JEM

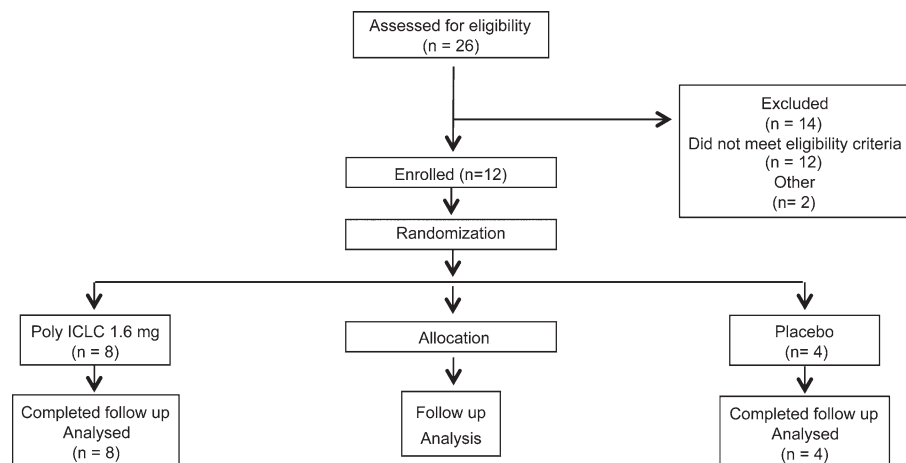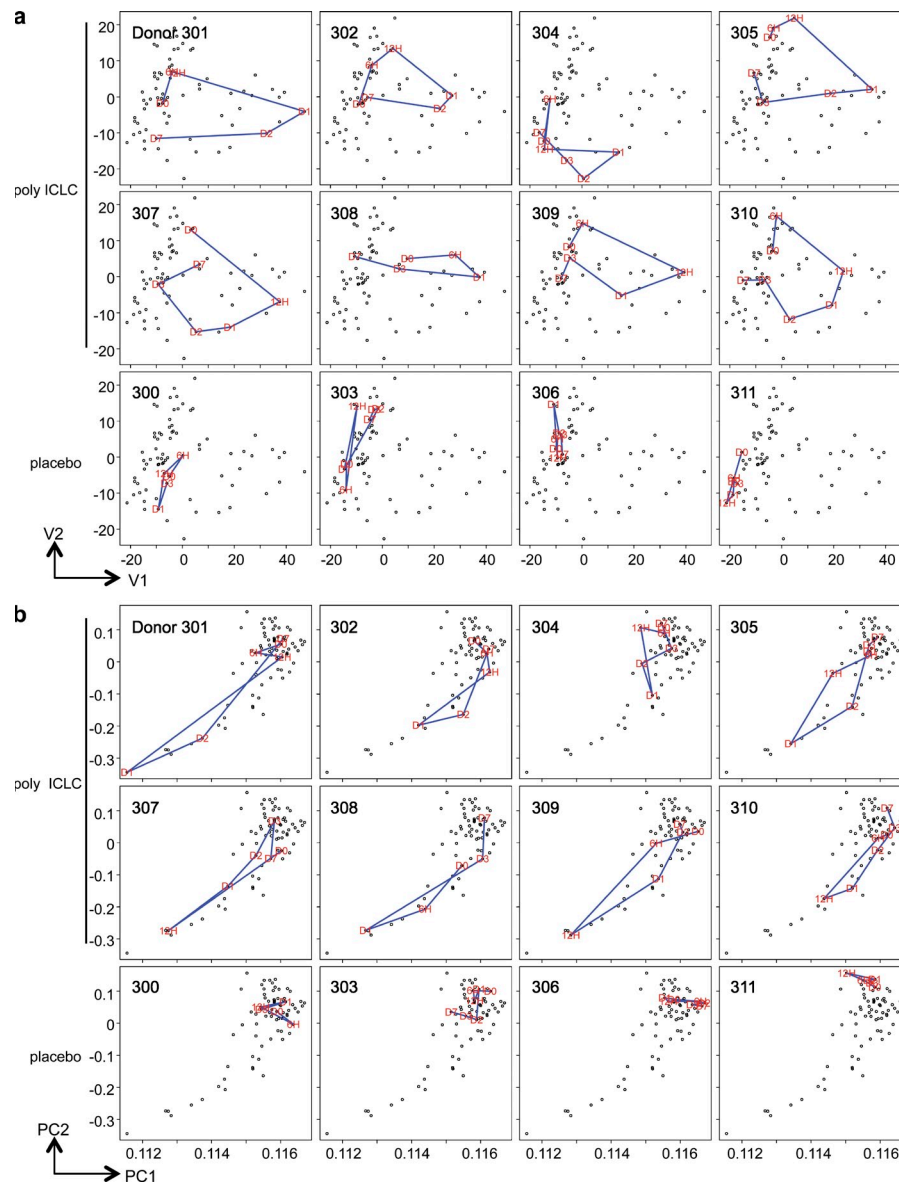**Figure S1.** Clinical trial participant flow diagram.

