

1 **Online supplementary materials and methods**

2 **Online Supplemental Table S1. Each ETC complex gene list used in this study.**

3

Complex I	Complex II	Complex III	Complex IV	Complex V
NDUFA1	SDHA	CYC1	COX4I1	ATP5F1A
NDUFA10	SDHB	UQCR10	COX4I2	ATP5F1B
NDUFA11	SDHC	UQCR11	COX5A	ATP5F1C
NDUFA12	SDHD	UQCRB	COX5B	ATP5F1D
NDUFA13		UQCRC1	COX6A1	ATP5F1E
NDUFA2		UQCRC2	COX6A2	ATP5IF1
NDUFA3		UQCRFS1	COX6B1	ATP5MC1
NDUFA5		UQCRH	COX6B2	ATP5MC2
NDUFA6		UQCRQ	COX6C	ATP5MC3
NDUFA7			COX7A1	ATP5MD
NDUFA8			COX7A2	ATP5ME
NDUFA9			COX7B	ATP5MF
NDUFAB1			COX7B2	ATP5MG
NDUFB1			COX7C	ATP5MPL
NDUFB10			COX8A	ATP5PB
NDUFB11			COX8C	ATP5PD
NDUFB2				ATP5PF
NDUFB3				ATP5PO
NDUFB4				
NDUFB5				
NDUFB6				
NDUFB7				
NDUFB8				
NDUFB9				
NDUFC1				
NDUFC2				
NDUFS1				
NDUFS2				

NDUFS3				
NDUFS4				
NDUFS5				
NDUFS6				
NDUFS7				
NDUFS8				
NDUFV1				
NDUFV2				
NDUFV3				

1 **Online Supplemental Table S2. Results of cis-eQTL analysis using RNA-seq and genotyping data from our IMD patients and**
2 **HCs.**

3

SLE GWAS Top	eQTL Top	Subset	r^2_{JPN}	r^2_{EUR}	eGene	Aliases and/or Function of eGene	References
rs1385374	rs3765107	DN B	0.955	1.000	SLC15A4		SLC15A4 in B cells regulates type I IFN production through regulation of TLR7/9 as well as mTORC1 signaling [1].
rs1385374	rs3765107	Naïve B	0.955	1.000	SLC15A4		
rs11059927	rs3765107	DN B	0.955	1.000	SLC15A4	Histidine transporter on lysosomes	
rs11059927	rs3765107	Naive B	0.955	1.000	SLC15A4		
rs2422345	rs11484635	USM B	0.995	0.995	TNFSF4		OX40L-expressing B cells supports plasma cell differentiation and Tfh maturation [2].
rs4916342	rs11484635	USM B	0.995	0.930	TNFSF4	OX40L	
rs10753074	rs11484635	USM B	0.995	0.991	TNFSF4		
rs4426778	rs7686702	Naive B	1.000	0.985	BANK1	B cell scaffold protein with ankyrin repeats 1	BANK1 on B cell promotes antigen presentation ability and autoantibody production [3].
rs11085725	rs11085727	SM B	0.962	1.000	TYK2	Tyrosine kinase 2	

rs11085725	rs35251378	DN B	0.991	0.995	TYK2		
rs11085725	rs35251378	Plasmablast	0.991	0.995	TYK2		
rs11085727	rs11085727	SM B	0.961	0.995	TYK2		
rs11085727	rs35251378	DN B	0.961	0.995	TYK2		
rs11085727	rs35251378	Plasmablast	0.961	0.995	TYK2		
rs1170426	rs1728797	USM B	0.992	1.000	ZFP90		
rs1170426	rs4783650	Naive B	1.000	0.849	ZFP90	Zink finger protein	
rs131658	rs5754467	SM B	0.956	0.800	UBE2L3		
rs3747093	rs5754467	SM B	0.996	0.974	UBE2L3	Ubiquitin conjugating enzyme E2L3	
rs2061831	rs2061831	Naive B	0.995	1.000	BLK		
rs2061831	rs2409780	USM B	0.995	1.000	BLK		
rs2254546	rs2254546	Plasmablast	0.937	0.993	BLK		
rs2618444	rs2061831	Naive B	0.990	1.000	BLK	B lymphoid tyrosine kinase	
rs2618444	rs2409780	USM B	0.995	1.000	BLK		
rs2618476	rs2061831	Naive B	0.924	0.950	BLK		
rs2618476	rs2409780	USM B	0.919	0.950	BLK		

