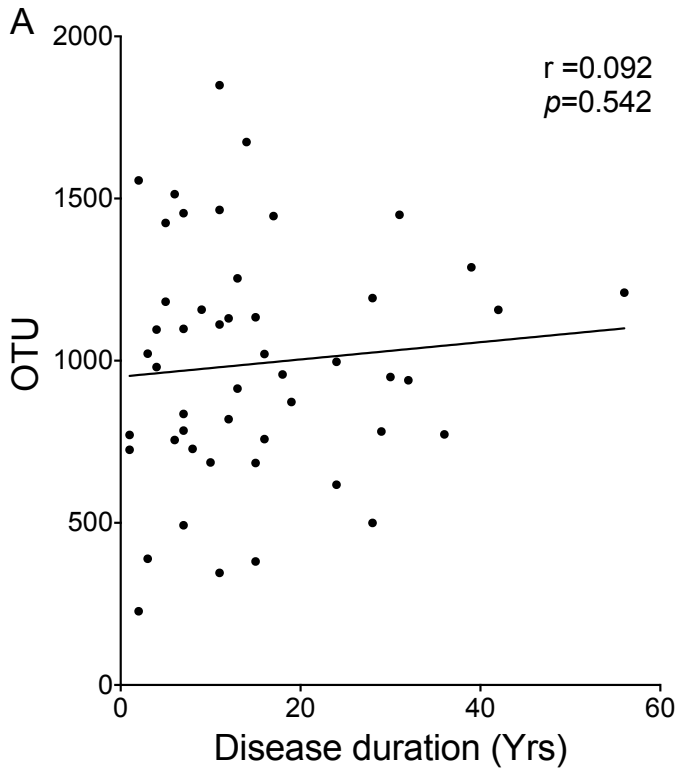
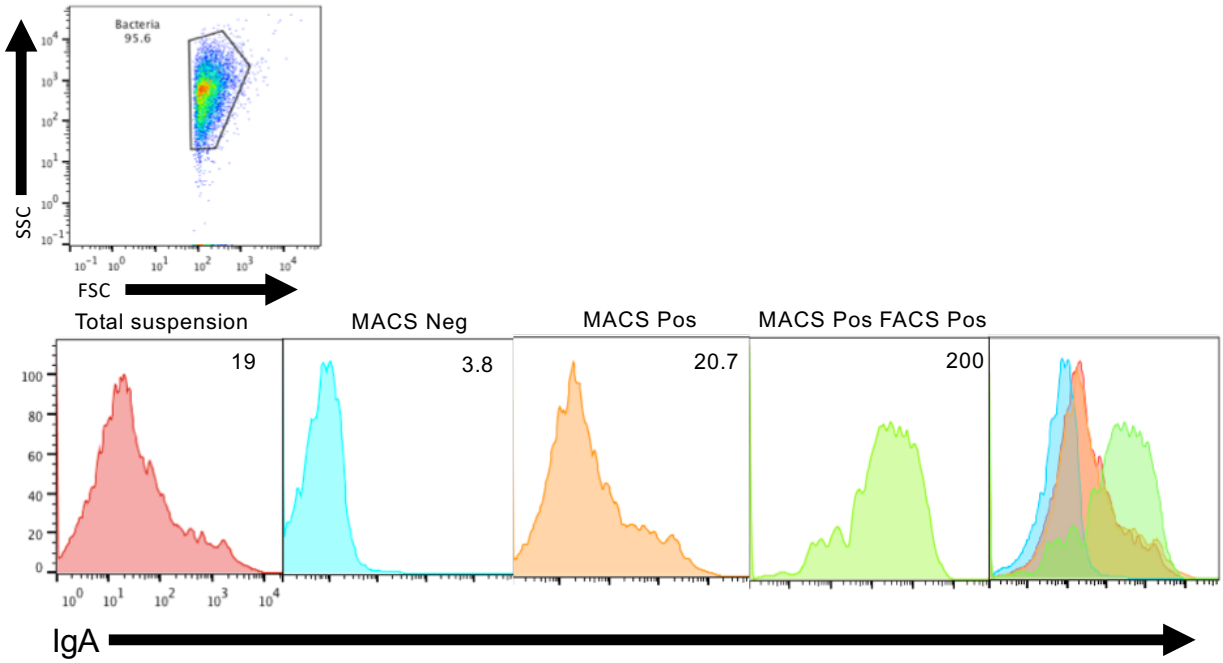
Supplementary Figure 1



