Supplementary Table S1. Demographics of subjects classified by each of the Sjögren's syndrome criteria.

	Complete Cohort	Complete data	AECG criteria		ACR criteria	
			Positive	Negative	Positive	Negative
	n=837	n=646	n=279	n=367	n=268	n=378
Age median (range)	55 (12-86)	57 (19-85)	57 (18-85)	54 (17-86)	56 (17-85)	54.5 (19-85)
Female (%)	761 (91%)	587 (91%)	253 (91%)	334 (91%)	247 (92%)	340 (90%)
Race						
Caucasian	617 (74%)	453 (70%)	195 (70%)	258 (70%)	188 (70%)	265 (70%)
African American	19 (2%)	14 (2%)	3 (1%)	11 (3%)	4 (2%)	10 (3%)
Asian	12 (1%)	8 (1%)	5 (2%)	3 (0.8%)	4 (2%)	4 (1%)
Native American	18 (2%)	18 (3%)	10 (4%)	8 (2%)	9 (3%)	9 (2%)
Pacific Islander	1 (0.1%)	1 (0.2%)	0 (0.0%)	1 (0.3%)	0 (0.0%)	1 (0.3%)
2 or more	166 (27%)	148 (23%)	65 (23%)	83 (23%)	62 (23%)	86 (23%)
Unknown	4 (0.5%)	4 (0.6%)	1 (0.4%)	3 (0.8%)	1 (0.4%)	3 (0.8%)

Ethnicity						
Hispanic	26 (3%)	22 (3%)	10 (4%)	12 (3%)	9 (3%)	13 (3%)
Non-Hispanic	809 (97%)	622 (96%)	268 (96%)	354 (97%)	258 (96%)	364 (97%)
Unknown	2 (0.2%)	2 (0.3%)	1 (0.4%)	1 (0.3%)	1 (0.4%)	1 (0.3%)

Supplementary Table S2. Number (%) of subjects of the 646 with complete data set that satisfy or do not satisfy each criterion, irrespective of classification.

	Criteria	
	(+)	(-)
	n (%)	n (%)
Items for AECG classification:		
Ocular symptoms	646 (100)	0 (0)
Oral symptoms	646 (100)	0 (0)
Ocular signs:		
Schirmer's I Test (≤5mm in 5 minutes)	251 (39)	395 (61)
Ocular Dye Score (≥ 4 van Bijsterveld's)	277 (43)	369 (57)
Histopathology (Focus Score ≥1)	273 (42)	373 (58)
Salivary gland involvement:		
Unstimulated salivary flow (≤1.5 ml in 15 min)	339 (52)	307 (48)
Autoantibodies:		
Ro/SSA (+)	174 (27)	472 (73)
La/SSB (+)	112 (17)	534 (83)
Items for ACR classification (not included in AECG classification):		
Positive Serology:		
Rheumatoid Factor (+) and ANA (+)	91 (14)	554 (86)
Keratoconjunctivitis sicca		
Ocular Stain Score (≥ 3)	429 (66)	217 (34)

Supplementary Table S3. Comparison of the performance of Schirmer's I testing of tear production, ocular dye score for evaluation of keratoconjunctivitis sicca (van Bijsterveld and OSS), whole unstimulated salivary flow at 15 minutes, presence of autoantibodies (anti-Ro or anti-La, ANA and rheumatoid factor) and histopathology in distinguishing subjects with primary Sjögren's syndrome by either set of criteria or both of them from those with non-Sjögren's sicca.

		Participant Classification			
		SS	DNMC	Performance (95% CI)	
Classification by ACR criteria:					
Schirmer's					
	Positive	131	102	Sensitivity	0.49 (0.43-0.55)
	Negative	137	258	Specificity	0.72 (0.67-0.76)
				PPV	0.56 (0.50-0.63)
				NPV	0.65 (0.60-0.70)
Ocular dye score: OSS ≥3					
	Positive	242	187	Sensitivity	0.90 (0.86-0.93)
	Negative	26	191	Specificity	0.51 (0.45-0.56)
				PPV	0.56 (0.52-0.61)
				NPV	0.88 (0.83-0.92)
WUSF					
	Positive	157	182	Sensitivity	0.59 (0.52-0.64)
	Negative	111	196	Specificity	0.52 (0.47-0.57)

