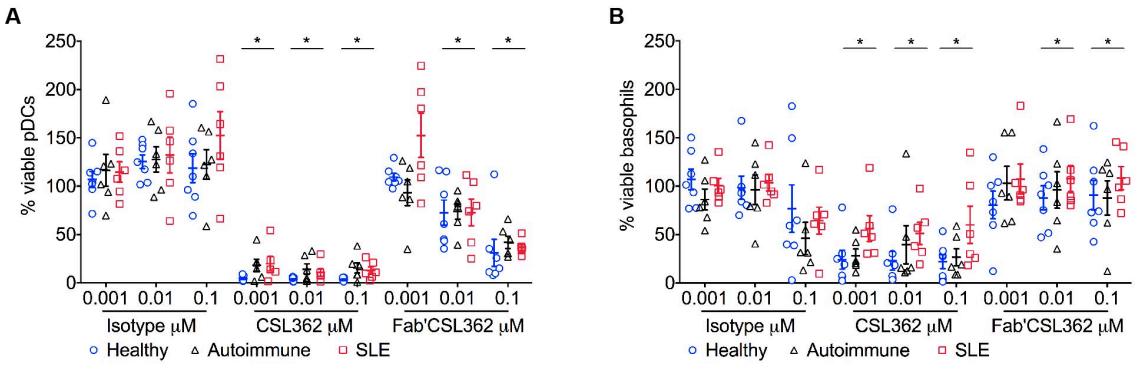
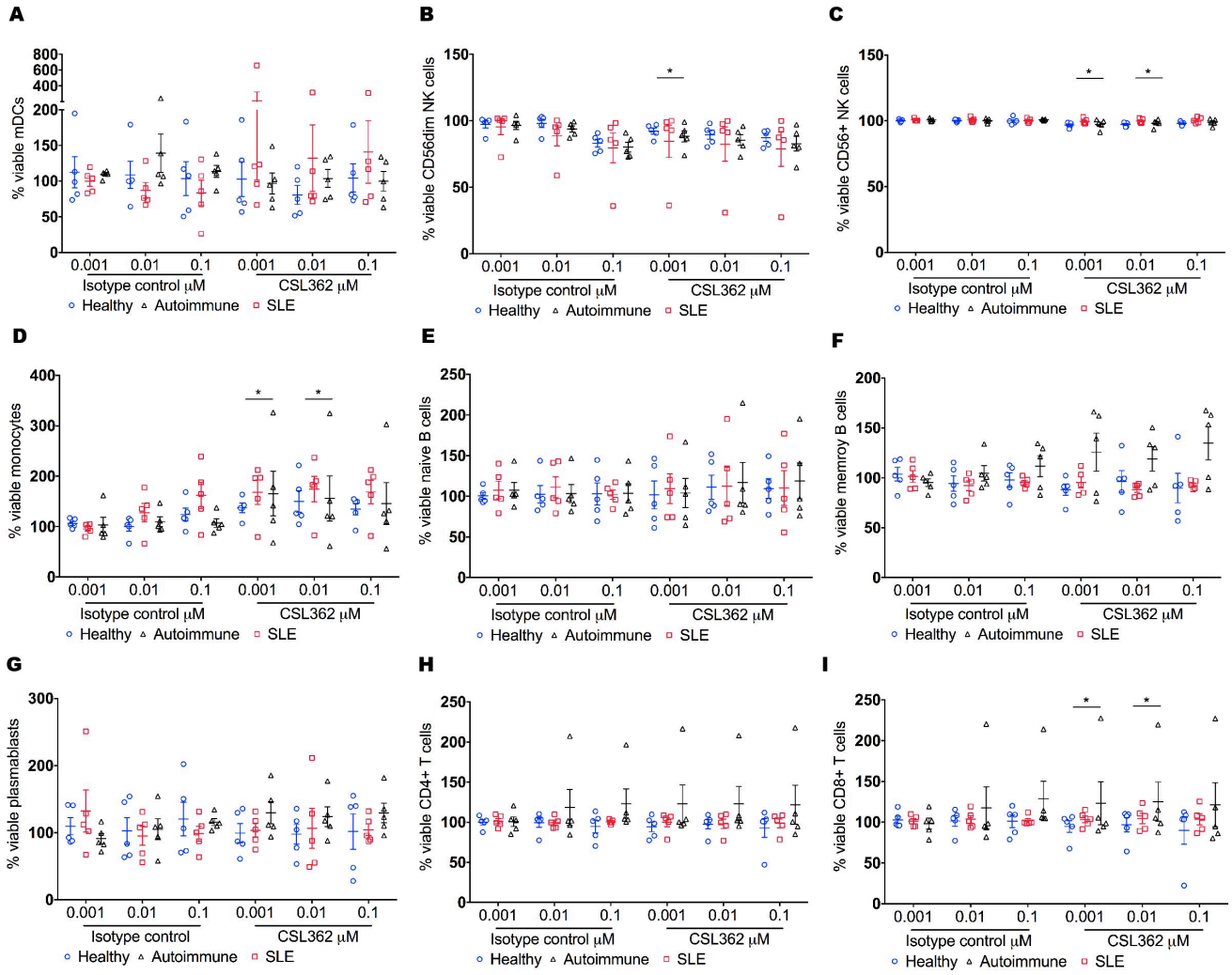
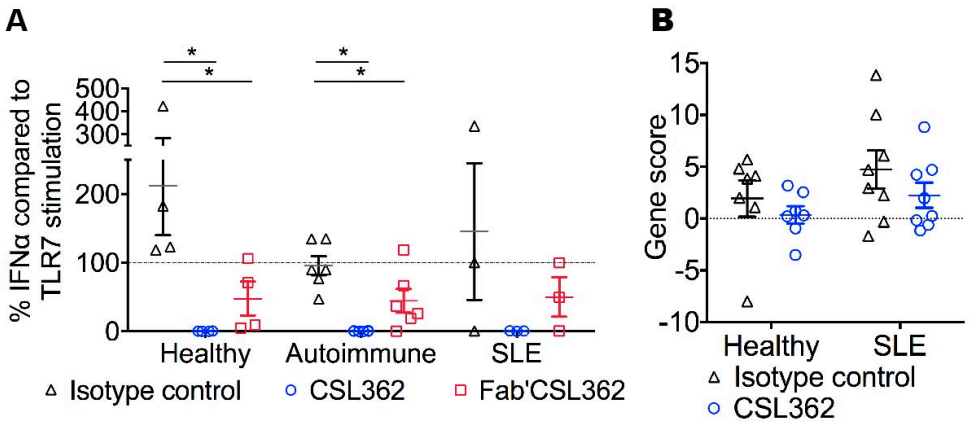