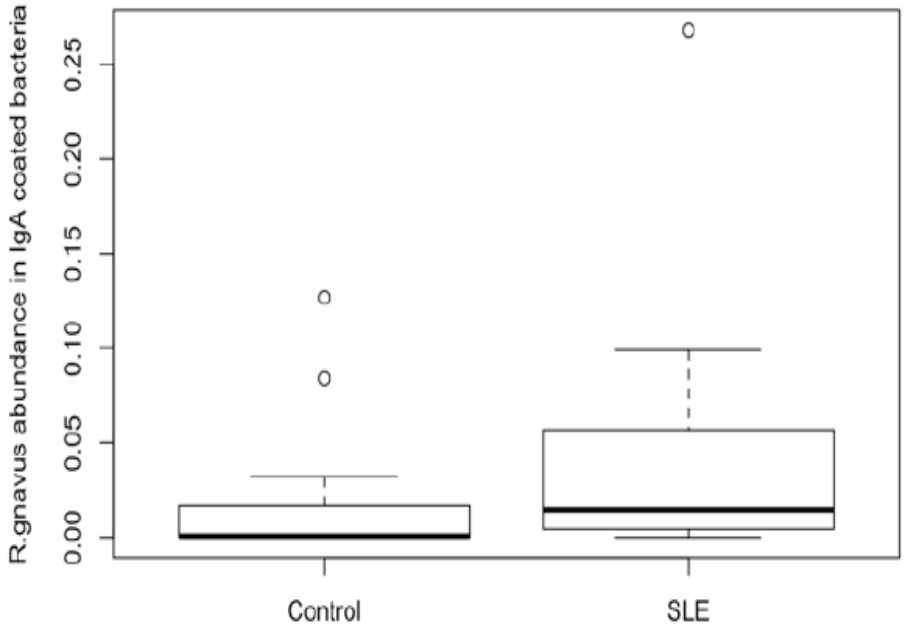
Supplementary Figure 1A. Level of alpha richness of fecal communities do not correlate with duration of disease. Values from Chao1 estimates in individual SLE libraries are shown (see methods).