				PPV	0.46 (0.41-0.52)
				NPV	0.64 (0.58-0.69)
Histopathology					
	Positive	230	43	Sensitivity	0.86 (0.81-0.90)
	Negative	38	335	Specificity	0.89 (0.85-0.92)
				PPV	0.84 (0.79-0.88)
				NPV	0.90 (0.86-0.93)
Serology (Ro/La OR ANA + RF)					
	Positive	171	21	Sensitivity	0.64 (0.58-0.70)
	Negative	97	357	Specificity	0.94 (0.92-0.96)
				PPV	0.89 (0.84-0.93)
				NPV	0.79 (0.75-0.82)
Classification by AECG criteria					
Schirmer’s					
	Positive	152	99	Sensitivity	0.54 (0.48-0.60)
	Negative	127	268	Specificity	0.73 (0.68-0.77)
				PPV	0.61 (0.54-0.67)
				NPV	0.68 (0.63-0.72)
Ocular dye score: vanBijsterveld score ≥4					
	Positive	171	106	Sensitivity	0.61 (0.55-0.67)
	Negative	108	261	Specificity	0.71 (0.66-0.76)
				PPV	0.62 (0.56-0.67)
				NPV	0.71 (0.66-0.75)

WUSF					
	Positive	182	157	Sensitivity	0.65 (0.59-0.71)
	Negative	97	210	Specificity	0.57 (0.52-0.62)
				PPV	0.54 (0.48-0.59)
				NPV	0.68 (0.63-0.74)
Histopathology					
	Positive	241	32	Sensitivity	0.86 (0.82-0.90)
	Negative	38	335	Specificity	0.91 (0.88-0.94)
				PPV	0.88 (0.84-0.92)
				NPV	0.90 (0.86-0.93)
Serology (Ro/La)					
	Positive	176	16	Sensitivity	0.63 (0.57-0.69)
	Negative	103	351	Specificity	0.96 (0.93-0.97)
				PPV	0.92 (0.87-0.95)
				NPV	0.77 (0.73-0.81)
All patients classified with Sjögren's syndrome* (n=303)					
Schirmer's					
	Positive	153	98	Sensitivity	0.50 (0.45-0.56)
	Negative	150	245	Specificity	0.71 (0.66-0.76)
				PPV	0.61 (0.55-0.67)
				NPV	0.62 (0.57-0.67)
Ocular dye score: vanBijsterveld score ≥4[1]					
	Positive	173	104	Sensitivity	0.57 (0.51-0.63)

	Negative	130	239	Specificity	0.70 (0.64-0.74)
				PPV	0.62 (0.56-0.68)
				NPV	0.65 (0.60-0.70)
Ocular dye score: OSS ≥3[2]					
	Positive	242	187	Sensitivity	0.80 (0.75-0.84)
	Negative	61	156	Specificity	0.45 (0.40-0.51)
				PPV	0.56 (0.52-0.61)
				NPV	0.72 (0.65-0.78)
WUSF					
	Positive	184	155	Sensitivity	0.61 (0.55-0.66)
	Negative	119	188	Specificity	0.55 (0.49-0.60)
				PPV	0.54 (0.49-0.60)
				NPV	0.61 (0.56-0.67)
Histopathology					
	Positive	256	17	Sensitivity	0.84 (0.80-0.88)
	Negative	47	326	Specificity	0.95 (0.92-0.97)
				PPV	0.94 (0.90-0.96)
				NPV	0.87 (0.83-0.91)
Serology (Ro/La OR ANA + RF)					
	Positive	192	19	Sensitivity	0.63 (0.58-0.69)
	Negative	111	324	Specificity	0.94 (0.91-0.97)
				PPV	0.91 (0.86-0.94)
				NPV	0.74 (0.70-0.78)

AECG=American European Consensus Group Classification Criteria for Sjögren's syndrome[19]

ACR=American College of Rheumatology Criteria Classification Criteria for Sjögren's syndrome[21]

pSS=primary Sjögren's syndrome; DNMC=did not meet criteria

*Sjögren's syndrome by either set of criteria (AECG, ACR or both)

Schirmer's I Test = Schirmer's test of tear production with <5 mm in 5 minutes considered abnormal (positive)

[1] Ocular dye score: for AECG criteria, ocular dye score (lissamine green + fluoresceine) = ≥ 4 according to van Bijsterveld's scoring system [24]; [2] for ACR criteria, ocular staining score (OSS lissamine green + fluoresceine) = ≥ 3 [23]

WUSF= Whole unstimulated salivary flow with <1.5 mls in 15 minutes considered abnormal (positive)

Supplementary Table S4. Comparison of the American-European Consensus Group criteria to the newly proposed American College of Rheumatology criteria. For AECG classification at least 4 criteria must be met and at least one of these must be either serology or histopathology. For ACR classification, 2 of 3 criteria must be satisfied.