Figure S2. Gene regulation was homogenous and peaked early on after s.c. poly ICLC. Plots of 2D classical MDS and the first two PCAs, displayed by individual subjects to show the evolution of their gene expression profiles through time. Global gene expression peaked at 24 h in five volunteers who received poly ICLC and at 12 h in the remaining three. In all eight volunteers, gene expression profiles returned to baseline levels 7 d after poly ICLC injection.
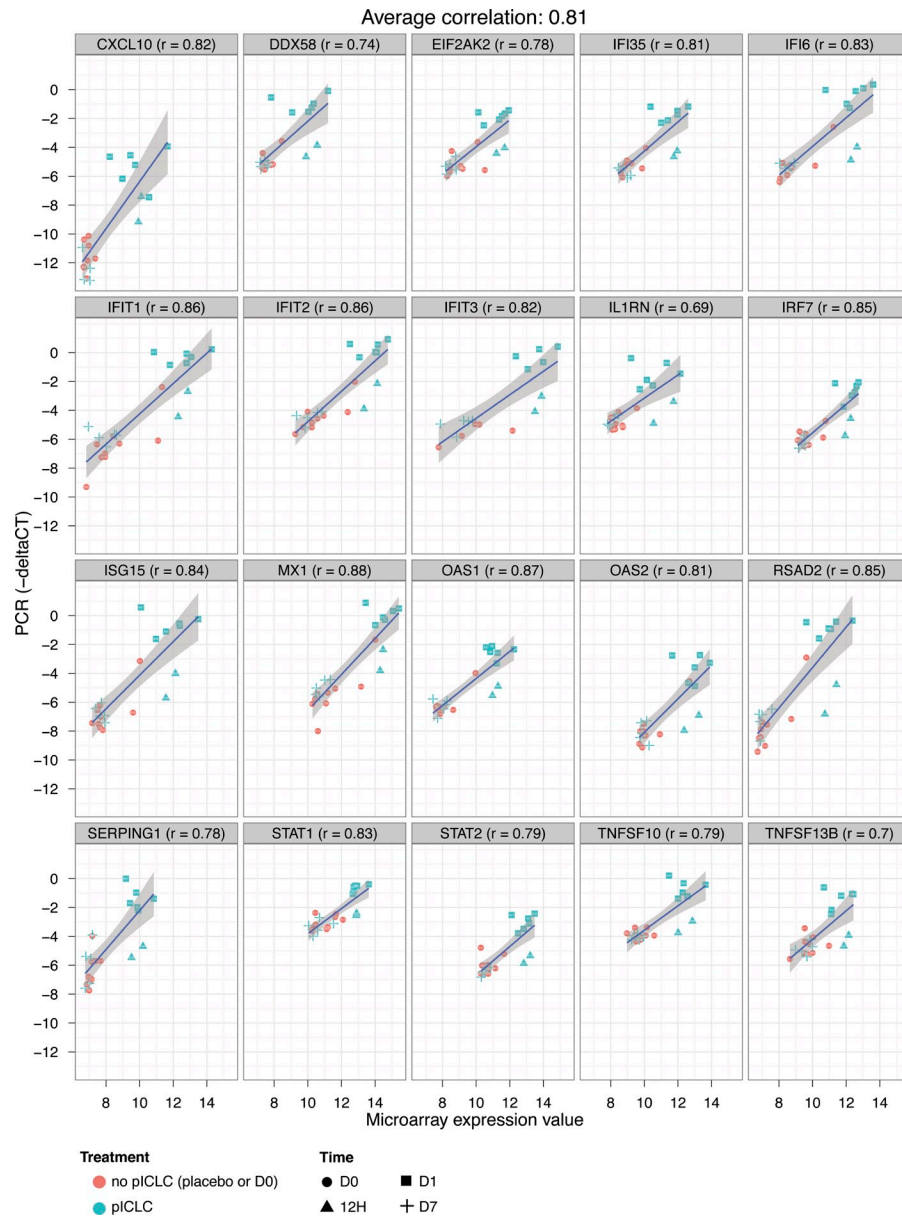
Figure S3. Gene expression values from the BeadArrays, plotted against the OpenArray real–time PCR −ΔCt values for each target gene.
PCR targets were mapped to BeadArray probes by matching the official gene symbols. Multiple matches were resolved by retaining only the most differentially expressed probe at Day 1. Correlations indicated are the sample Pearson correlation coefficients. The TaqMan gene expression assay primer identifiers used in the OpenArray experiment were: CXCL10 Hs00171042_m1, DDX58 Hs00204833_m1, EIF2AK2 Hs00169345_m1, IFI35 Hs00382709_m1, IFI6 Hs00242571_m1, IFIT1 Hs00356631_g1, IFIT2 Hs00533665_m1, IFIT3 Hs00155468_m1, IL1RN Hs00277299_m1, IRF7 Hs01014809_g1, ISG15 Hs01921425_s1, MX1 Hs00895608_m1, OAS1 Hs00973637_m1, OAS2 Hs00213443_m1, RSAD2 Hs00369813_m1, SERPING1 Hs00163781_m1, STAT1 Hs01014005_m1, STAT2 Hs01013123_m1, TNFSF10 Hs00921974_m1, and NFSF13B Hs00198106_m1.