B

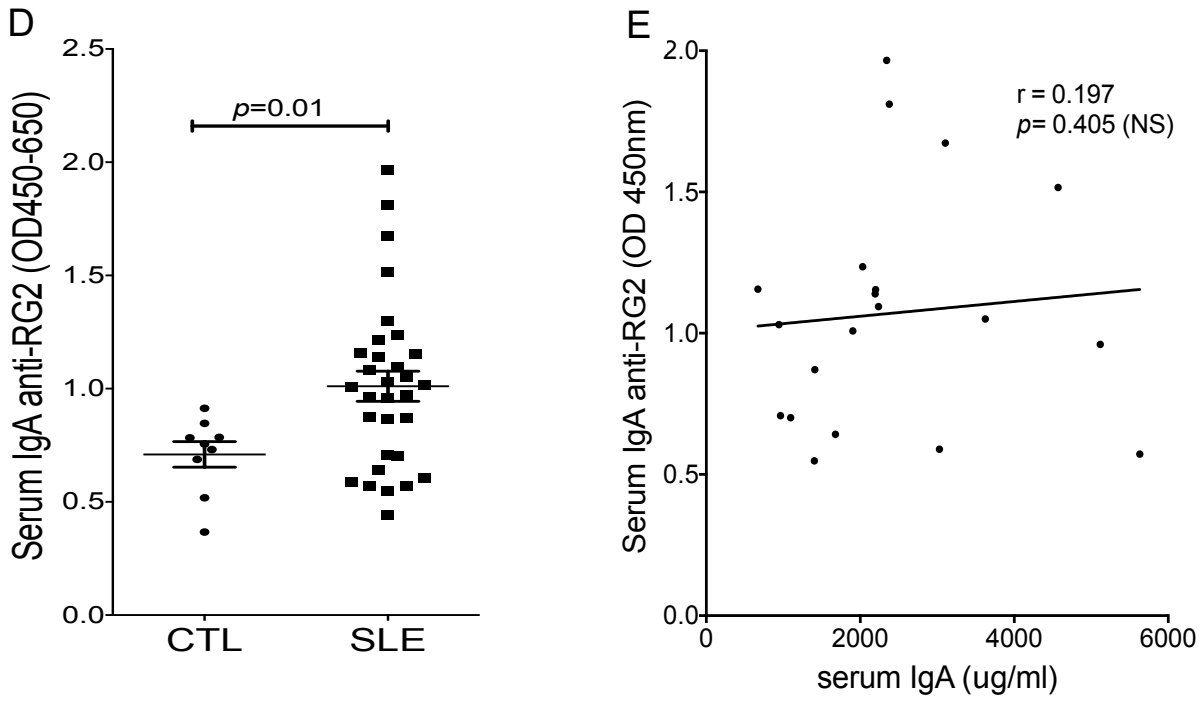


Supplementary Figure 1B. Isolation of sIgA-coated bacteria based on a two-step purification approach. The top row shows the scattergram of washed fecal bacteria based on side and forward scatter. “Total suspension” represents the original sample, which is shown to be highly heterogeneous with an overall mean fluorescence intensity (MFI) of only 19. After depletion of IgA-bound bacteria the “MACS negative” sample has a lower MFI for IgA staining (MFI value 3.8), while MACS positive sample is higher, and the MACS positive FACS positive double-enriched fraction displays a IgA MFI of 200.

C

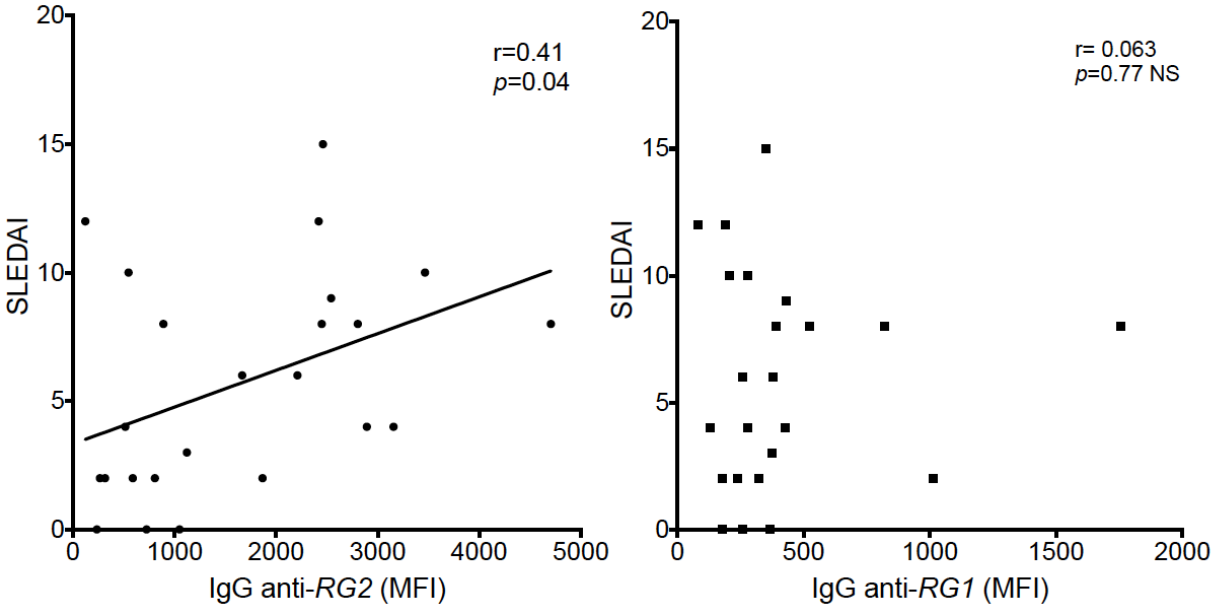


Supplementary Figure 1C. Lupus fecal sIgA-coated bacteria communities are numerically enriched for representation of *R. gnavus*. Results are shown for the 16S rRNA gene analyses of libraries generated for sIgA-coated bacteria obtained from a two-step purification process. Results are for 17 healthy female adult controls and 23 SLE patients, depicted as mean ± SD for controls 0.0186±0.037, SLE 0.035±0.059, p=0.1404, NS by Wilcoxon rank sum test (ratio = 1.88).