Tyk2 tyrosine kinase expression is required for the maintenance of mitochondrial respiration in primary pro-B lymphocytes [4].

ZFP90 transgenic mice showed altered expression of OXPHOS related genes [5].

UBE2N, UBE2L3, and UBE2D2/3 contribute to Parkin-mediated mitophagy [6].

BLK and BANK1 act through PLC gamma 2 in B cell signaling [7].

rs2736332	rs2061831	Naive B	0.995	0.876	BLK		
rs2736332	rs2409780	USM B	1.000	0.876	BLK		
rs2736337	rs2061831	Naive B	0.962	0.995	BLK		
rs2736337	rs2409780	USM B	0.957	0.995	BLK		
rs2736340	rs2061831	Naive B	0.957	0.995	BLK		
rs2736340	rs2409780	USM B	0.952	0.995	BLK		
rs7812879	rs2254546	Plasmablast	0.911	0.986	BLK		
rs13277113	rs2061831	Naive B	0.897	0.990	BLK		
rs13277113	rs2409780	USM B	0.893	0.990	BLK		
rs2299864	rs1322178	Plasmablast	0.981	0.964	ATG5		Mitochondrial quality control after oxidative damage.
rs9373839	rs1322178	Plasmablast	0.981	0.959	ATG5	Autophagy related 5	Localizes to punctae on mitochondria [8].
rs2732549	rs146368551	Naive B	0.821	0.913	CD44	Cell surface glycoprotein	CD44 ^{lo} to CD44 ^{hi} conversion of esophageal keratinocytes induces mitochondrial dysfunction and OXPHOS [9].
rs3794060	rs732934	Naive B	1.000	1.000	NADSYN1		
rs3794060	rs732934	USM B	1.000	1.000	NADSYN1	NAD synthetase 1	

rs6445975	rs4681845	Naive B	0.914	0.971	PXK	PX domain containing serine/threonine kinase like	PXK influenced the rate of BCR internalization [10].
rs6445975	rs4681845	SM B	0.914	0.971	PXK		
rs6445975	rs4681845	USM B	0.914	0.971	PXK		
rs7258015	rs2304237	Naive B	1.000	0.979	ICAM3	Ig-like adhesion molecule	ICAM-3 crosslinking induced the production of reactive oxygen species (ROS), which are known to be involved in the control of endothelial cell-cell contacts [11].
rs7258015	rs2304237	USM B	1.000	0.979	ICAM3		
rs73366469	rs73366469	Plasmablast	0.853	1.000	NCF1	Subunit of NADPH oxidase	
rs9782955	rs2104125	DN B	0.990	0.959	LYST	Lysosomal trafficking regulator	Lyst mutation results in elevated levels of oxidative damage to lipid membranes [12].
rs9782955	rs2104125	Naive B	0.990	0.959	LYST		
rs9782955	rs2104125	SM B	0.990	0.959	LYST		

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2 References

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- 1 Online Supplemental Table S3. Parent subset common DEGs in test and validation cohorts with the information of *cis*-eQTL
 2 analysis

Gene	subset common DEGs								eQTL & GWAS				
	B test	validation	CD4 test	validation	DC test	validation	Mono test	validation	B	CD4	DC	Mono	others
CLSPN													
GCA													
IL18R1			*							*			
IL18RAP													
IL7	*		*						*	*			
LGALS9	*				*		*		*		*	*	
NCF2													
NEU1													
PDHX													
PHKG2													
PKIA	*		*						*	*			
PRDM1													
PRDX6	*								*				
PRNP													
PYCARD			*							*			
RGS1			*							*			
RPL10A							*					*	
SERBP1													

- 3 An asterisk (*) indicates a candidate gene which was picked up as a DEG in both cohorts and also eGene from eQTL and GWAS.