Table S1. Subject demographics

Study ID	Study drug	Age	Gender	Race	Ethnicity
		yr			
301	Poly ICLC	19	Female	African-American	Hispanic
302	Poly ICLC	30	Male	White	Hispanic
304	Poly ICLC	29	Female	African-American	Non-Hispanic
305	Poly ICLC	42	Male	White	Hispanic
307	Poly ICLC	25	Female	White	Non-Hispanic
308	Poly ICLC	23	Female	White	Non-Hispanic
309	Poly ICLC	23	Female	White	Non-Hispanic
310	Poly ICLC	34	Male	White	Non-Hispanic
300	Placebo	32	Male	White	Non-Hispanic
303	Placebo	53	Male	White	Non-Hispanic
306	Placebo	43	Male	White	Non-Hispanic
311	Placebo	37	Male	African-American	Non-Hispanic

Table S6. Selected canonical pathways and their genes commonly modulated after poly ICLC at day 1 and YF17D at day 7

Ingenuity canonical pathways	−log(p-value) poly ICLC	Ratio poly ICLC	−log(p-value) YF-17D	Ratio YF-17D	Common regulated genes after poly ICLC and YFV
Role of PRRs in recognition of bacteria and viruses	7.83	0.41	3.46	0.34	TLR8, C1QC, C1QA, C1QB, IFIH1, TICAM1, TLR7, CASP1, NOD1, RIPK2, NLRC4, ATM, OAS1, NLRP3, OAS2, MYD88, C5, OAS3, TLR4, IRF7, NOD2, TLR5, DDX58, IL1B, EIF2AK2, and C3AR1
Apoptosis signaling	4.4	0.35	1.9	0.32	NFKBIE, BCL2, PRKCE, CHUK, CASP8, BIRC3, PRKCA, RRAS, BAK1, and CASP2
IFN signaling	4.25	0.47	3.48	0.47	IFIT3, SOCS1, OAS1, IRF9, MX1, IFI35, JAK2, PSMB8, TAP1, BAK1, BCL2, IFIT1, IFITM1, STAT2, and STAT1
DC Maturation	3.29	0.24	6.26	0.2	HLADOA, NFKBIE, LTB, JAK2, CREB5, FCGR2B, HLAA, CHUK, LTBR, CD1C, IL23A, STAT1, ATM, MYD88, RELB, IL15, TLR4, IL1RN, FCER1G, CD86, IL1B, STAT2, and CCR7
NF-κB signaling	2.98	0.27	3.06	0.31	PRKACB, TLR8, LTBR, TRAF5, TNFSF13B, ATM, HDAC2, RRAS, IL1RN, KLK2, MAP2K6, NFKBIE, TLR7, CHUK, EGFR, MYD88, RELB, TLR4, CSNK2A2, RIPK1, TLR5, BCL10, FCER1G, and IL1B
Activation of IRF by cytosolic PRRs	2.11	0.28	1.66	0.29	DHX58, NFKBIE, ZBP1, IRF9, ADAR, ISG15, IFIH1, IRF7, RIPK1, DDX58, STAT2, CHUK, and STAT1
Antigen presentation pathway	1.88	0.32	1.86	0.34	PSMB9, HLA-DOA, NLRC5, PSMB8, CD74, TAP1, MR1, HLA-A, and HLA-E
IL-10 signaling	1.83	0.28	2.68	0.34	MAP2K6, NFKBIE, FCGR2B, HMOX1, CCR1, BLVRA, IL1RN, CD14, and IL1B
Cross talk between DCs and NK cells	1.79	0.27	2.16	0.32	IL15RA, ACTA2, LTB, KIR3DL2, TNFSF10, MICB, HLAA, TLR7, LTBR, IL15, TLR4, HLA-E, CD86, and CCR7
TLR signaling	1.61	0.29	2.32	0.36	MAP2K6, MYD88, TLR8, TLR4, TLR5, TLR7, CD14, and CHUK

The column −log(p-value) represents the statistical significance for each pathway. The column ratio represents the ratio of regulated gene number/pathway gene number after poly ICLC or YF17D.

Table S2, listing DEGs 1 d after s.c. administration of poly ICLC in comparison to placebo, Table S3, listing IRGs, Table S4, showing the canonical pathways significantly regulated at 1 d after poly ICLC s.c., and Table S5, listing the top commonly regulated genes in whole blood 1 d after poly ICLC s.c. and after in vitro stimulation of PBMCs with poly IC, are provided as Excel files.