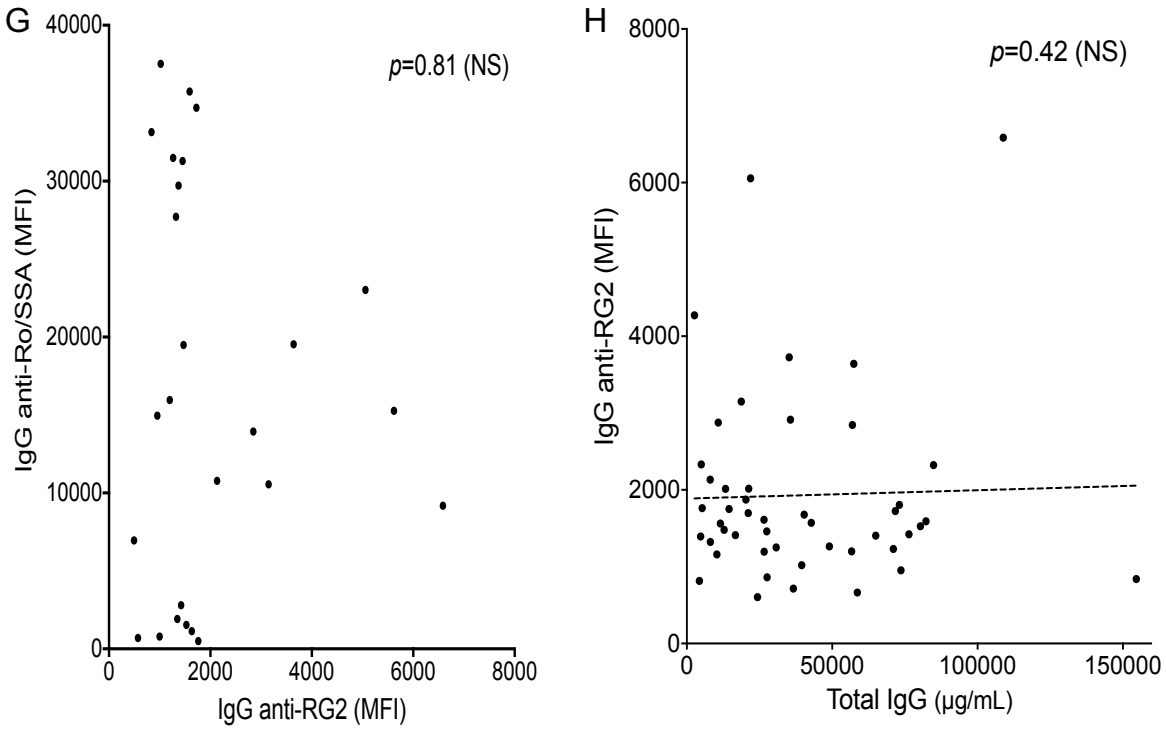


Supplementary Figures 1D&E. Serum IgA levels to *RG2* are significantly higher in SLE patients (*D)* but there is no correlation between IgA anti-*RG2* and serum total IgG levels (*E)*. Assays were performed by ELISA using individual serum samples at 1:200 dilution.