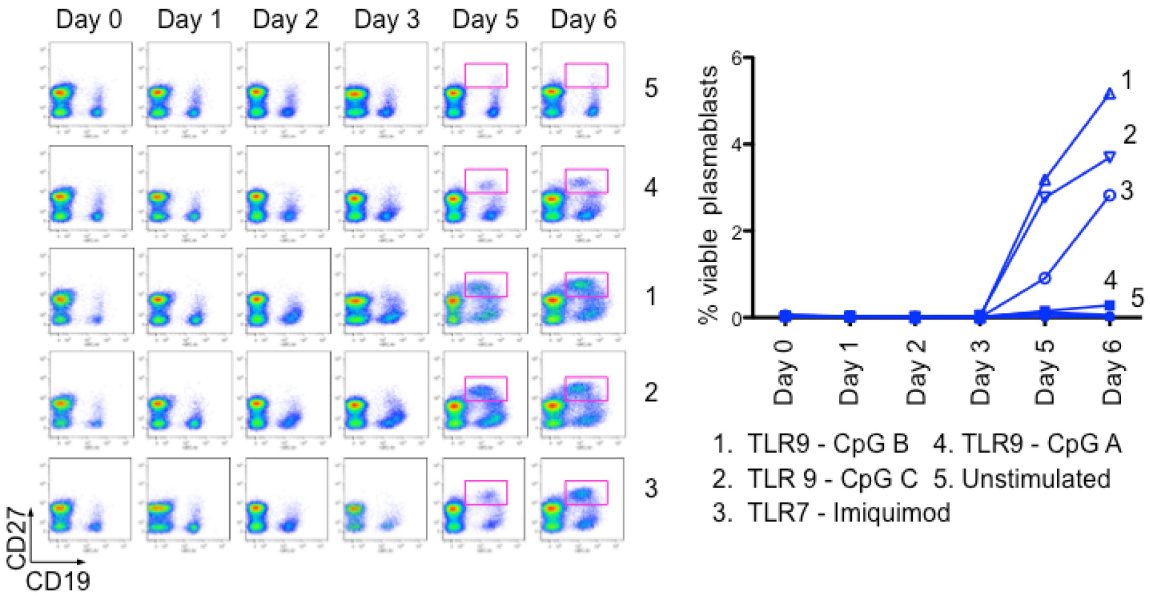
Supplemental Figure 1. IL-3 blockade with Fab'CSL362 depletes plasmacytoid dendritic cells (pDCs), but not basophils, at higher doses. Percentage of viable (**A**) pDCs (Sytox Blue-, Lin1-, HLADR+, BDCA2++) and (**B**) basophils (Sytox Blue-, Lin1-,CCR3+) following 24 hour culture with CSL362, Fab'CSL362 and isotype control at three doses (0.001 μM, 0.01 μM and 0.1 μM) compared to media alone. Data expressed as mean ± SEM, * $p < 0.05$ (Mann Whitney test), compared to equivalent dose isotype control, from SLE (n = 6), autoimmune (n = 6) and healthy (n = 7) donors.