1 **Online Supplemental Table S4. Gene lists of each type I IFN signaling-related gene cluster.**
 2

C1	C2	C3	C4	C5	C6
RNF135	ITCH	POLR1D	TRIM25	RIPK2	POLR3H
MB21D1	TRAIP	PCBP2	ADAR	PTPN22	HSP90AB1
IKBKE	IRF4	RPS27A	STAT2	TBK1	HSPD1
PTPN6	DHX9	UBA52	DHX58	PTPN2	XRCC5
UBC	SAMHD1	TRAF3IP1	OAS3	POLR2K	XRCC6
CDC37	CTNNB1	PRKDC	IRF7	POLR3GL	FADD
UBA7	ZC3HAV1	CRCP	OAS2	TAX1BP1	IRF2
IRF1	POLR3B	CREBBP	C19orf66	UBE2K	GBP2
RELA	EP300	RNF216	IRF9	MRE11A	HAVCR2
HLA-A	POLR3A	PTPN11	TRIM38	IFNAR1	PYCARD
MYD88	ZBTB20	LRRFIP1	DDX58	IFNAR2	PIN1
TNFAIP3	JAK1	DHX36	IFIH1		POLR2L
IRF5	REL	PPM1B	STAT1		POLR2F
NLRC5	IRF8	TRAF3	SP100		UBB
STAT6	RNASEL	OTUD5	IFI16		HMGB2
TYK2	POLR3F	RELB	NMI		ISG20
PTPN1	TRIM32	NFKB1	UBE2L6		HMGB1
TICAM1	LSM14A	NFKB2	BST2		POLR3K
NLRX1	CYLD	IRAK1	IFI35		POLR1C
TRIM56	DDX3X	PLCG2	MX2		POLR3C
POLR3E		POLR2H	OASL		IP6K2
MAVS		POLR3D	HERC5		HLA-E
TIRAP			XAF1		HLA-F
HLA-B			IFIT1		
HLA-C			IFIT3		
HLA-H			IFITM1		
MUL1			IFI6		
TMEM173			IFI27		
DDX41			MX1		
SHMT2			RSAD2		
HLA-G			OAS1		
FLOT1			ISG15		
IRF3			USP18		

POLR2E			IFITM2		
			IFITM3		
			TREX1		
			PSMB8		
			TRIM21		

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1 **Online Supplemental Table S5. Correlation of C1 to C5 signatures with the OXPPOS signature in each immune cell subset**