F

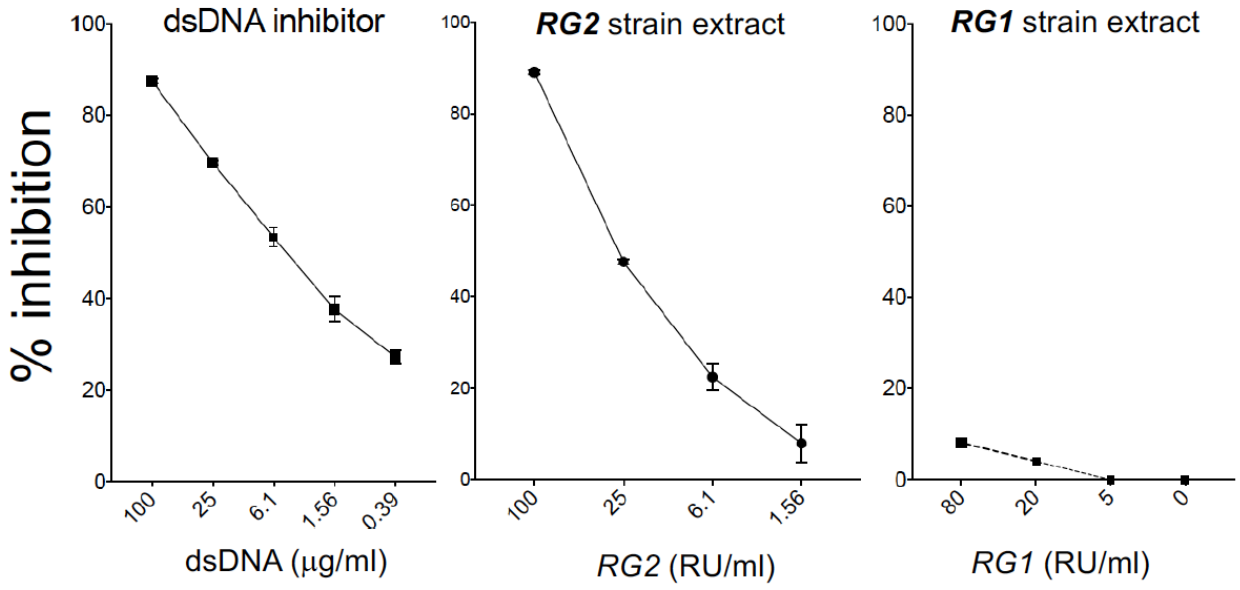


Supplementary Figure 1F. Serum levels of circulating IgG anti-*RG2* strain antibodies weakly correlated with SLEDAI disease composite score. A relationship was found between SLEDAI and levels of matched serum IgG anti-*RG2* strain (left) but not with the *RG1* strain (right). N=24. SLEDAI represents a composite score for SLE disease activity, and the serum IgG anti-*RG2* levels were determined with a custom bead-based assay with nuclease-treated *RG2* bacterial extract to detect serum IgG reactivity.



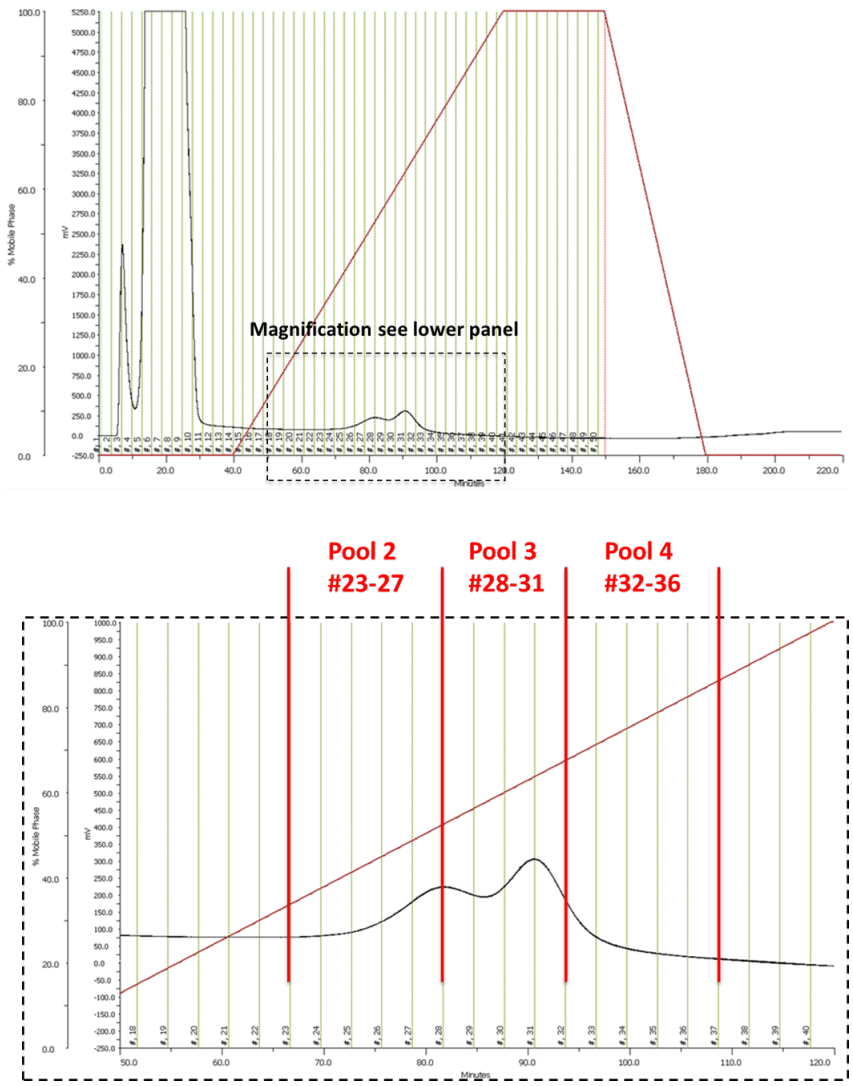
Supplementary Figure 1 G&H. Levels of serum IgG anti-*RG2* neither correlated with IgG anti-Ro52 (SSA) (*G)*, nor with total IgG levels (*H)*). IgG anti-*RG2* levels were determined by bead-based assays while total IgG used an in-house ELISA and anti-Ro52 by commercial ELISA kit.

