Supplemental Figure 1. The four types of Xist RNA localization patterns in mouse T cells. Xist RNA FISH images with DAPI (left) and a cartoon for each type of pattern (right). Type I nuclei have clustered Xist RNA transcripts in a nuclear territory/space encompassing the Xi. Type II nuclei have dispersed Xist RNA signals in the nuclear area of the Xi. The Xi nuclear territory was previously defined using sequential Xist RNA then DNA FISH using X-paints (21). Type III nuclei have Xist signals disperse all across the nucleus, beyond the territory of the Xi. Type IV nuclei have no detectable Xist RNA signals.

Supplemental Figure 2. Sequential Xist RNA FISH and IF for H3K27me3 images for double-positive (DP) thymocytes. DPs were isolated from one female mouse; the experiment was repeated three times (using 3 different mice), and representative images from one experiment is shown. Arrows indicate a H3K27me3 focus.

Supplemental Figure 3. Quantification of Xist RNA FISH localization patterns in splenic T cells (*left*: circulating labeled as 'naïve'; *right: in vitro* activated) from NZB/W F1 mice from 3 disease stages: (A) pre-disease, (B) early-stage and (C) late-stage disease and age-matched controls (n= 4-5 mice/group) for each timepoint. Statistical significance was determined using one-tailed t-tests for comparisons of each type of Xist RNA localization pattern, making comparisons within each stage of disease between WT and NZB/W samples. Not significant, n.s.

Supplemental Figure 4. Quantification of XIST RNA FISH localization patterns (Type I-IV) in SLE patient T cells and healthy age-matched controls. (A) Circulating T cells. (B) In vitro activated (using CD3/CD28) T cells. Statistical significance was determined using unpaired two-tailed t tests for comparisons of each type of XIST RNA localization pattern, making comparisons within each stage of disease between healthy control ("control") and SLE samples. Not significant, n.s.

Supplemental Figure 5. (A) XIST RNA expression is similar between SLE patients and healthy age-matched controls. XIST RNA reads (FPKM) for each SLE patient and controls were determined using RNAseq data set from Figure 7. The samples are not statistically significantly different using one way ANOVA test for the 3 groups; also not statistically significant between female controls and SLE patients (two-tailed t test). (B) X to Autosome ratio for gene expression for SLE patient T cells and healthy controls. The samples are not statistically significant, testing with two-tailed t test.

Supplemental Figure 6. X-linked gene transcripts downregulated in SLE patient T cells (high SLEDAI) compared to healthy controls. Gene names for each transcript are listed on the left; complete transcript information is shown in Supplemental Table 3.

Supplemental Table 1. All X-linked gene transcripts that are differentially expressed between all healthy control (HC) females (n = 4) and all SLE female patients (SLE/HC), shown as mean normalized read counts. Genes with the GO term 'immunity' are highlighted in yellow. Fold change was considered significant at FDR < 0.05.

Supplemental Table 2. X-linked gene transcripts (normalized read counts) that are differentially expressed between healthy control (HC) female and High SLEDAI SLE female (SLE/HC) patients. Shown are all upregulated gene transcripts that are greater than 1 for log2FC, and downregulated gene transcripts have negative values (log2FC less than 1). Gene transcripts with GO term 'immunity' are highlighted in yellow. Fold change is considered significant at FDR < 0.05. XCI escape status was inferred for each gene from Reference (29).

Supplemental Table 3. X-linked differentially expressed gene transcripts (shown as normalized read counts) between healthy control (HC) female and low SLEDAI SLE female samples (SLE/HC). Upregulated gene transcripts have positive log2FC values; downregulated gene transcripts have negative values. Genes with the GO term 'immunity' are highlighted in yellow. Fold change was considered significant at FDR < 0.05. XCI escape status for each gene was inferred from Reference (29).

