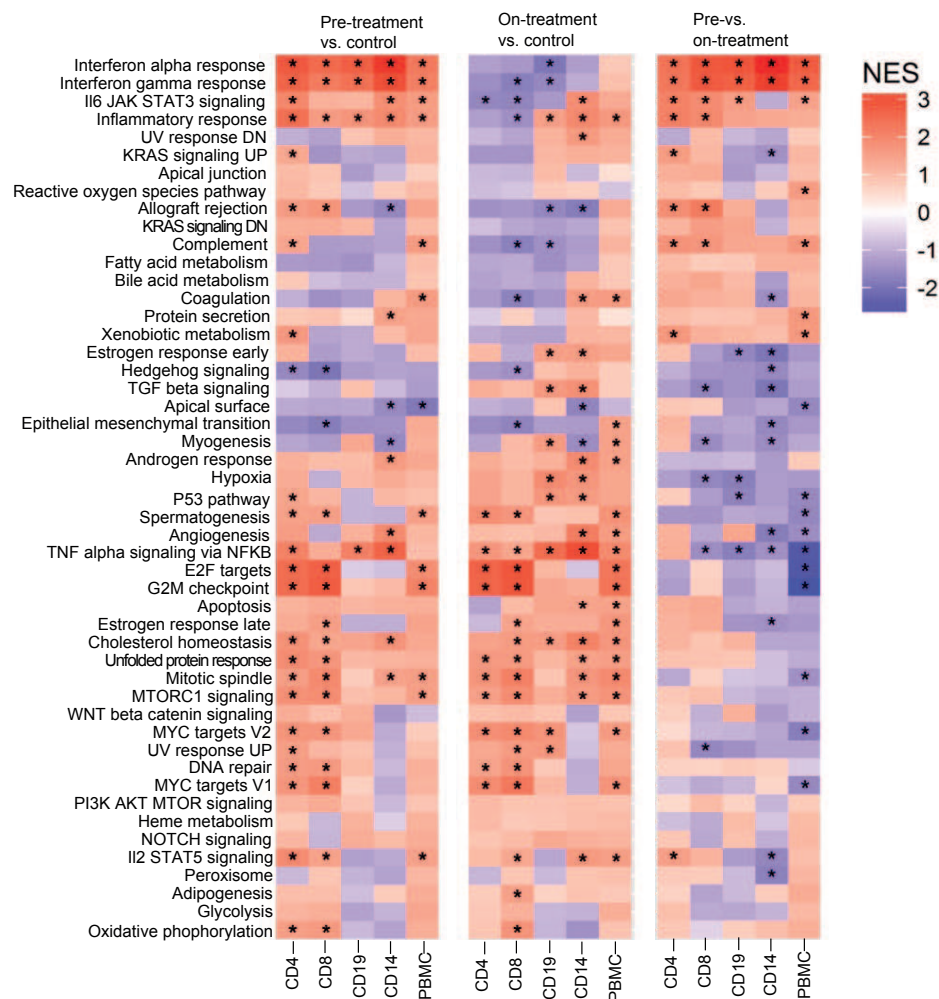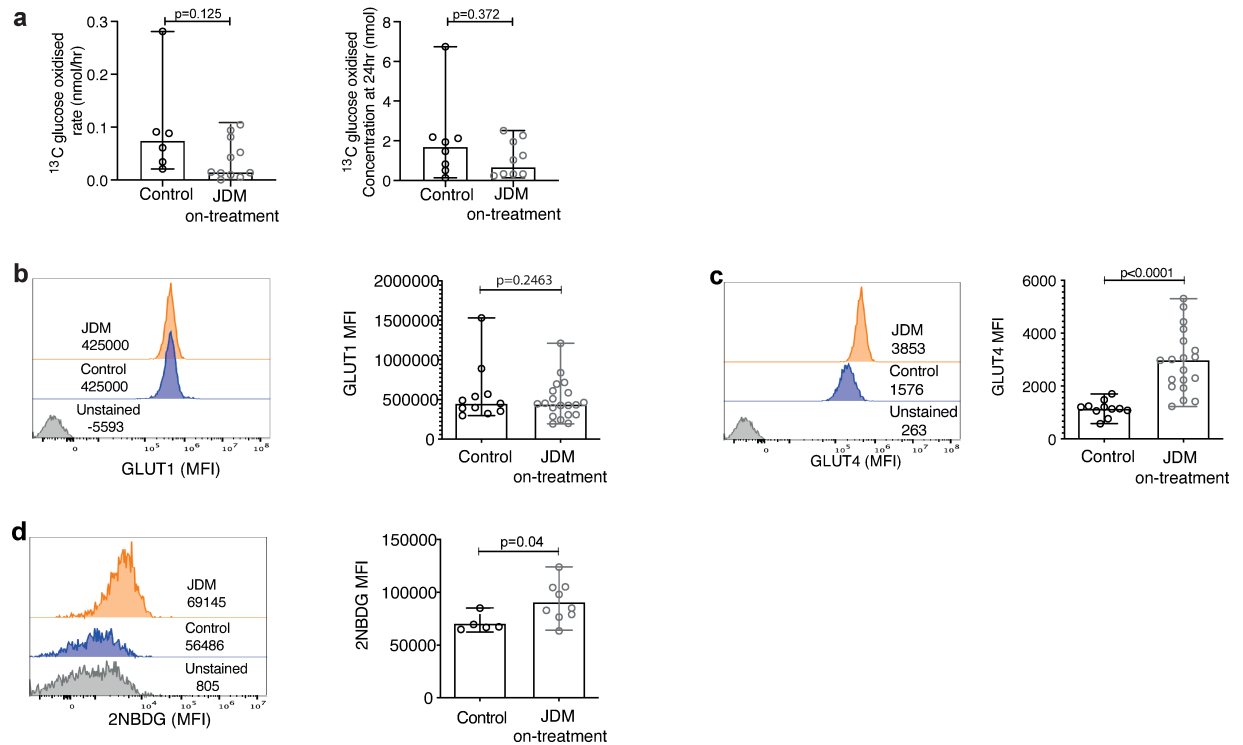# Supplementary Figure 1