I

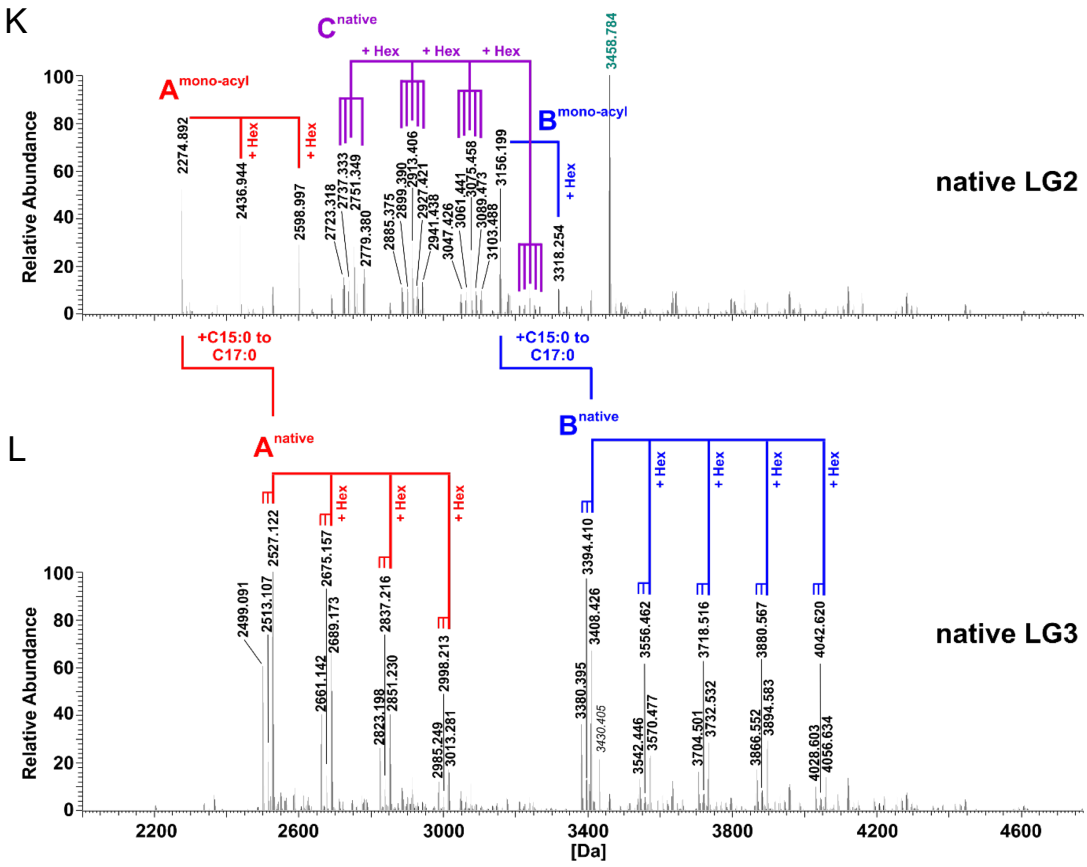


Supplementary Figure 1l. *RG2* extracts displayed dose-dependent inhibition of the binding of Lupus serum IgG to native DNA, akin to dsDNA itself. However an equivalent preparation of another *R. gnavus* strain, *RG1*, was without inhibitory activity. Bacterial strains were prepared with lysozyme and a broad DNA/RNA nuclease that was then neutralized with PMSF before use (see methods). Strains are described in Supplementary Table 5.