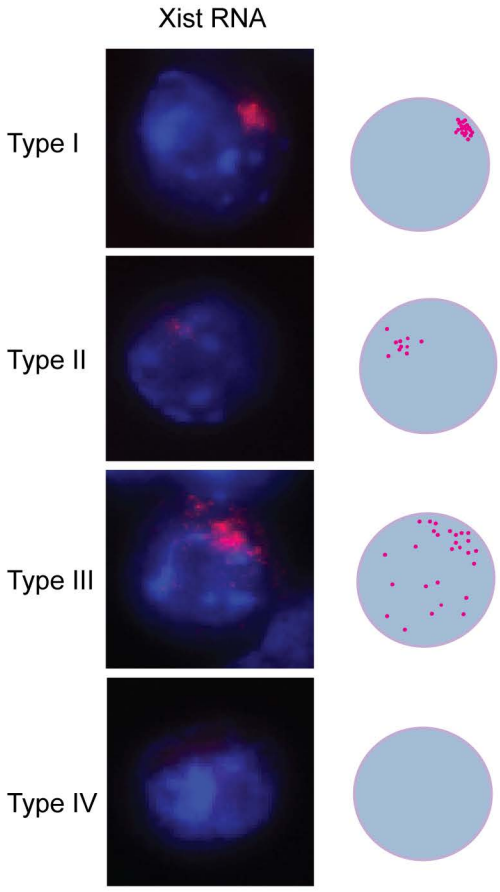
Supplemental Table 4. X-linked gene transcripts uniquely expressed in high SLEDAI SLE patients (56 gene transcripts) and low SLEDAI SLE patients (4 gene transcripts). The 16 X-linked gene transcripts overexpressed in both high and low SLEDAI samples is shown in the box. The three genes that escape XCI are noted.

Supplemental Table 5. X-linked differentially expressed gene transcripts between SLE male vs SLE female (female/male). Genes with GO term 'immunity' are highlighted in yellow. Fold change was considered significant at FDR < 0.05.

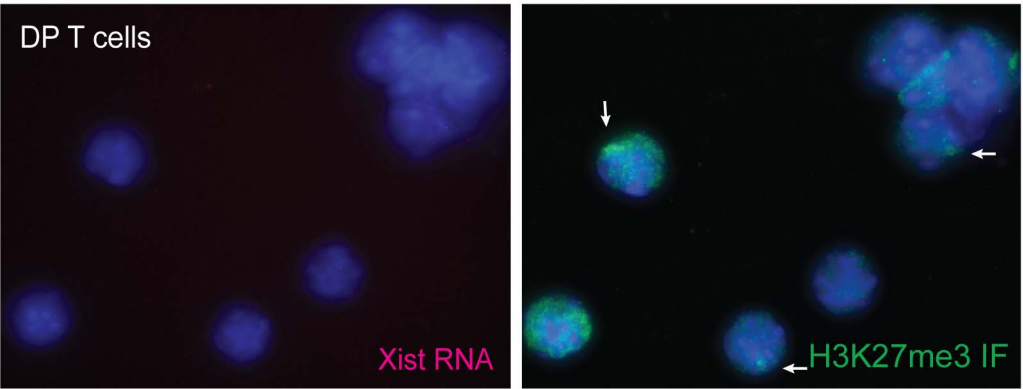
Supplemental Table 6. X-linked differentially expressed gene transcripts between SLE male vs healthy control (HC) female (female/male). Genes with GO term 'immunity' are highlighted in yellow. Fold change was considered significant at FDR < 0.05.

