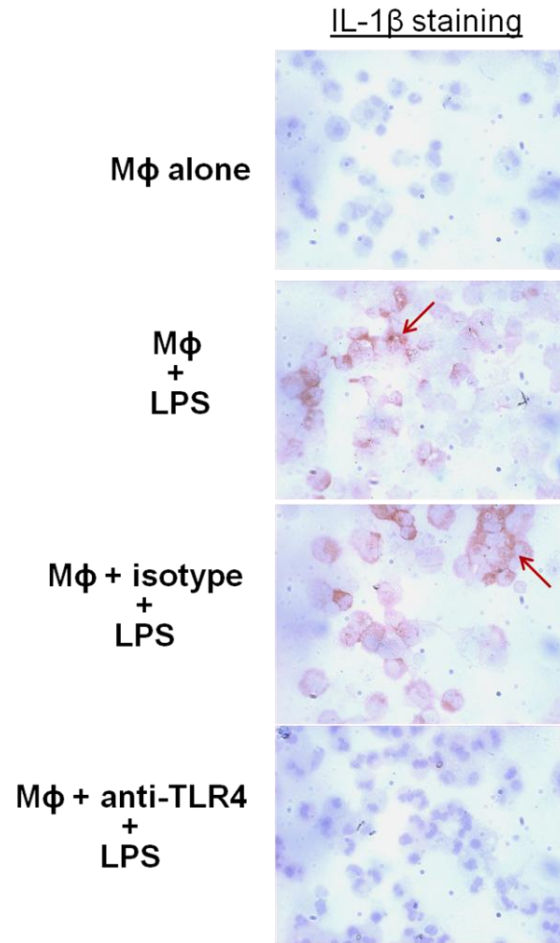
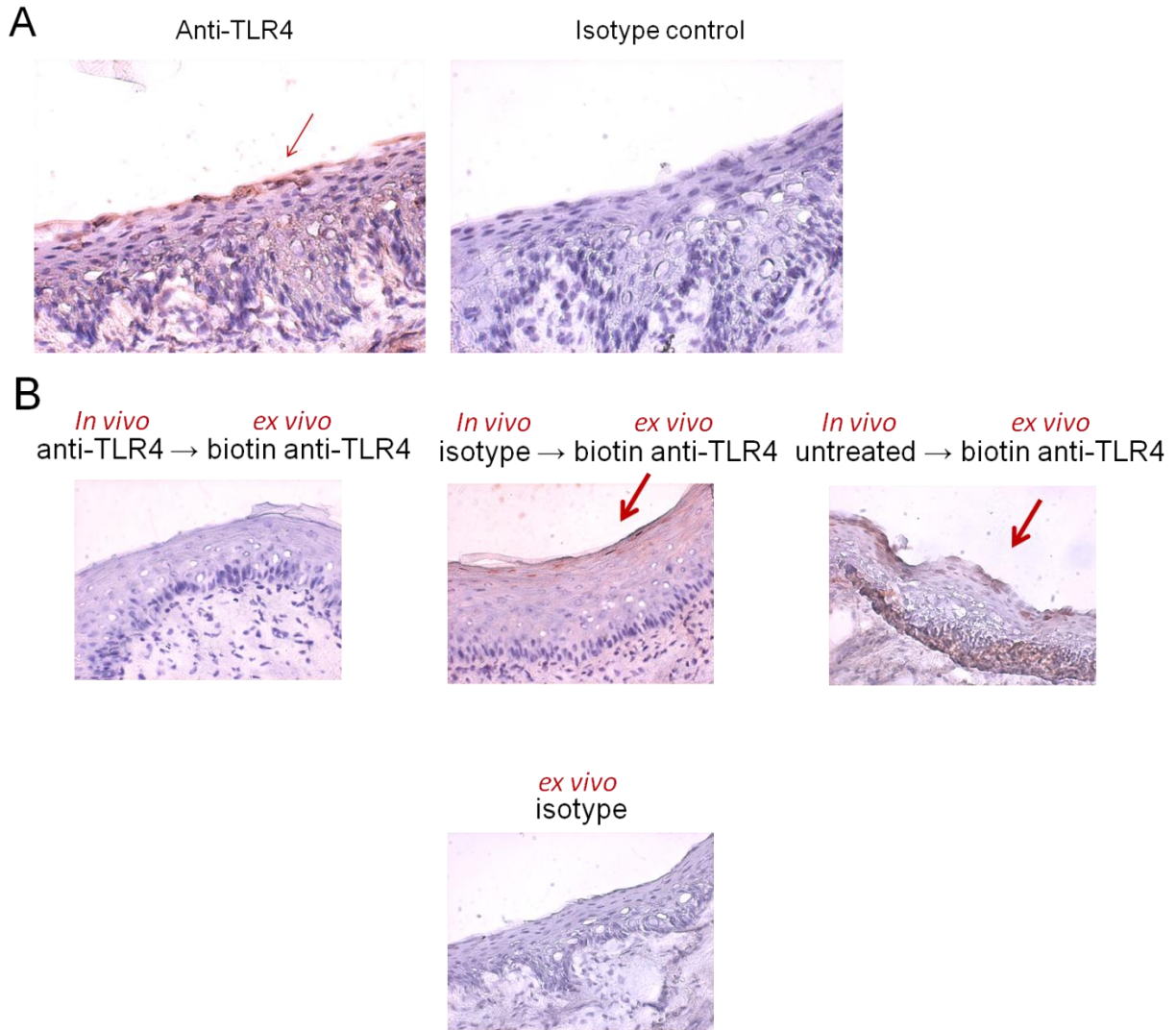


