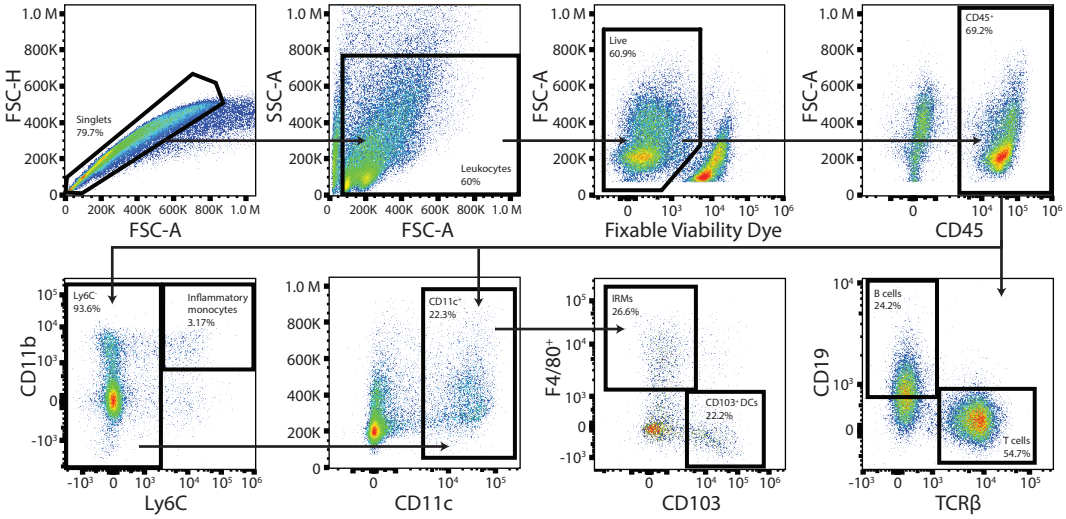
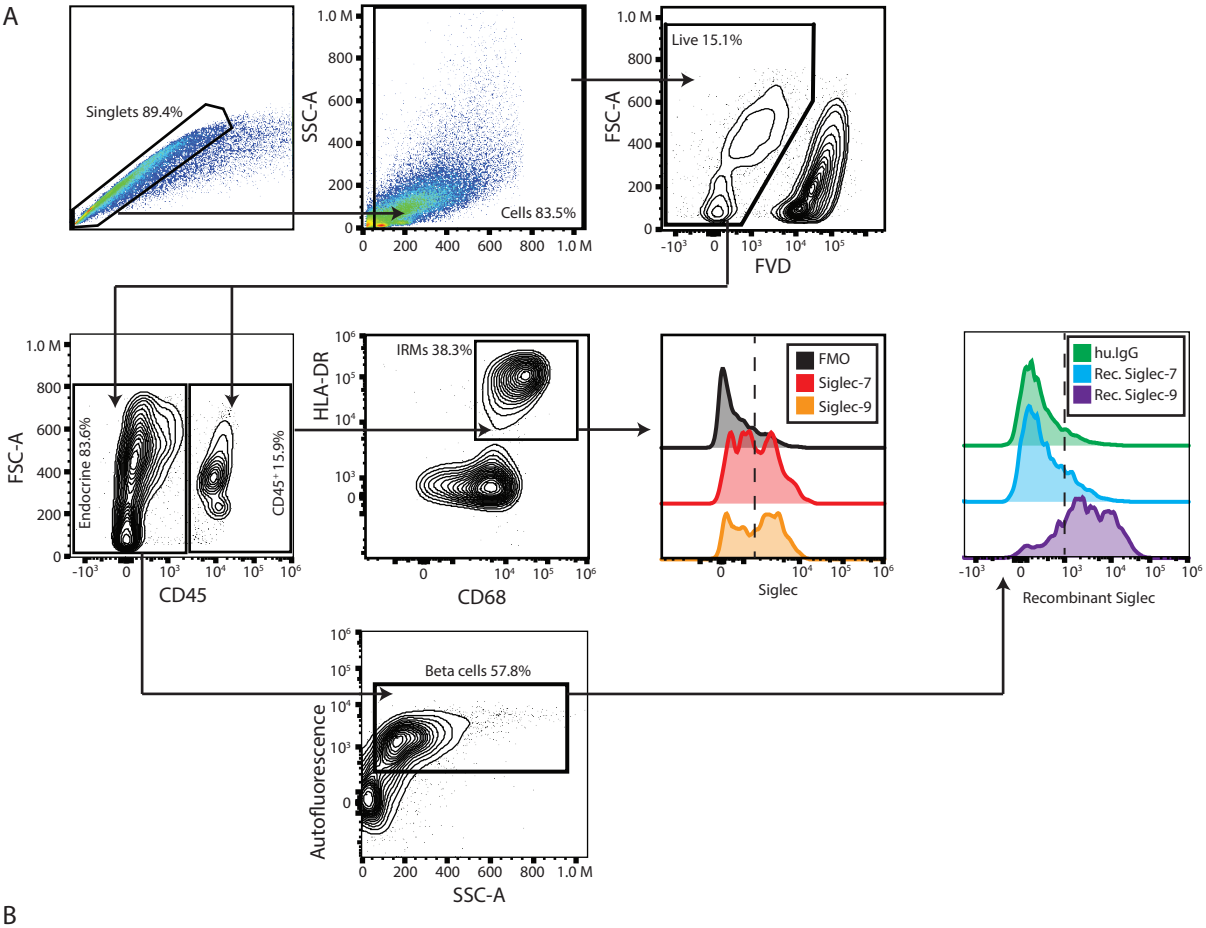
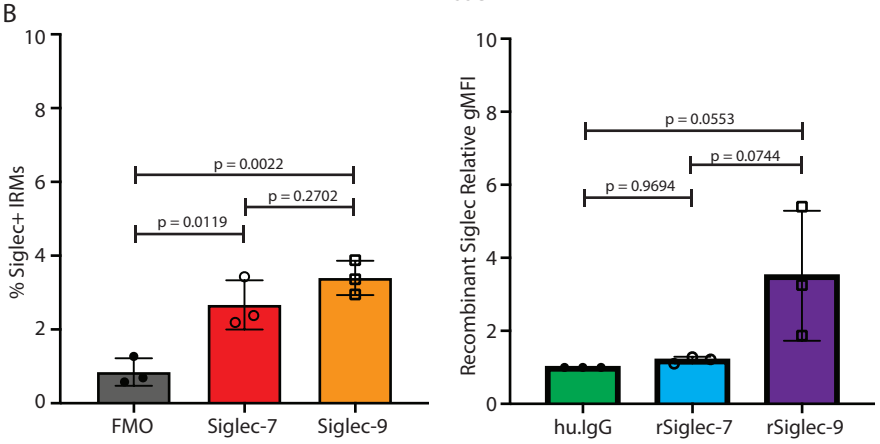
Supplemental Figure 1



Gating scheme for identifying islet-associated IRMs, Ly6C$^-$ IRMs, T, and B cells. After non-enzymatic cell dissociation, live, single CD45$^+$ cells were further categorized as T, B, and either CD11c$^+$ F4/80$^+$ CD103$^-$ IRMs or Ly6C-excluded CD11c$^+$ F4/80$^+$ CD103$^-$ IRMs.