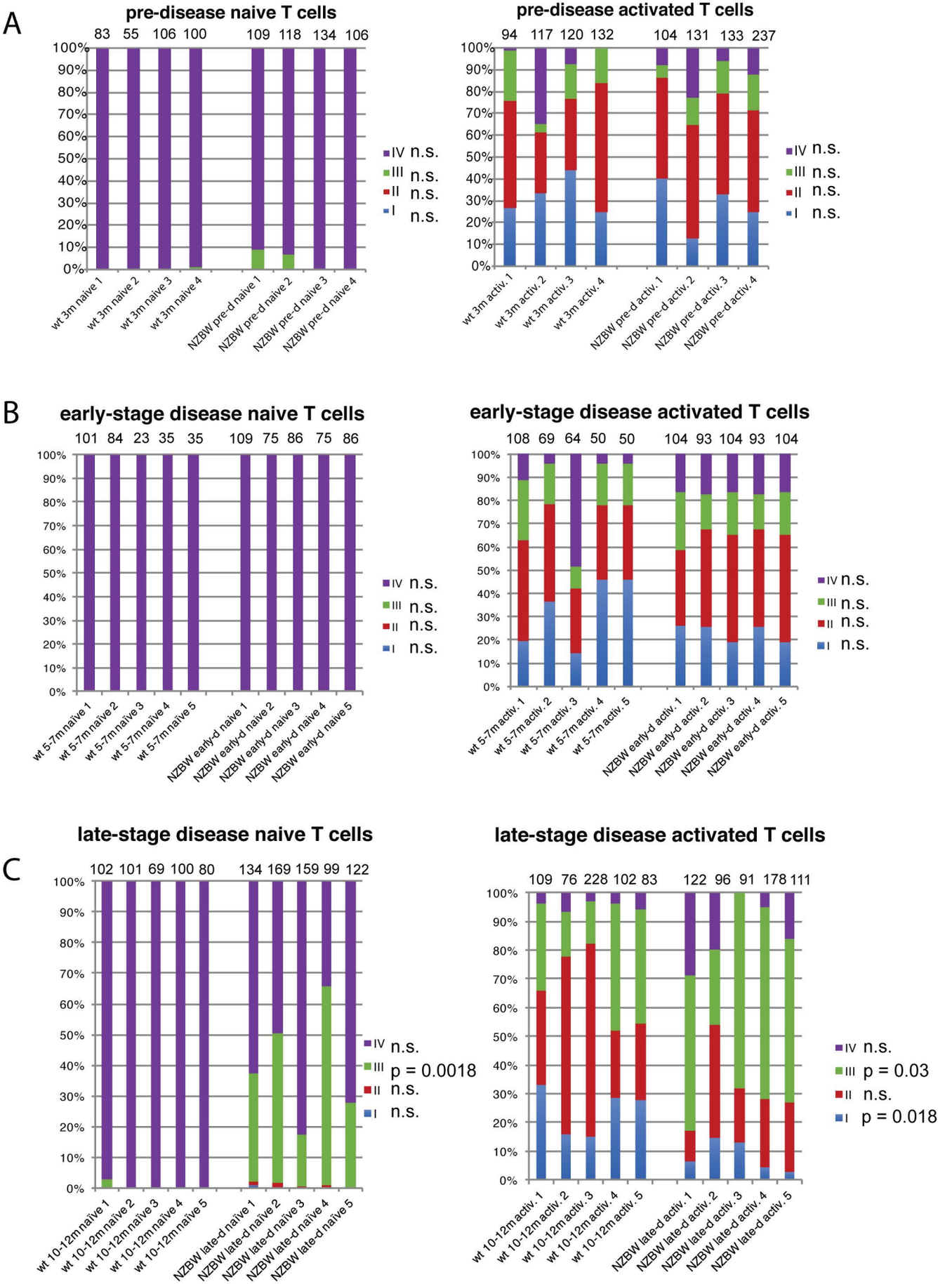
Supplemental Table 7. Differentially expressed XIST interacting protein coding genes between healthy control (HC) female and High SLEDAI SLE female (SLE/HC), upregulated genes are above 1; down-regulated genes are less than 1. Genes with GO term 'immunity' are highlighted in yellow. Fold change was considered significant at FDR < 0.05.