**FIG S1.** Schematic of S100A8 and S100A9 expression and processing in *C. albicans*. A fusion gene encoding for Sap2 leader peptide of *C. albicans* together with a codon optimized S100A8 or S100A9 coding sequence was placed under the control of the *C. albicans ACT1* promoter. The construct was transformed into *C. albicans CAI4 (ura3<sup>-/-</sup>)* to reconstitute the *URA3* gene at its native locus. Following entry into the ER and transport to Golgi, the leader peptide is cleaved off by Kex2 protease at Lys-Arg dipeptides. Resulting S100A8 or S100A9 protein products are then transported to the cell surface followed by extracellular release via exocytosis.

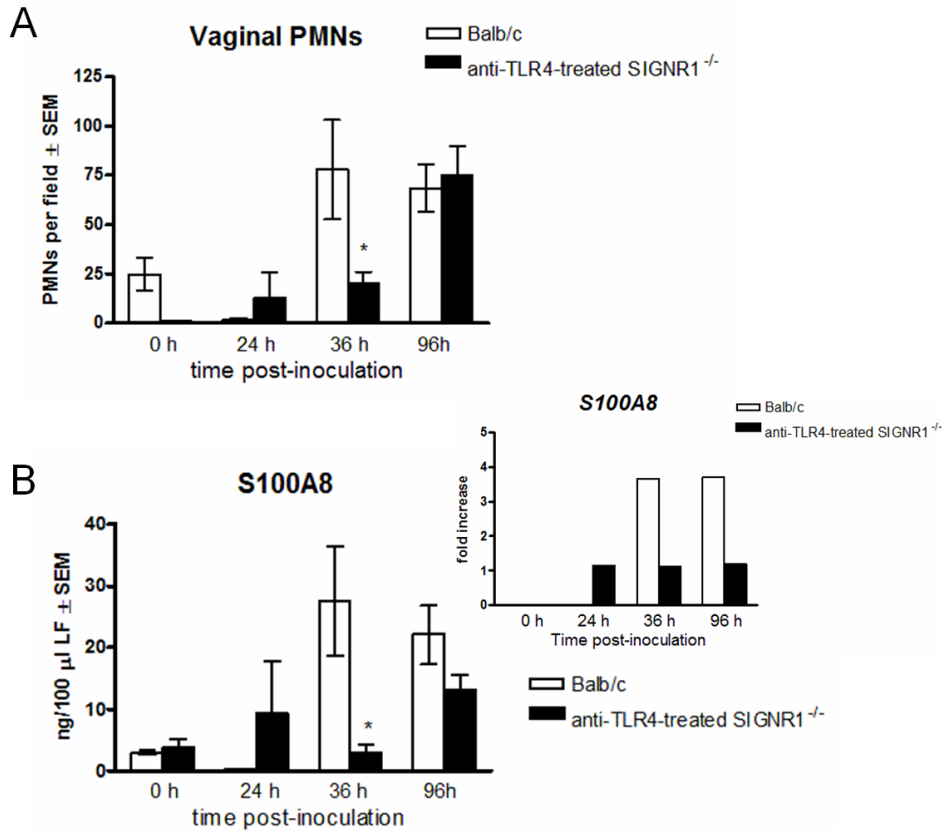


**FIG S2.** Abrogation of LPS-induced inflammatory response by anti-TLR4 antibody treatment in mouse macrophages. Primary mouse macrophages (M $\phi$ ) were isolated from peritoneal exudates 16h after intraperitoneal injection of 10% casein and enriched by Ficoll-paque gravity centrifugation. M $\phi$  were treated with anti-TLR4 or isotype control antibodies (100  $\mu$ g/ml) for 2 h, followed by LPS (100 ng/ml) stimulation. After 18 h, M $\phi$  were collected, and cytospin preparations of the M $\phi$  were stained for IL-1 $\beta$  by immunocytochemistry using anti-IL-1 $\beta$  antibody (0.4  $\mu$ g/ml). Images are shown at  $\times$ 400 magnification. Arrows represent M $\phi$  stained positive for IL-1 $\beta$ . Images are representative of two repeats experiments including 4 mice per group.

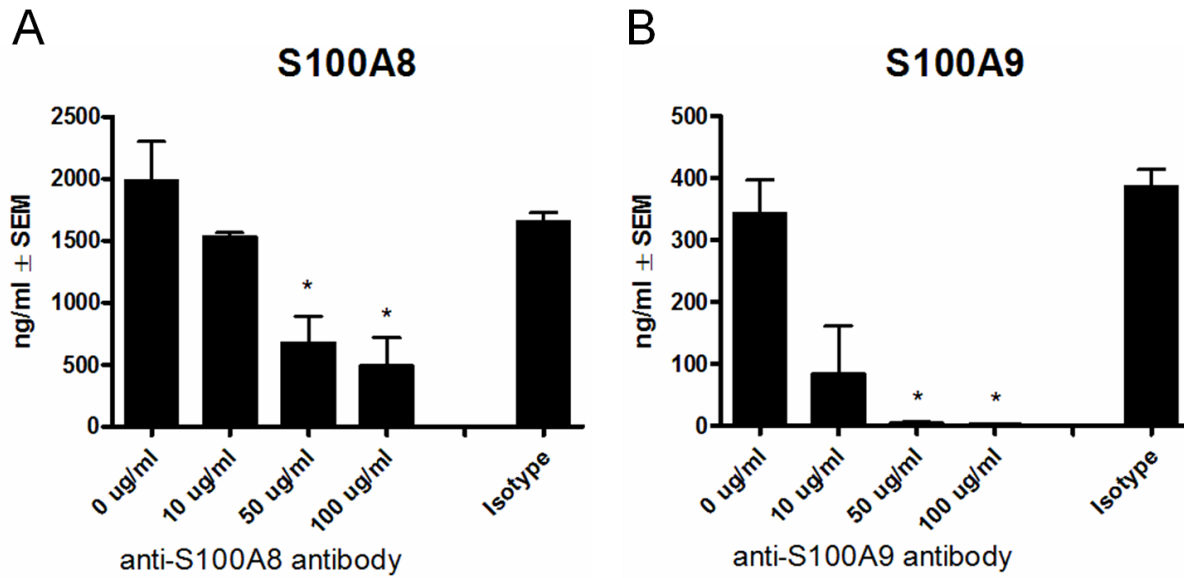


**FIG S3.** Effects of TLR4-SIGNR1 double-deficient conditions on vaginal PMN migration in response to *C. albicans*. (A) Expression of TLR4 in vaginal epithelium. Vaginal tissue sections of estrogenized SIGNR1<sup>-/-</sup> mice were stained with anti-TLR4 antibody (10 µg/ml) by immunohistochemistry. (B) Intravaginal antibody neutralization of TLR4. Estrogenized SIGNR1<sup>-/-</sup> mice were given intravaginal treatments with anti-TLR4 or isotype control antibodies (100 µg/ml in PBS) in a volume of 20 µl at 12 h intervals over a 24 h period (3 treatments total) (indicated as “*in vivo*”). Vaginae were removed 2 day after the final treatment, and tissue sections