J

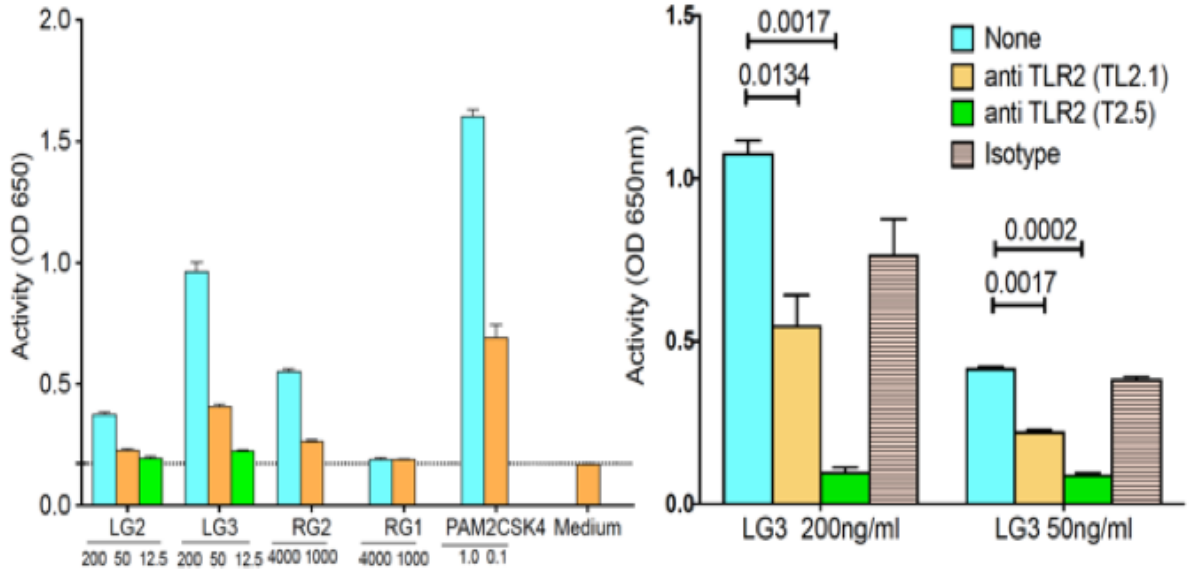


Supplementary Figure 1J. Chromatogram of the hydrophobic interaction chromatography (HIC) performed with the material recovered from the aqueous phase of the butanol-water extraction of *RG2* cells. Studies showed the phosphate content of the fractions #20-40 was zero, indicating the absence of Lipoteichoic Acid (LTA) molecules in *RG2*. The fractions were combined as indicated in top panel, higher magnification in lower panel, resulting in the following yields: pool 2, 0.94 mg; pool 3, 2.86 mg; pool 4, 0.23 mg. The mass spectra of pool 2 (LG2) and pool 3 (LG3) are depicted in Figure 3 and Supplementary Figures 1 K&L. Experience from other studies indicate that the main UV active signals in fractions #20-40 can at times represent non-lipoglycan species such as lipoproteins.