Supplemental Figure 1



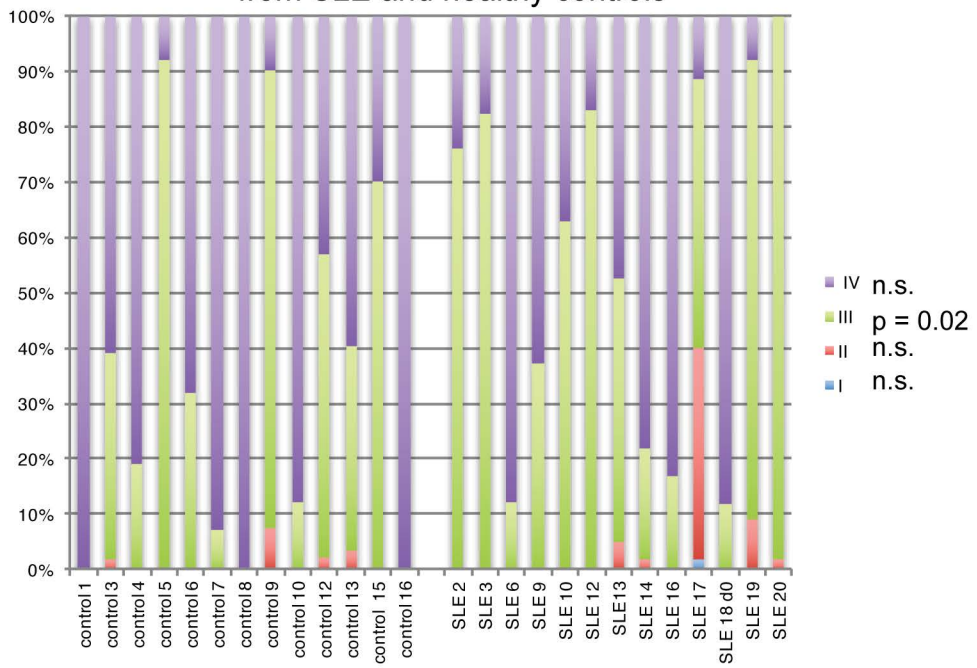
Sequential Xist RNA FISH and IF for DP thymocytes