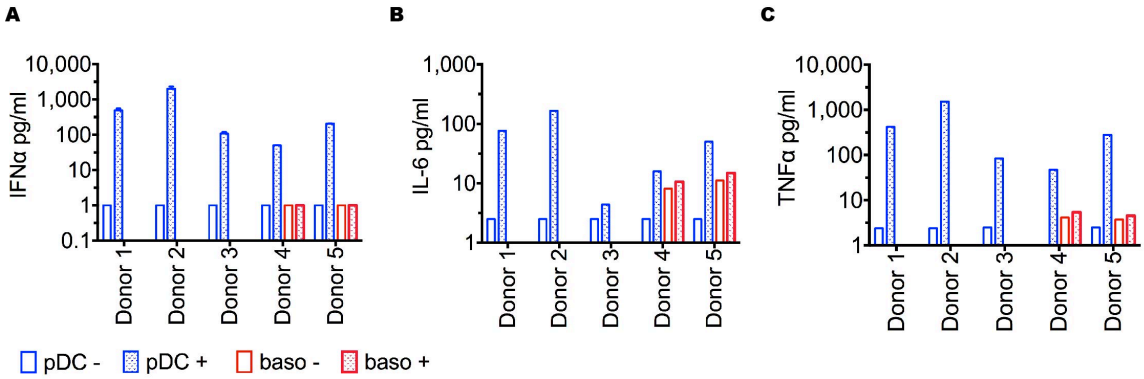
Supplemental Figure 2. No depletion of myeloid dendritic cells (mDCs), monocytes, NK, B and T cell subsets with CSL362 treatment. Percentage of viable (Sytox Blue-) (**A**) mDCs (Lin1-, HLADR+, CD11c+, BDCA2-, BDCA1+), (**B**) CD56 dim NK cells (CD14-, CD3-, CD56dim), (**C**) CD56+ NK cells (CD14-, CD3-, CD56+), (**D**) monocytes (CD3-, CD14+, CD11b+), (**E**) naïve B cells (CD19+, CD27-), (**F**) memory B cells (CD19+, CD27+), (**G**) plasmablasts (CD19+, CD27++), (**H**) CD4+ T cells (CD3-, CD4+, CD8-) or (**I**) CD8+ T cells (CD3-, CD8+, CD4-), following 24 hour culture with CSL362 and isotype control at three doses (0.001 μM, 0.01 μM or 0.1 μM) compared to no treatment. Data expressed as mean ± SEM, * $p < 0.05$ (Mann Whitney test), compared to equivalent dose isotype control from SLE, autoimmune and healthy donors (n = 5 each).



Supplemental Figure 3. CSL362 inhibits TLR7-induced IFNα production and IFN-inducible gene expression. (**A**) IFNα production from SLE (n = 3), autoimmune (n = 6) and healthy (n = 4) donor PBMCs and, (**B**) IFN-inducible gene expression, expressed as a single gene score for SLE (n = 8) and healthy (n = 7) donor PBMCs stimulated with TLR7 agonist imiquimod, following CSL362, Fab'CSL362 ((**A**) only) or isotype control pre-treatment. Gene score represents the average $\log_2$ fold change in expression of 11 IFN-inducible genes (*IFI44L, IFIT1, IFIT3, IRF7, ISG15, MX1, MX2, OAS1, OAS2, SERPING1, XAF1*) for each treatment compared to no treatment. IFN-inducible gene expression determined by qPCR, IFNα production by ELISA. Data expressed as mean ± SEM, * $p < 0.05$ (Mann Whitney test).



Supplemental Figure 4. Expansion of plasmablasts is maximal after six days of stimulation with TLR7 and TLR9 agonists. Representative data from a single healthy donor showing plasmablast (CD19+, CD27++) expansion in response to stimulation with TLR9 agonists CpG A, B and C, and TLR7 agonist imiquimod at days 0, 1, 2, 3, 5 and 6.