2

3 Test cohort

subset	Cluster1			Cluster2			Cluster3			Cluster4			Cluster5		
	<i>r</i>	<i>q</i>		<i>r</i>	<i>q</i>		<i>r</i>	<i>q</i>		<i>r</i>	<i>q</i>		<i>r</i>	<i>q</i>	
Naive B	-0.34	0.03	*	-0.24	0.11		-0.21	0.24		0.3	0.09		0.33	0.05	*
SM B	0.03	0.85		-0.63	1.3 xE-5	****	0.47	7.2 xE-3	**	0.53	5.1 xE-4	***	0.31	0.05	*
USM B	-0.11	0.49		-0.46	3.8 xE-3	**	0.29	0.12		0.3	0.09		0.41	0.03	*
DN B	-0.44	2.9 xE-3	**	-0.6	3.9 xE-5	****	-0.08	0.7		0.02	0.91		0.24	0.11	
Plasma- blast	-0.5	4.8 xE-4	***	-0.5	9.0 xE-4	***	-0.23	0.21		0.45	6.4 xE-3	**	0.37	0.03	*
Th1	-0.51	3.3 xE-4	***	-0.51	5.4 xE-4	***	-1.7 xE-3	0.99		0.66	4.8 xE-6	*****	0.28	0.07	
Th2	-0.59	4.9 xE-5	****	-0.24	0.11		-0.22	0.21		0.29	0.09		0.27	0.08	
Th17	-0.56	7.6 xE-5	****	-0.36	0.01	*	-0.22	0.21		0.24	0.15		0.45	8.3 xE-3	**
Tfh	-0.57	7.6 xE-5	****	-0.37	0.01	*	-0.37	0.05	*	0.32	0.07		0.35	0.04	*
Naive CD4	-0.42	4.3 xE-3	**	-0.37	0.01	*	-0.28	0.12		0.25	0.14		0.38	0.03	*
Mem CD4	-0.7	3.2 xE-7	*****	-0.16	0.26		-0.27	0.12		0.29	0.09		0.51	3.4 xE-3	**
Fr. II eTreg	-0.58	5.1 xE-5	****	-0.39	8.1 xE-3	**	-0.33	0.07		0.07	0.68		0.46	8.3 xE-3	**
Naive CD8	-0.43	2.9 xE-3	**	-0.38	9.8 xE-3	**	-0.17	0.32		0.33	0.07		0.1	0.53	

Mem CD8	-0.35	0.02	*	-0.52	5.3 xE-4	***	-0.07	0.7		0.64	5.5 xE-6	*****	0.33	0.05	*
mDC	-0.56	7.6 xE-05	****	-0.59	3.9 xE-05	****	-0.41	0.02	*	0.13	0.43		0.31	0.05	*
pDC	-0.38	9.6 xE-03	**	-0.43	3.8 xE-03	**	-0.11	0.57		0.21	0.18		0.3	0.05	*
CD16p Mono	-0.63	1.2 xE-05	****	-0.64	1.3 xE-05	****	-0.49	6.8 xE-03	**	-0.12	0.45		0.19	0.21	
CD16n Mono	-0.58	4.9 xE-05	****	-0.4	8.1 xE-03	**	-0.28	0.12		0.22	0.18		0.37	0.03	*
NK	-0.34	0.02	*	-0.47	1.6 xE-03	**	0.05	0.77		0.35	0.06		-0.07	0.64	

1 **Online Supplemental Table S6. Clinical characteristics of the enrolled SLE patients**

Characteristics	HC		SLE	
	Test cohort	Validation cohort	Test cohort	Validation cohort
	n = 37	n = 55	n = 49	n = 58
Age	52.2 ± 13.8	44.2 ± 15.0	49.3 ± 10.6	45.9 ± 13.3
Gender, female	32 (86.5%)	37 (67.3%)	44 (89.8%)	50 (86.2%)
Disease duration	NA	NA	19.5 ± 12.0	13.2 ± 10.8
SLEDAI-2K	NA	NA	5.2 ± 3.5	6.9 ± 5.2
SDI	NA	NA	1.0 ± 1.2	0.9 ± 1.4
Complement decrease	NA	NA	22 (44.9%)	28 (48.3%)
Leukopenia	NA	NA	41 (85.4%)	46 (80.7%)
Lymphopenia	NA	NA	35 (71.4%)	44 (77.2%)
Plasmablast (% in total B)	1.4 ± 1.6	2.6 ± 2.7	9.0 ± 8.9	9.9 ± 9.8
Anti-dsDNA positive	NA	NA	16 (32.7%)	22 (38.6%)
Anti-dsDNA titer	NA	NA	21.2 ± 31.9	24.7 ± 60.2
Anti-Sm positive	NA	NA	3 (6.1%)	9 (16.4%)
Anti-RNP positive	NA	NA	14 (28.6%)	20 (37.0%)
APA positive	NA	NA	16 (32.7%)	19 (36.5%)
Daily PSL dose (mg/day)	NA	NA	5.4±2.4	7.5±10.4
PSL	NA	NA	46 (93.9%)	49 (84.5%)
Azathioprine	NA	NA	3 (6.1%)	7 (12.1%)
Cyclophosphamide (p.o.)	NA	NA	1 (2.0%)	0 (0%)
Cyclosporin A	NA	NA	6 (12.2%)	6 (10.3%)
Tacrolimus	NA	NA	8 (16.3%)	6 (10.3%)
Mycophenolate mofetil	NA	NA	2 (4.1%)	9 (15.6%)