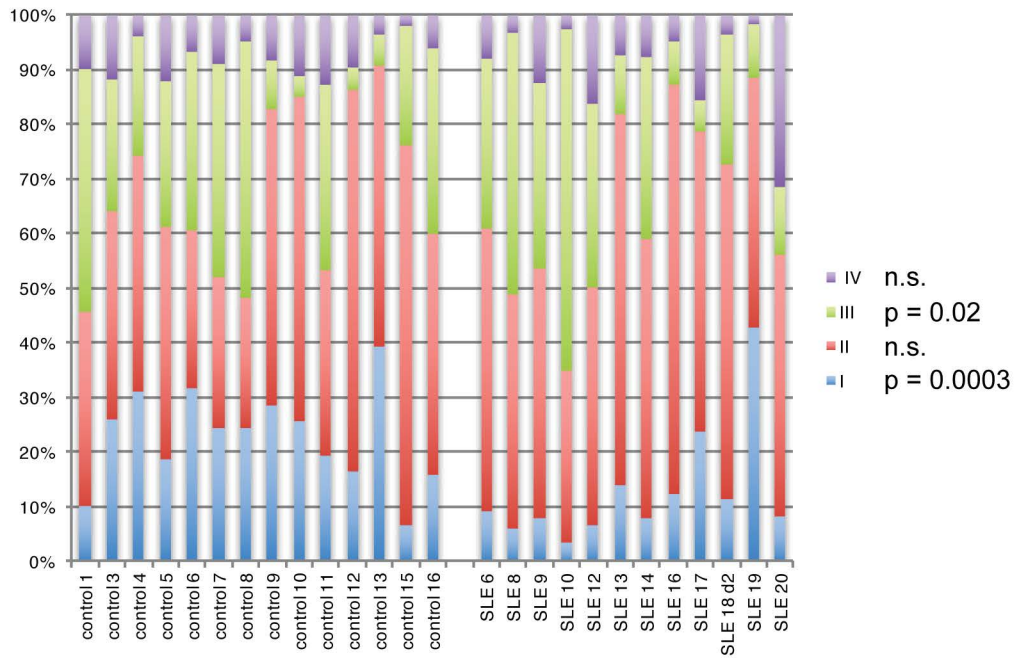


Supplemental Figure 3

A

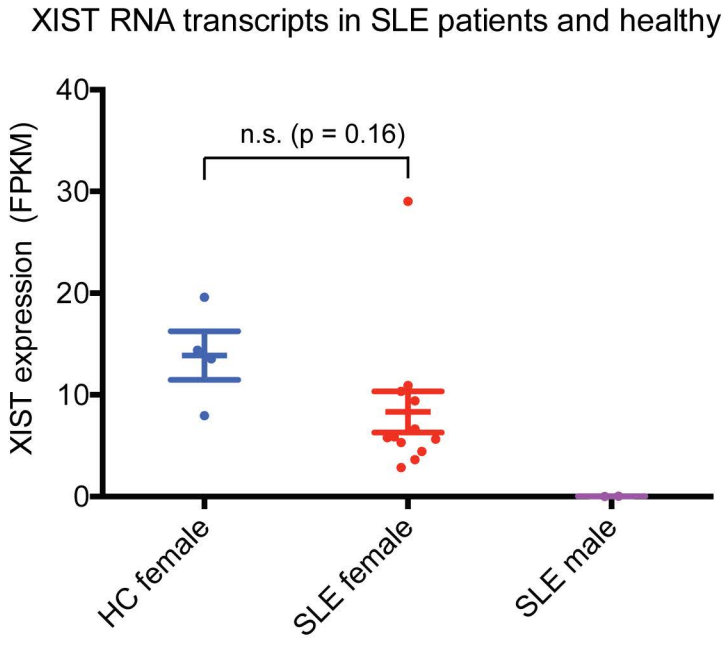


B

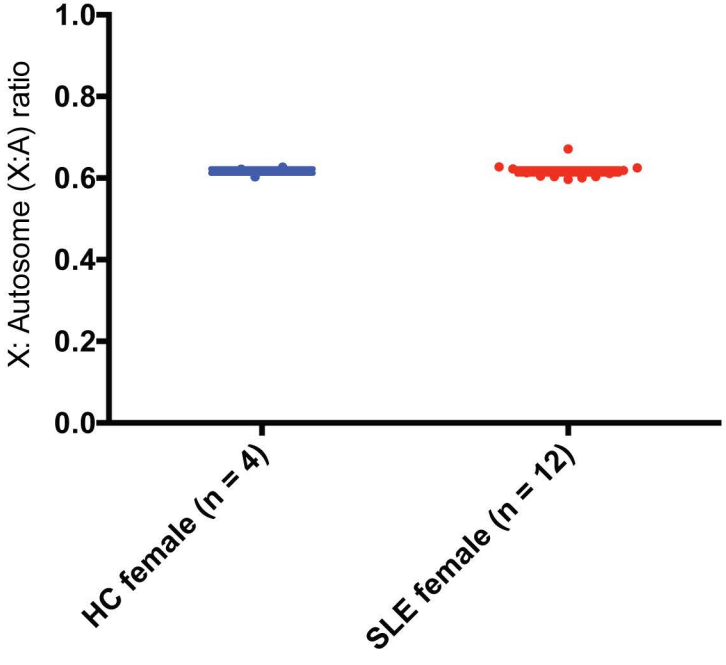


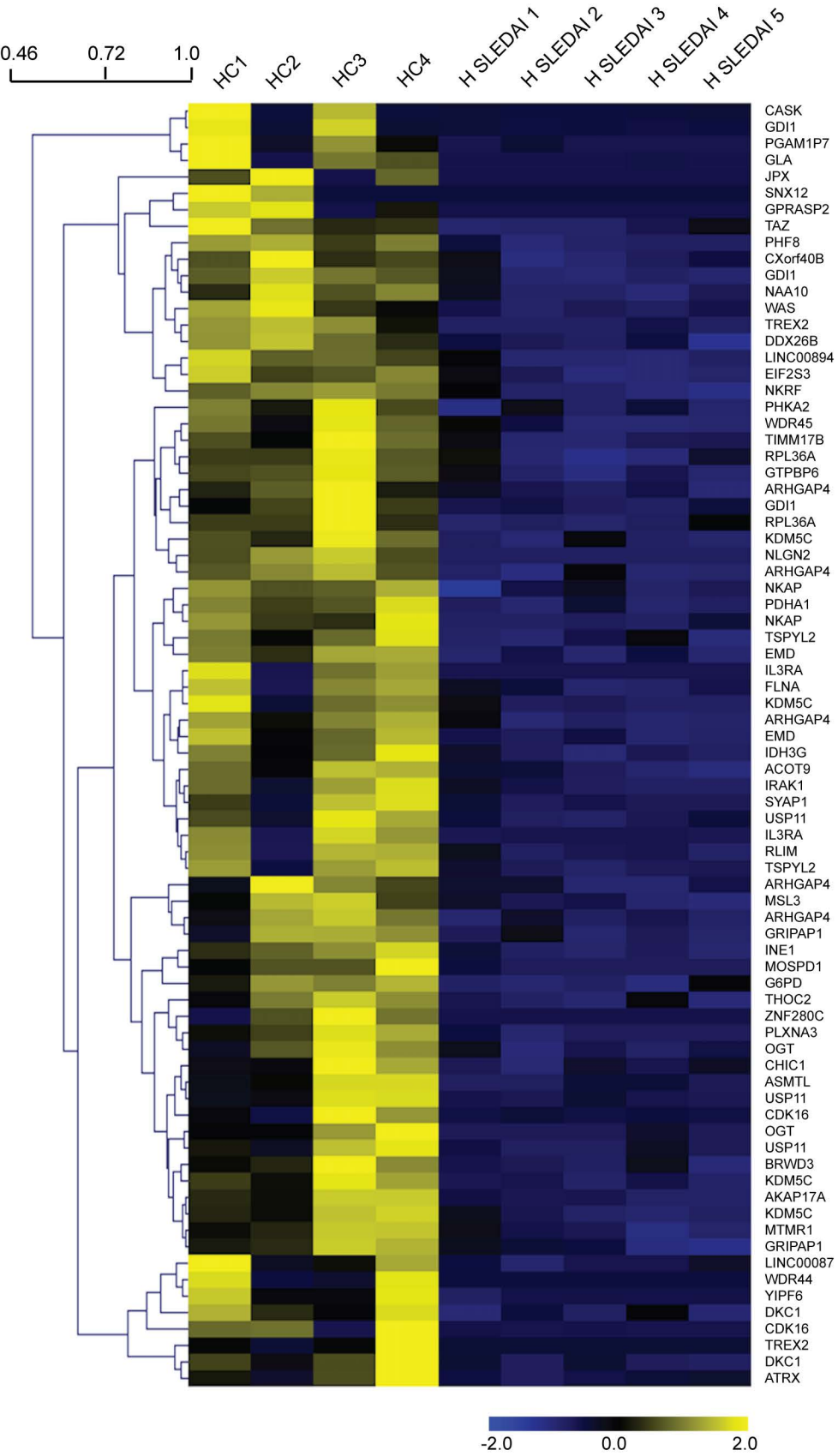
Supplemental Figure 4

A


XIST RNA transcripts in SLE patients and healthy controls
XIST expression (FPKM)
40
30
20
10
0
n.s. (p = 0.16)
HC female
SLE female
SLE male

B


X: Autosome ratio for SLE patient T cells
X: Autosome (X:A) ratio
1.0
0.8
0.6
0.4
0.2
0.0
HC female (n = 4)
SLE female (n = 12)


X-linked down-regulated gene transcripts in SLE T cells
0.46
0.72