Supplemental Figure 5. IFNα, IL-6 and TNFα are elevated in conditioned medium produced by stimulating pDCs with CpG C. Levels of (**A**) IFNα (**B**) IL-6 and (**C**) TNF-α in conditioned medium, as determined by ELISA (IFNα) and Luminex assay (IL-6 and TNFα). pDC+ and pDC- represent conditioned media from isolated pDCs stimulated (+) or not (-) with CpG C. Baso+ and baso– represent the same for stimulated (+) or not (-) basophils. Levels of BAFF, GM-CSF, IFNγ, MIP-3α, TNFβ, IL-1β, IL-2, IL-3, IL-4, IL-5, IL-9, IL-10, IL-12p70, IL-13, IL-15, IL-17A, IL-17E/IL25, IL-17F, IL-21, IL-22, IL-23, IL-27, IL-28A, IL-31 and IL-33 were negligible.

Supplemental Table 1. SLE donor characteristics

Age (mean, range)	38.6, 18-70 (years)
Gender (female, male)	91, 9 (%)
Disease duration (mean, range)	9.5, 0.25-25 (years)
Ethnicity	
- Caucasian	65 (%)
- Asian	32
- African	3
SLEDAI (mean, range)	5, 0-14
Disease manifestations (current or past)	
- Rash	65 (%)
- Arthritis	76
- Cardiorespiratory	41
- Renal	29
- Neuropsychiatric	9
- Cytopenia	50
- Positive anti-dsDNA antibody	79
- Hypocomplementaemia	47
Current medications	
- No immunosuppression	9 (%)
- Steroids	59
- Hydroxychloroquine	76
- Methotrexate	9
- Azathioprine	24
- Mycophenolate	12
- Rituximab	3

Supplemental Table 2. Antibodies and reagents

Application	Reagent	Company	Category number
CD123 expression	Anti-CD123 PE	BD Biosciences	555644
Plasmacytoid dendritic cells, basophils	Lineage cocktail 1 – Lin1 (CD3, CD14, CD16, CD19, CD20, CD56) FITC	BD Biosciences	340546
Plasmacytoid dendritic cells, basophils	Anti-HLADR APC	BD Biosciences	641393
Plasmacytoid dendritic cells, basophils	Anti-HLADR APCH7	BD Biosciences	561358
Plasmacytoid dendritic cells	Anti-BDCA2 PECy7	E-Bioscience	25-9818-42
Plasmacytoid dendritic cells	Anti-BDCA2 APC	Miltenyi Biotec	130-090-905
Basophils	Anti-CCR3 AF647	BD Biosciences	561745
Basophils	IgE FITC	KPL	02-10-04
Myeloid dendritic cells	Anti-CD11c BV421	BD Biosciences	562561
Myeloid dendritic cells	Anti-CD11c APC	BD Biosciences	340544
Myeloid dendritic cells	Anti-BDCA1 PE	Miltenyi Biotec	130-098-007
Myeloid dendritic cells	Anti-CD123 BV510	BD Biosciences	563702
NK cells, monocytes, T cells	Anti-CD3 PECy7	BD Biosciences	557851
NK cells	Anti-CD56 FITC	BD Biosciences	340410
NK cells	Anti-Nkp46 APC	BD Biosciences	558051
NK cells	Anti-CD107a APCH7	BD Biosciences	561343
B cells	Anti-CD19 PECy7	BD Biosciences	557835
B cells	Anti-CD19 APC	BD Biosciences	555415
B cells	Anti-CD20 FITC	BD Biosciences	556632
B cells	Anti-CD27 V500	BD Biosciences	561222
B cells	Anti-CD38 BV421	BD Biosciences	562444
B cells	Anti-CD38 PECy7	BD Biosciences	335790
Monocytes, NK cells	Anti-CD14 APCH7	BD Biosciences	561384
Monocytes	Anti-CD14 APC	BD Biosciences	555399
Monocytes	Anti-CD11b APC	BD Biosciences	09546
Monocytes, granulocytes	Anti-CD16 FITC	BD Biosciences	555406
Granulocytes and eosinophils	Anti-CD49d APC	BD Biosciences	559881
T cells	Anti-CD4 FITC	BD Biosciences	555346
T cells	Anti-CD8 APC	BD Biosciences	555369
T cells	Anti-CD8 APCH7	BD Biosciences	561423
Dead cell stain	Sytox Blue	Life Technologies	S11348
Cell proliferation dye	CFSE	Life Technologies	C34554
NK cell activation	Golgistop	BD Biosciences	554754