(CD68+CD163-) (23.7%), 21.6 – 31.7), M2 Macrophages (CD68+CD163+) (35.9%, 26.4 – 40.7), and CD16+ cells (25.7%, 20.4 – 29.5) (figure 3). Further verification using a Z-axis overlay of intracellular markers on tSNE plots of immune cell clusters identified by CyTOF confirmed low expression of IFN-1 and the interferogenic pathway, phosphorylated stimulator of interferon genes (pSTING), in the pDCs (figure 2B).

Conclusions Taken together, these findings suggest pDCs may not play the central role in CLE as major IFN-1 producers and myeloid cells are larger contributors of IFN-1 in numbers and as a percent. pDCs may have a pathogenic role in CLE through IFN-1-independent mechanisms.

Molecular Biology of Lupus

902 LOSS-OF-FUNCTION VARIANTS IN SAT1 CAUSE X-LINKED CHILDHOOD-ONSET SYSTEMIC LUPUS ERYTHEMATOSUS

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Objectives Families that contain multiple siblings affected with childhood-onset of systemic lupus erythematosus (SLE) likely have strong genetic predispositions. We performed whole-exome sequencing (WES) to identify familial rare risk variants and to assess their effects in lupus.

Methods Sanger sequencing validated the two ultra-rare, predicted pathogenic risk variants discovered by WES and identified additional variants in 562 additional SLE patients. Effects of a splice site variant and a frameshift variant were assessed using a Minigene assay and CRISPR/Cas9-mediated knock-in (KI) mice, respectively.

Results The two familial ultra-rare, predicted loss-of-function (LOF) SAT1 variants exhibited X-linked recessive Mendelian inheritance in two unrelated African-American families. Each LOF variant was transmitted from the heterozygous unaffected mother to her two sons with childhood-onset SLE. The p. Asp40Tyr variant affected a splice donor site causing deleterious splicing. The young hemizygous male and homozygous female Sat1p.Glu22Leufs*6 KI mice spontaneously developed splenomegaly, enlarged glomeruli with leukocyte infiltration, proteinuria and elevated expression of type I interferon inducible genes. SAT1 is highly expressed in neutrophils and