1.0
HC1
HC2
HC3
HC4
H SLEDAI 1
H SLEDAI 2
H SLEDAI 3
H SLEDAI 4
H SLEDAI 5
CASK
GDI1
PGAM1P7
GLA
JPX
SNX12
GPRASP2
TAZ
PHF8
CXorf40B
GDI1
NAA10
WAS
TREX2
DDX26B
LINC00894
EIF2S3
NKRF
PHKA2
WDR45
TIMM17B
RPL36A
GTPBP6
ARHGAP4
GDI1
RPL36A
KDM5C
NLGN2
ARHGAP4
NKAP
PDHA1
NKAP
TSPYL2
EMD
IL3RA
FLNA
KDM5C
ARHGAP4
EMD
IDH3G
ACOT9
IRAK1
SYAP1
USP11
IL3RA
RLIM
TSPYL2
ARHGAP4
MSL3
ARHGAP4
GRIPAP1
INE1
MOSPD1
G6PD
THOC2
ZNF280C
PLXNA3
OGT
CHIC1
ASMTL
USP11
CDK16
OGT
USP11
BRWD3
KDM5C
AKAP17A
KDM5C
MTMR1
GRIPAP1
LINC00087
WDR44
YIPF6
DKC1
CDK16
TREX2
DKC1
ATRX
-2.0
0.0
2.0