	AECG	ACR
Subjective/Symptomatic†	Dry eyes Dry mouth	None
Objective oral	WUSF*	None
Objective ocular	Ocular dye score** (Rose Bengal or other); or Schirmer's I test	Ocular staining score*** (Lissamine green/fluoresceine)
Serological	anti-Ro or anti-La	anti-Ro or anti-La; or, ANA and RF
Histopathology	Focus score ≥1	Focus score ≥1

† See methods for specific AECG questions concerning sicca symptoms
* Whole unstimulated salivary flow
** Score ≥ 4 according to vanBijsterveld scoring system [24]
*** Score ≥ 3 according to Ocular Staining Score [23]
ANA: Antinuclear antibodies; RF: Rheumatoid Factor

SUPPLEMENTARY METHODS

Serology. We determine anti-Ro (or SSA) and anti-La (or SSB) autoantibodies by multiple methods (Supplemental materials). These include double immunodiffusion using rabbit thymus extract as antigen, as previously described;[1] a commercial immunoassay (Inno-Lia ANA Update, Innogenetics NV, Gent, Belgium) to measure anti-Ro60, anti-Ro52 and anti-La, as has been previously reported for anti-Ro/La.[2] Additionally, we use the Bio-Rad BioPlex 2200 ANA (Bio-Rad, Hercules, CA) system, which utilizes dyed magnetic beads to simultaneously perform multiple automated measurements. We follow the recommendations of the manufacturer, loading undiluted sera samples to detect antibodies to 60 kD Ro, 52kD Ro, and La, as we have previously reported.[3] ANAs and anti–double-stranded DNA (anti-dsDNA) were measured using IIF (using HEp-2 cells for detection of ANAs and *Crithidia luciliae* for detection of anti-dsDNA; Inova Diagnostics). The IIF assays were manually read by clinical immunology laboratory personnel, using a Nikon Optiphot fluorescence microscope (HBO bulb 100W mercury lamp, 20 objective). Precipitating levels of autoantibodies directed against soluble tissue antigens (Sm, nRNP, P, Jo-1, and anti-Scl70) were detected by immunodiffusion using calf thymus extract (CTE), or rabbit thymus extract (RTE) for anti-Scl70.

Peripheral Blood mRNA Transcript Measurements. Total RNA obtained by blood collection into PaxGene tubes (BD Company) and extracted following manufacturer's protocols (Qiagen). Excess globin transcripts were removed using GLOBINclearTM (Ambion). RNA concentrations were determined using the Nanodrop spectrophotometer

and RNA quality was assessed with the Agilent 2100 Bioanalyzer. Double stranded cDNA was synthesized using a T7 promoter, and biotin-labeled cRNA was transcribed using the Illumina TotalPrep RNA Amplification System (Ambion). Samples were hybridized to Human WG-6 v3.0 BeadChip microarrays (Illumina, San Diego) containing 48,803 mRNA transcripts in 37,805 unique genes per array. Microarrays were washed under high stringency and labeled with streptavidin-Cy3, and subsequently fluorescent intensity-based gene expression data were collected using Illumina's BeadStation 500 scanner and iScan.

Statistical Analysis of gene expression data. For the gene expression data, unless stated, all statistical analyses were performed in the R. Raw intensity values for two microarray experiments were background subtracted using Illumina BeadStudio software. Identification of outlier and poor-performing samples was accomplished by applying the package arrayQualityMetrics (AQM) to log-transformed GEP data from each experiment. Quality control measures were applied to each dataset to filter transcripts expressed in < 10% of samples (detection call threshold of $P < 0.05$) and probes with differential missingness ($P < 0.001$ by Fisher's exact test) between the two datasets. Remaining probes were then compared against data tables from the Re-annotation and Mapping of Oligonucleotide Array Technologies (ReMOAT), in which Illumina BeadArray probe quality was extensively assessed and re-annotated. Each dataset was then independently normalized using Robust Multiarray Average (RMA), followed by log2 transformation and quantile normalization. ComBat was subsequently applied to the combined dataset to adjust for non-biological experimental variation (i.e.

batch effects). After QC and normalization, 15,063 probes (in 12,248 genes) remained, for which Welch's t-tests, q-values, and fold changes (FC) were calculated. Differentially expressed genes were selected by Q <0.05 and FC>1.25 or <0.80. Final re-annotation of probe IDs was undertaken using the DAVID gene ID conversion tool and ReMOAT data tables; unresolved probe IDs were verified individually in Entrez Gene and discontinued probes removed. Pathway analysis for differentially expressed genes was carried out in Genomatix. Cluster 3.0 was used to perform unsupervised hierarchical clustering by average linkage for both genes and arrays, and these results were visualized as heat maps using Java TreeView.

REFERENCES:

1. Clark G, Reichlin M, Tomasi TB Jr. Characterization of a soluble cytoplasmic antigen reactive with sera from patients with systemic lupus erythematosus. *J Immunol* 1969;**102**:117-22.
2. Gordon P, Khamashta MA, Rosenthal E, et al. Anti-52 kDa Ro, anti-60 kDa Ro, and anti-La antibody profiles in neonatal lupus. *J Rheumatol* 2004;**31**:2480-7.
3. Aggarwal R, Namjou B, Li S, et al. Male only systemic lupus. *J Rheumatol* 2010;**37**:1480-7.