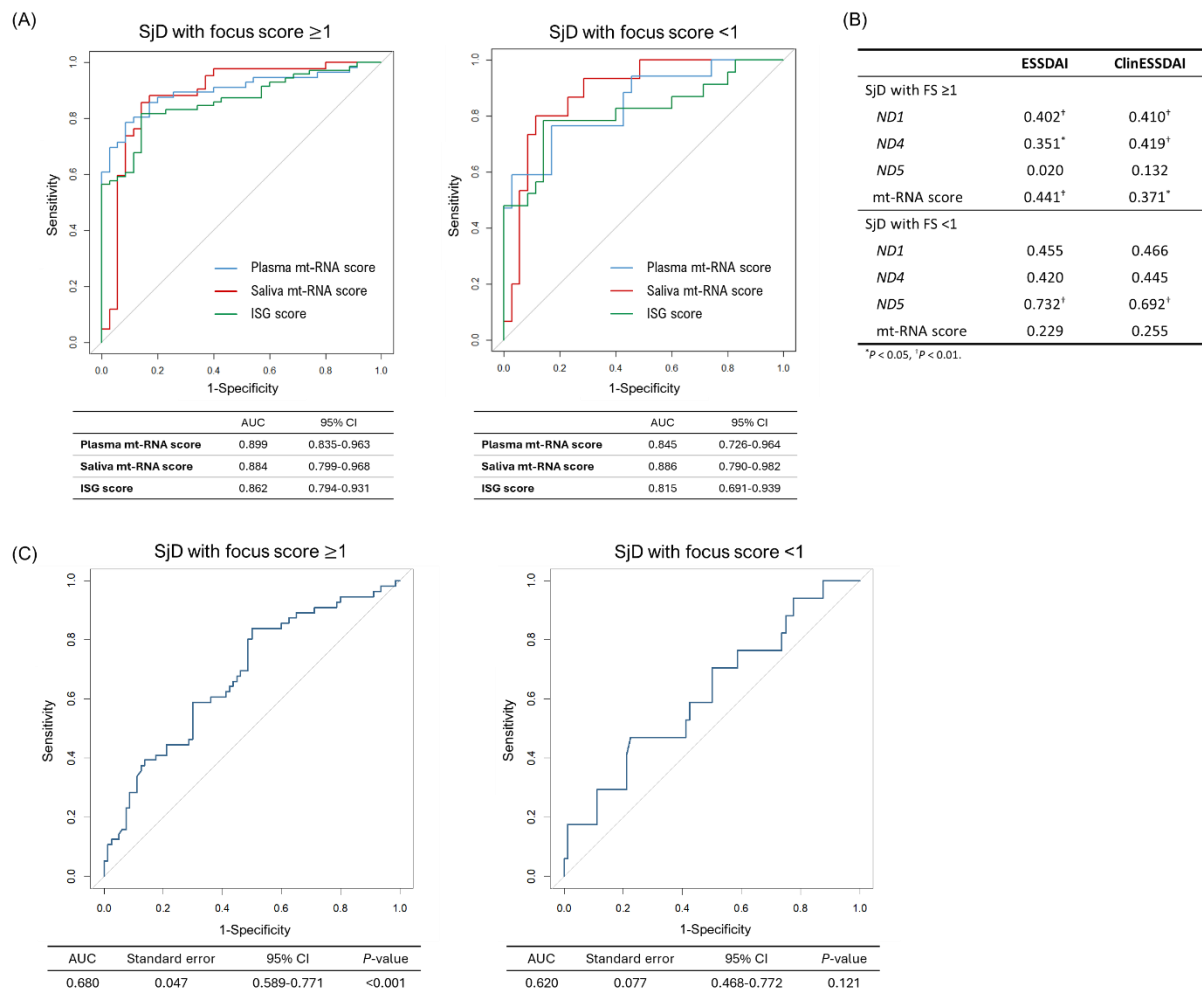
Supplementary Figure S3 The receiver operating characteristics curve of plasma mt-RNA score to differentiate Sjögren disease (SjD) among pooled data from SjD, rheumatoid arthritis, and systemic lupus erythematosus.



Supplementary Figure S4 Sensitivity analysis including only patients with Sjögren disease (SjD) who were anti-SSA/Ro positive (n=101) or negative (n=10). (A) Receiver operating characteristics (ROC) curve for distinguishing patients with SjD from healthy controls. (B) Pearson correlation coefficients between SjD disease activity and saliva levels of *ND1*, *ND4*, or *ND5* mitochondrial (mt)-RNA and mt-RNA scores. (C) ROC curve for distinguishing patients with SjD from those with rheumatoid arthritis and systemic lupus erythematosus.



Supplementary Figure S5 Sensitivity analysis including only patients with Sjögren disease (SjD) who had focus score ≥ 1 ($n=77$) or <1 ($n=24$). (A) Receiver operating characteristics (ROC) curve for distinguishing patients with SjD from healthy controls. (B) Pearson correlation coefficients between SjD disease activity and saliva levels of *ND1*, *ND4*, or *ND5* mitochondrial (mt)-RNA and mt-RNA scores. (C) ROC curve for distinguishing patients with SjD from those with rheumatoid arthritis and systemic lupus erythematosus.



Supplementary Figure S6 Sensitivity analysis including only patients with Sjögren disease (SjD) who had serum total IgG ≥ 1.8 g/dL (n=74) or <1.8 g/dL (n=37). (A) Receiver operating characteristics (ROC) curve for distinguishing patients with SjD from healthy controls. (B) Pearson correlation coefficients between SjD disease activity and saliva levels of *ND1*, *ND4*, or *ND5* mitochondrial (mt)-RNA and mt-RNA scores. (C) ROC curve for distinguishing patients with SjD from those with rheumatoid arthritis and systemic lupus erythematosus.