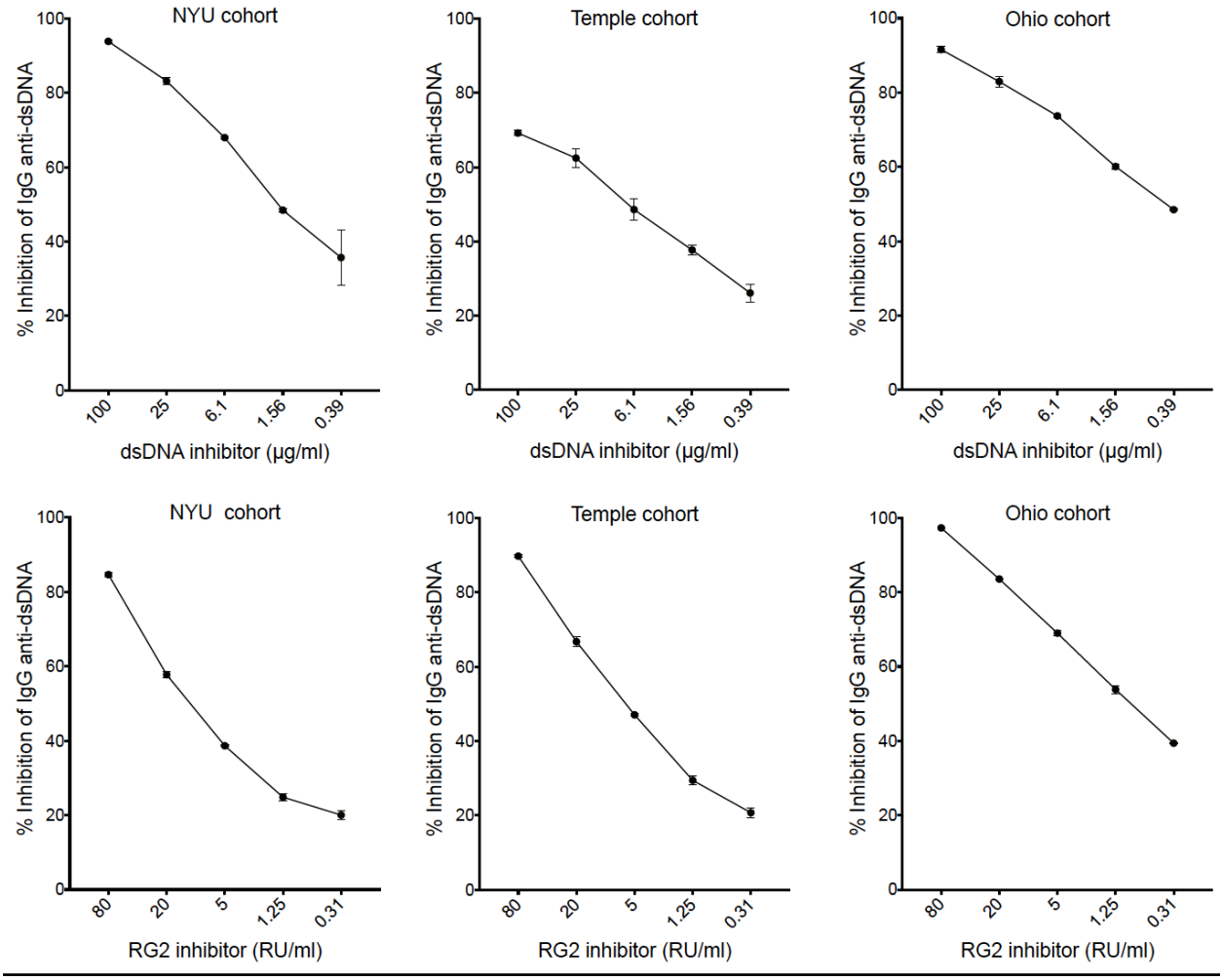
Supplementary Figures 1K&L. Lipoglycan preparations LG2 and LG3 differ in their respective lipoglycan content. The charge-deconvoluted MS spectrum of negative ion mode analysis of lipoglycan preparations, LG2 and LG3, obtained after hydrophobic interaction chromatography (HIC) are shown. ***K)*** LG2 contains one major series of lipoglycan molecules (series C^{native}, purple), which represent a series of further hexose-substituted (Δm = +162.05 Da) molecular species. ***L)*** LG3 contains two of such major series, starting from 2499.091/2513.107/2527.122 Da (series A^{native}, red) and 3380.395/3394.410/3408.426 Da (series B^{native}, dark blue), respectively. Interestingly, in LG2 mono-acyl variants of lipoglycans of series A and B (series $A^{mono\text{-}acyl}$ and $B^{mono\text{-}acyl}$) were also observed (see ***K***). In panel ***K)***, the signal at 3458.784 Da results from a molecule of currently unknown nature. Sodium adducts can be recognized by Δm = 21.98 Da and are labeled in *italic* style. Abundances were normalized to the respective base peak of the depicted spectral region.

M



Supplementary Figure 1M. *RG2* extracts and LG2 and LG2 have TLR2 stimulatory capacity while *RG1* extracts do not. Left) LG2 and LG3 and extract of *RG2* strain, but not *RG1*, induce dose-dependent activation of human TLR2-transfected HEK cells. Right) Incubation with anti-TLR2 monoclonal antibody significantly inhibited the HEK cell line stimulation by a component of LG3. For stimulation with LG3 at 200 ng/mL, TL2.1 mAb incubation resulted in 49% inhibition and T2.5 >98% inhibition of HEK cell activation. For stimulation with LG3 at 50 ng/ml, there was 46% and >98% inhibition of cellular activation, respectively. Each condition was assessed in triplicate. Dotted line represents the background level of medium alone. Values represent mean ± SD based on a standard curve.

N



Supplementary Figure 1N. Pooled serum IgG anti-native DNA from three independent adult Lupus cohorts are significantly inhibited in a dose-dependent manner with *RG2* extract. Samples were prepared and studies performed by ELISA the same as in Supplementary Figure 1I and Supplementary Figure 2. Each point is the mean of measurements in triplicate with error bars representing SD.