1 **Table S7. Sorting Panel of Each Immune Cell Subset**

Parent	Subset Name	Gating Strategy	Comment
B cell	Naïve B	CD3-CD19+IgD+CD27-	
	Switched memory B (SM B)	CD3-CD19+IgD-CD27+	test cohort only
	Switched memory B (SM B)	CD3-CD19+IgD-CD27+CD38-	validation cohort only
	Unswitched memory B (USM B)	CD3-CD19+IgD+CD27+	
	Double Negative B (DN B)	CD3-CD19+IgD-CD27-	
	Plasmablast	CD3-CD19+IgD-CD27++CD38+	
T cell	Th1	CD3+CD4+CD25-CD45RA-CXCR5-CCR5-CXCR3+	test cohort only
	Th1	CD3+CD4+CD8-CD25-CCR4-CCR6-CXCR3+CXCR5- in non-NaiveCD4	validation cohort only
	Th2	CD3+CD4+CD25-CD45RA-CXCR5-CCR5-CXCR3-	test cohort only
	Th2	CD3+CD4+CD8-CD25-CCR4+CCR6-CXCR3-CXCR5- in non-NaiveCD4	validation cohort only
	Th17	CD3+CD4+CD25-CD45RA-CXCR5-CCR5+CXCR3-	test cohort only
	Th17	CD3+CD4+CD8-CD25-CCR6+CXCR3-CXCR5- in non-NaiveCD4	validation cohort only
	Tfh	CD3+CD4+CD25-CXCR5+	test cohort only
	Tfh	CD3+CD4+CD8-CD25-CXCR5+ in non-NaiveCD4	validation cohort only
	Naïve CD4 T (Naïve CD4)	CD3+CD4+CD45RA+	test cohort only
	Naïve CD4 T (Naïve CD4)	CD3+CD4+CD8-CCR7+CD45RA+	validation cohort only
	Memory CD4 T (Mem CD4)	CD3+CD4+CD25-CD45RA-	test cohort only
	Memory CD4 T (Mem CD4)	CD3+CD4+CD8-CD25- in non-NaiveCD4	validation cohort only
	Fraction II effector regulatory T (Fr. II eTreg)	CD3+CD4+CD25 ^{high} CD45RA-	test cohort only

	Fraction II effector regulatory T (Fr. II eTreg)	CD3+CD4+CD8-CD25highCD45RA-	validation cohort only
	Naïve CD8 T (Naïve CD8)	CD3+CD19-CD8+CD45RA+	test cohort only
	Naïve CD8 T (Naïve CD8)	CD3+CD4-CD8+CD45RA+CCR7+	validation cohort only
	Memory CD8 T (Mem CD8)	CD3+CD19-CD8+CD45RA-	test cohort only
	NK	CD3-CD19-CD56+CD14-	test cohort only
Monocyte	CD16 positive monocytes (CD16p Mono)	CD3-CD19-CD56-HLADR+CD14+CD16+	
	CD16 negative monocytes (CD16n Mono)	CD3-CD19-CD56-HLADR+CD14+CD16-	
Dendritic Cell	Myeloid Dendritic Cells (mDC)	CD3-CD19-CD56-HLADR+CD14-(CD16-)CD11c+CD123-	
	Plasmacytoid Dendritic Cells (pDC)	CD3-CD19-CD56-HLADR+CD14-(CD16-)CD11c-CD123+	