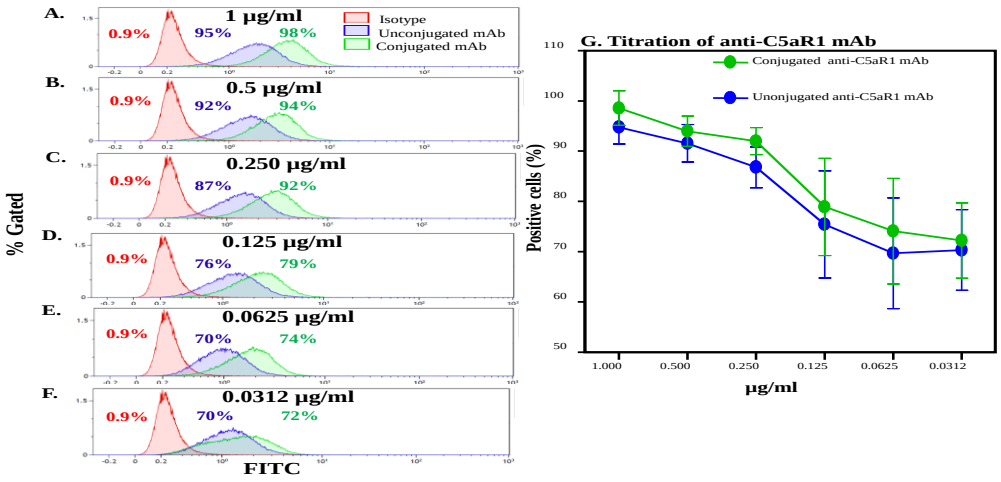

FIGURE S1. Effect of conjugation on mAb (20/70) binding properties. C5aR1 binding was measured on RAW cells using conjugated or unconjugated anti-C5aR1 mAb at a concentration of 1ug, 0.5ug, 0.250ug, 0.125ug, 0.0625ug and 0.0315 ug per $5x10^5$ cells/ml. RAW cells were stained with a matched isolytpe (Rat IgG2b-FITC) (red-shaded line) or various concentration of the primary anti-C5aR1 unconjugated mAb (blue-shaded line) or anti-C5aR1 conjugated mAb (green-shaded line). Cells were incubated with primary unconjugated or conjugated anti-C5aR1 mAb for 1 hr followed by two washes with 1xPBS containing 1%BSA and incubation for 30 minutes at 4^0C with secondary anti-Rat IgG2b-FITC antibody. After washing two times cells were subjected to flow cytometric analysis. A total of 50,000 cells were counted to generating these titration curves. RAW cells without any stain were also analyzed and these histograms were identical to the matched isotype (data not shown). **A.** 1µg/ml of unconjugated or conjugated anti-C5aR1 mAb **B.** 0.5µg/ml of unconjugated or conjugated anti-C5aR1 mAb **C.** 0.250µg/ml of unconjugated or conjugated anti-C5aR1 mAb **D.** 0.125µg/ml of unconjugated or conjugated anti-C5aR1 mAb **E.** 0.0625µg/ml of unconjugated or conjugated anti-C5aR1 mAb **F.** 0.0312 µg/ml of unconjugated or conjugated anti-C5aR1 mAb. These six panels **(A-F)** of FACS histograms represent one of the four independent experiments with almost identical results. **G.** Pooled data from FACS analysis from four independent titration experiments. X axis shows various concentrations of the conjugated anti-C5aR1 or unconjugated anti-C5aR1 mAb. Y axis shows percent positive cells for unconjugated anti-C5aR1 mAb (blue line) and conjugated anti-C5aR1 mAb (green line). Results of the mean ± SEM of four experiments have been shown. Although visually it appears from FACS histograms **(A-F)** that conjugated anti-C5aR1 was little bit superior at all concentrations but statistically these differences comparing with unconjugated anti-C5aR1 mAb were non-significant ($p > 0.05$) comparing all concentrations.