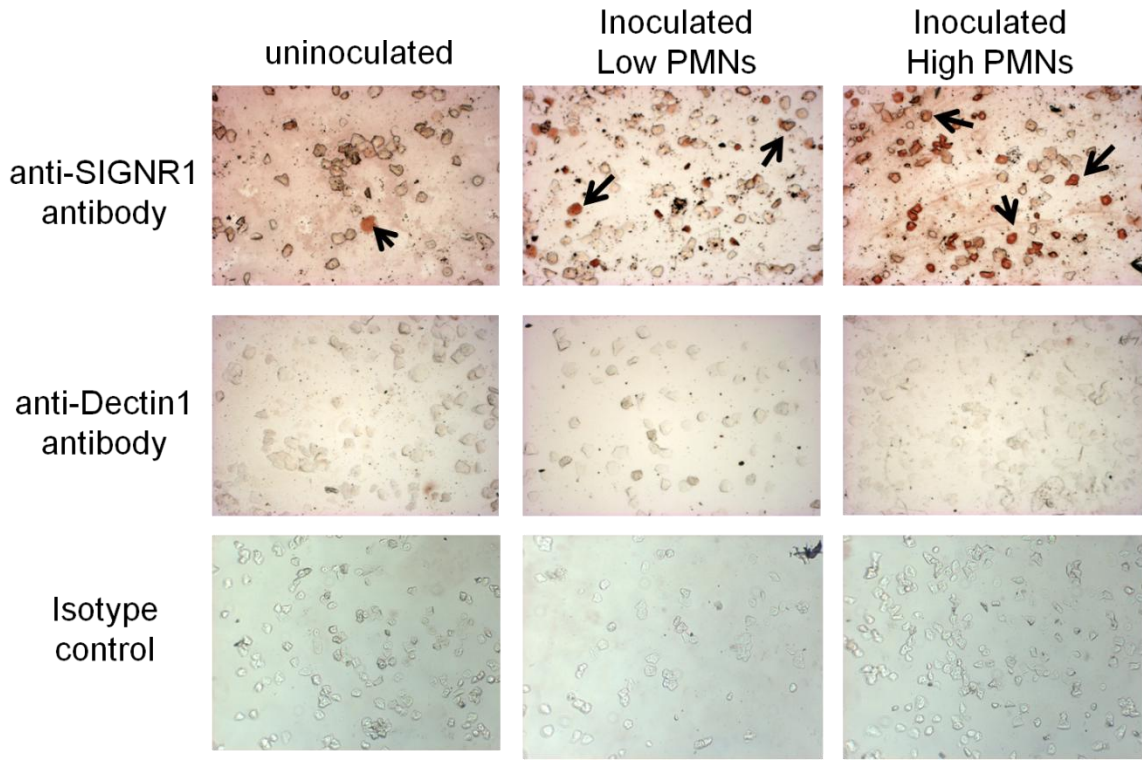
were stained with biotin anti-TLR4 or isotype antibodies (10  $\mu\text{g/ml}$ ) by immunohistochemistry (indicated as “*ex vivo*”). Arrows indicate positively stained vaginal epithelium. Images are representative of two repeat experiments including 3 mice per group.



**FIG S4** Early responses by S100A8 and PMNs in TLR4-neutralized SIGNR1<sup>-/-</sup> mice following inoculation. Estrogenized SIGNR1<sup>-/-</sup> mice were treated with anti-TLR4 or isotype control antibodies (100 μg/ml in PBS) in a volume of 20 μl at -4, 16 and 24h post-inoculation. Vaginal lavage fluids and vaginal tissues were collected at 24, 36 and 96 h post-inoculation, and (A) PMN infiltration and (B) S100A8 concentrations were assessed. Insert represents *S100A8* mRNA expression by vaginal epithelial cells quantified by real-time PCR. Figure represents cumulative data from two repeat experiments (samples were pooled for real-time PCR) consisting of 6 to 10 mice per strain. \*, P<0.05 compared to the wild-type control group. SEM, standard error of the mean.



**FIG S5** Binding capacity of anti-S100A8 and anti-S100A9 antibodies. (A) S100A8- or (B) S100A9-containing *C. albicans* culture supernatants were treated with varying concentrations of polyclonal anti-S100A8 or S100A9 (100 µg/ml), respectively, or isotype control antibody for 45 min at 37°C. The antibody-treated culture supernatants were subjected to ELISA to detect unbound S100A8 or S100A9 protein. Figure represents cumulative data from 2 repeat experiments. SEM, standard error of the mean. \*, P < 0.05 compared to the isotype-treated culture supernatants.



**FIG S6** SIGNR1 and dectin-1 expression on vaginal epithelial cells following interaction with *C. albicans*. Cytospin preparations of cellular fractions in vaginal lavage fluid from estrogenized uninoculated or inoculated mice with high or low PMNs were stained by immunocytochemistry using antibodies (10 µg/ml) specific for PRRs listed in Table 1 or isotype controls. Images show representative positive (arrowed) and negative staining for SIGNR1 and dectin-1, respectively, at 100x magnification. Images are representative data from 2 repeat experiments testing specimens collected on day 4 post-inoculation.