Supplementary Figure 1. Transcriptional analysis validates strong IFN type 1 signaturein in all cell types in JDM pre-treatment.
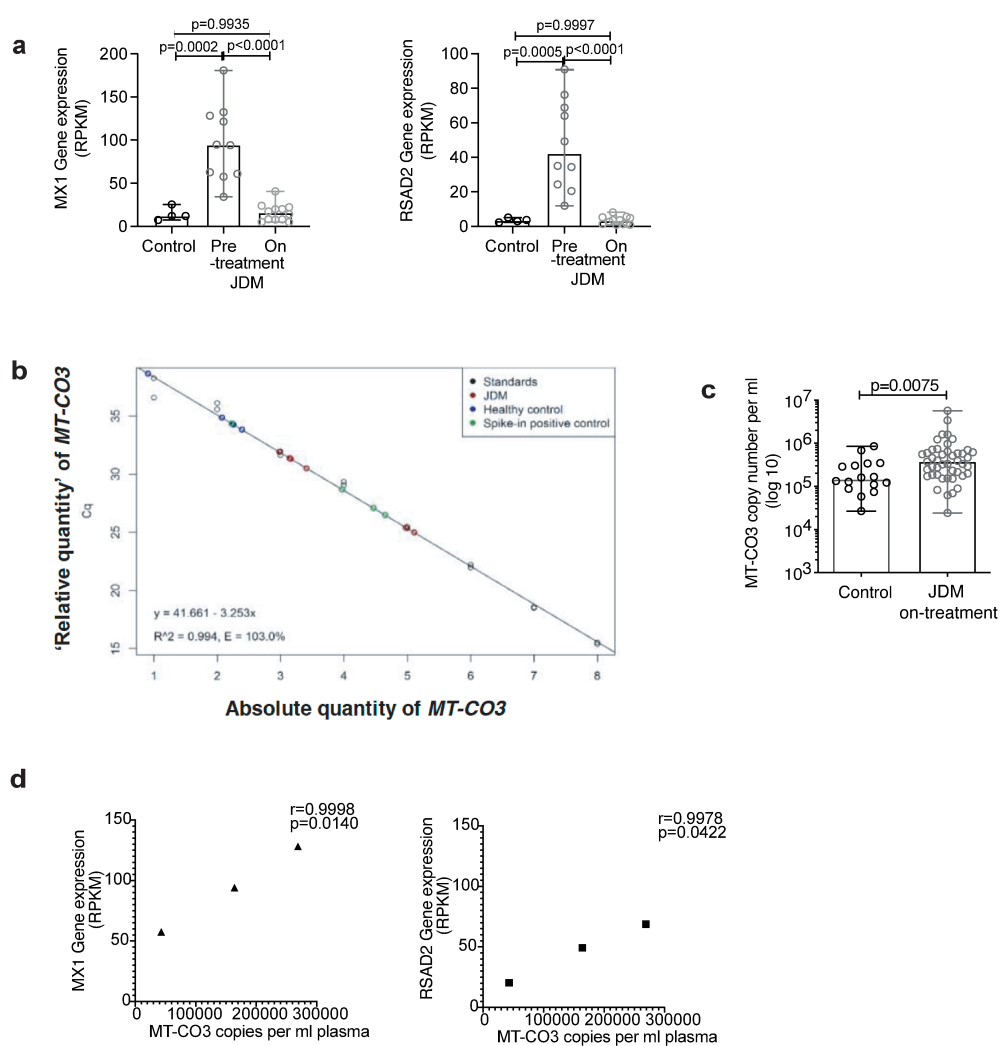Transcriptomic analysis of flow-sorted CD4+, CD8+, CD19+ and CD14+ cells from JDM patients taken pre-treatment [n=10] and 12 months on-treatment [n=11], and age-matched healthy controls [n=4]. Heatmap of Gene-Set Enrichment Analysis (GSEA) for enriched Hallmark gene-sets. For each cell type every gene was ranked comparing pre-treatment vs. control, on-treatment vs. control and pre- vs. on-treatment. Normalised Enrichment Score (NES): red represents an up-regulated pathway and blue a down-regulated pathway, stars represent adjusted p-values (* $p<0.05$).