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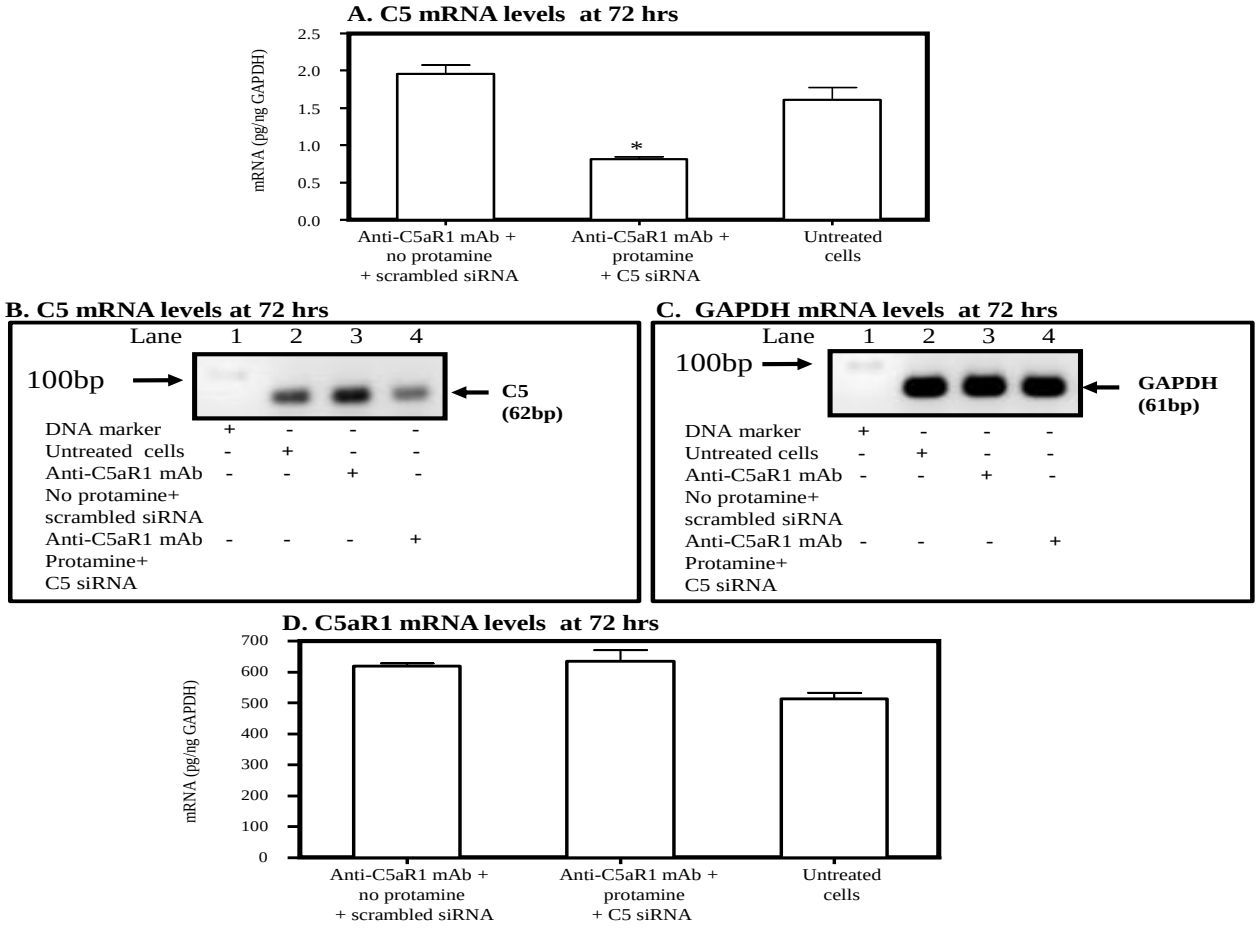

FIGURE S2. Specificity of C5 siRNA for C5 mRNA used to conjugate with protamine-anti-C5aR1 mAb (20/70). C5 siRNA specifically inhibited the mRNA for C5 not for the C5aR1. RAW cells were transfected with C5aR1 mAb-no protamine - scrambled siRNA or C5aR1 mAb - protamine - C5 siRNA or untreated. A mixture of four C5 siRNA was used for these studies. After 72 hrs of culturing transduced RAW cells the mRNA levels for C5, GAPDH and C5aR1were determined by qRT-PCR using Taqman probes. Untreated cells (control RAW cells) were neither treated with anti-C5aR1 mAb - protamine - C5 siRNA or anti-C5aR1 mAb - no protamine - no C5 siRNA nor with scrambled siRNA. **A.** C5 mRNA levels specifically decreased 72 hrs after treating cells with a conjugate of anti-C5aR1 mAb protamine + C5siRNA but not after treating cells with unconjugated mixture of anti-C5aR1 mAb + no protamine scrambled siRNA. No decrease in the C5 mRNA was noticed in untreated cells at 72 hrs **B.** A 2% Agarose gel showing a specific decrease in the C5 mRNA levels in RAW cells, DNA marker (lane 1), untreated cells (lane 2), anti-C5aR1 mAb + no protamine + scrambled siRNAs (lane 3), and anti-C5aR1 mAb + protamine + C5 siRNAs (lane 4). **C.** A 2% Agarose gel for samples in panel B showing no off target effect on the GAPDH mRNA. DNA marker (lane 1), untreated cells (lane 2), anti-C5aR1 mAb + no protamine + scrambled siRNAs (lane 3) and anti-C5aR1 mAb + protamine + C5 siRNAs (lane 4). **D.** No change in the C5aR1 mRNA levels 72 hrs after transduction of RAW cells with anti-C5aR1 mAb + no protamine + scrambled siRNA or anti-C5aR1 mAb + protamine + C5 siRNAs or untreated cells. Data were normalized to 18S rRNA. The levels of mRNA expressed in ng/pg. Exact amounts of each mRNA were determined by standard curves generated with synthetic cDNAs. *$p < 0.05$ in comparison to the cells treated with scrambled siRNA or untreated cells.