Supplemental material

BMJ Publishing Group Limited (BMJ) disclaims all liability and responsibility arising from any reliance placed on this supplemental material which has been supplied by the author(s)

Ann Rheum Dis

Supplementary Figure 2

Supplementary Figure 2. There is abnormal cellular metabolism in JDM CD14+ monocytes.
(**a**) Bar graphs show 13C labelled glucose metabolism rate (left) and final concentration into oxidised glucose in CD14+ monocytes from JDM [n=6] and controls [n=6]. Representative histogram (left) and bar graphs (right) show (**b**) GLUT1 and (**c**) GLUT4 MFI in CD14+ monocytes from JDM [n=20] vs. control [n=11]. (**d**) Representative histogram (left) and bar graphs (right) show 2NBDG MFI in JDM CD14+monocytes [n=9] compared to controls [n=5]. All bar graphs: median with range shown. Statistical analysis: non-parametric Mann-Whitney test, p-value.

Supplementary Figure 3

Supplementary Figure 3. Non-oxidised mitochondrial DNA correlated with increased ISG in pre-treatment JDM
(**a**) Gene expression analysis of CD14+ monocytes from JDM patients taken pre-treatment [n=10] and 12 months on-treatment [n=12], and controls [n=3]. Reads per kilobase pair of transcript (RPKM) gene expression of *MX1* and *RSAD2* (left to right). (**b**) Standard curve of MT-CO3 for standards, spike-in positive controls, JDM and age-matched healthy control samples. (**c**) MT-CO3 copy number per ml of plasma (mtDNA) for JDM pre-treatment [n=45] and controls [n=16]. (**d**) MT-CO3 copy number per ml of blood for JDM pre-treatment [n=3] correlated to matched sample RPKM gene expression values for MX1 and RSAD2 (left to right).Bar graph: median with range shown.Statistical analysis: (**a**) Non-parametric Kruskal-Wallis test with Dunn's multiple comparisons, adjusted p-values. (**c**) Non-parametric Mann-Whitney tests, p-values. (**d**) r and p-values calculated by Pearson correlation.