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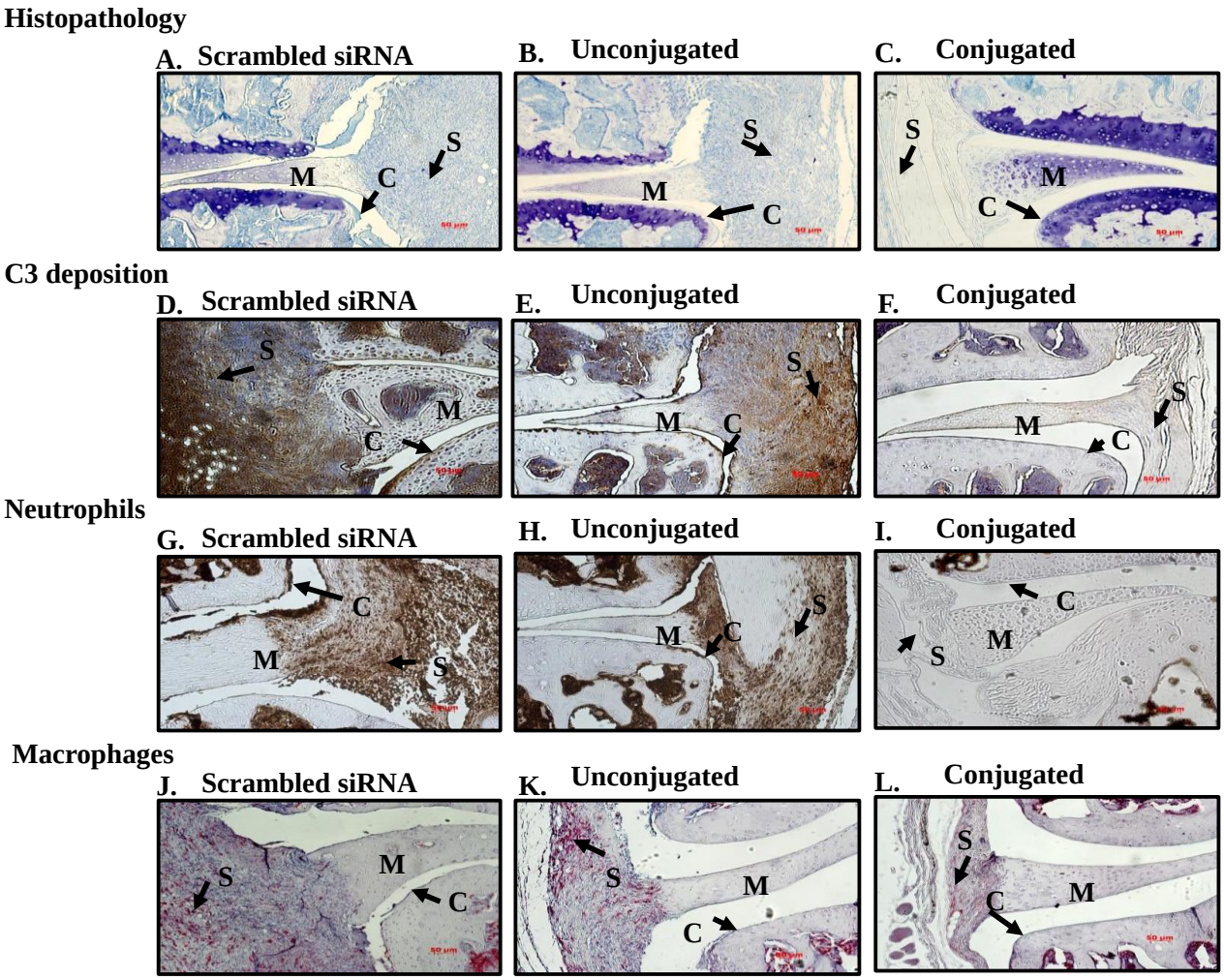

FIGURE S3. Representative histopathology, C3 deposition, neutrophil and macrophage images from the knee joints of mice injected three times i.p. with Scrambled siRNA or anti-C5aR mAb-no protamine-C5siRNA (unconjugated) or anti-C5aR mAb- protamine-C5siRNA (conjugated) followed by injection of mixture of five anti-CII mAb and LPS. The top three panels from left to right (A, B & C) show staining with toluidine-blue (T-blue)(blue color) from the knee joints of WT mice treated with only Scrambled siRNA (left panel) or with unconjugated (center panel) or with conjugated complex (right panel). The second three panels from left to right (D, E & F) show C3 deposition staining with anti-C3 Ab (brown color) from the knee joints of WT mice treated with only Scrambled siRNA (left panel) or with unconjugated (center panel) or with conjugated complex (right panel). The third set of three panels from left to right (G, H & I) show staining with F4/80 for macrophage (red color) from the knee joints of mice treated with Scrambled siRNA (left panel) or with unconjugated (center panel) or with conjugated complex (right panel). The fourth set of three panels from left to right (J, K & K) show staining for neutrophil (brown color) from the knee joints of mice treated with Scrambled siRNA (left panel) or with unconjugated (center panel) or with conjugated complex (right panel). Areas of staining of synovium (S-black arrow), cartilage (C-black arrow) and meniscus (M) are identified. Magnification for all knee joint images shown is 10X and the scale bar is 0.5μm (shown by red color line at the lower bottom of right hand side corner).

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