Supplementary Figure 4
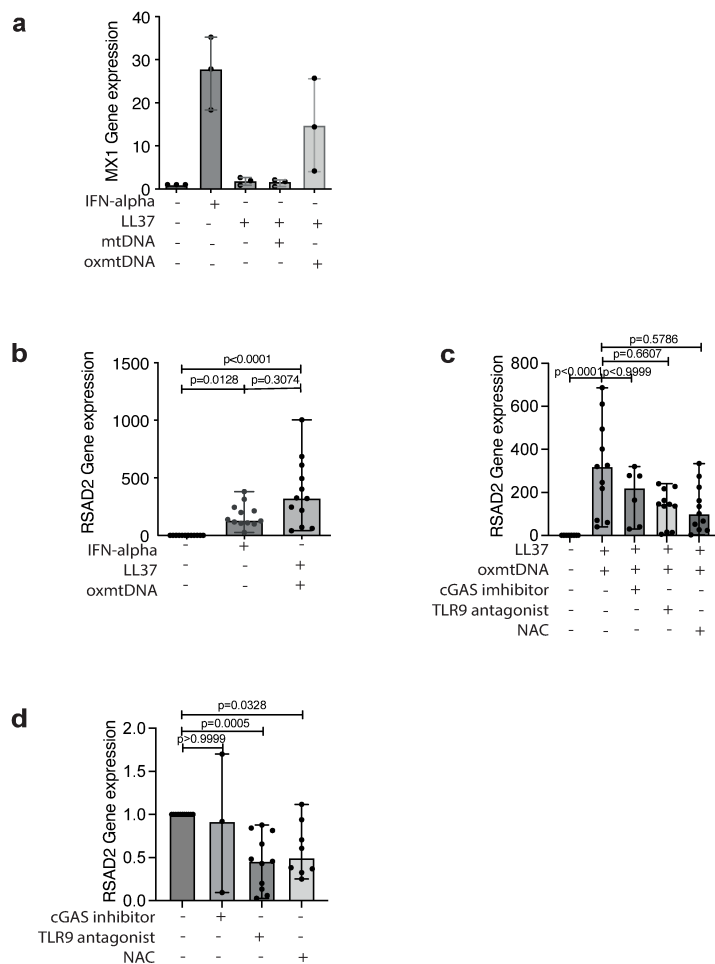
Supplementary Figure 3. Non-oxidised mitochondrial does not induce ISG, but oxidised does and can be blocked by TLR9 antagonist and NAC

(**a**) Bar graph shpws relative expression of IFN stimulated gene (ISG) *MX1* in control PBMC [n=3] incubated with IFN-alpha, LL37, mtDNA (+LL37), oxidised mtDNA (with LL37) or no stimuli. (b) Bar graphs show relative expression of ISG *RSAD2* in control PBMC [n=12] incubated with IFN-alpha, oxmtDNA (with LL-37) or no stimuli (unstim). (c) Bar graphs show relative expression of ISG *RSAD2* in control PBMC incubated with no stimuli, oxmtDNA (+LL-37) [n=12] with or without cGAS inhibitor [n=6], TLR-9 antagonist [ODN TTAGGG(A151)] [n=11] or N-acetylcysteine (NAC) [n=11]. (d) Bar graphs show gene expression of ISG *RSAD2* in PBMC from JDM patients pre-treatment cultured with or without cGAS inhibitor [n=3], TLR-9 antagonist [n=11], NAC [n=8] or in medium alone (untreated) [n=6]. Bar graph: median with range shown.Statistical analysis: (**a-d**) Non-parametric Kruskal-Wallis test with Dunn's multiple comparisons, adjusted p-values.