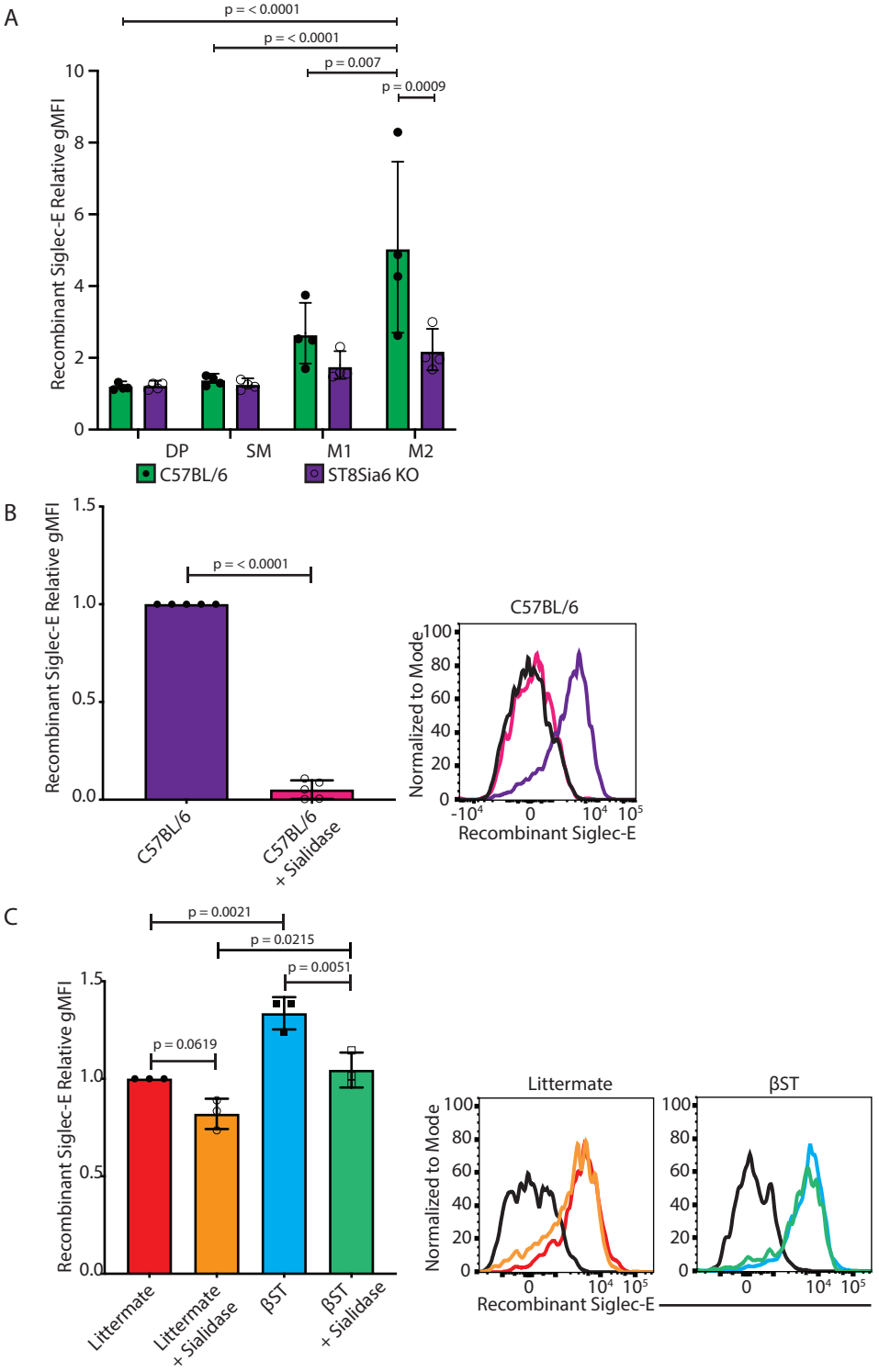
Supplemental Figure 2





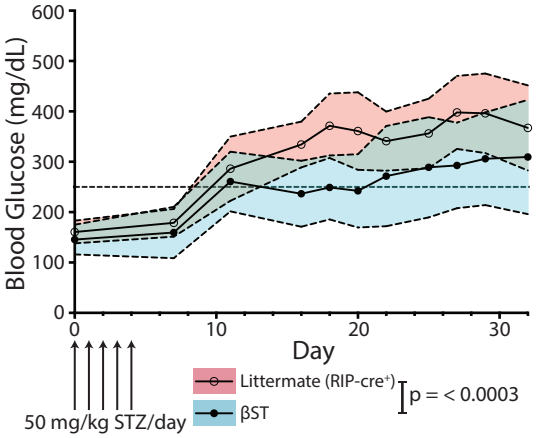
Binding of recombinant Siglecs to human beta cells, and Siglec expression on human IRMs. Nondiabetic cadaveric human islets (n = 3) were commercially obtained (Prodo Laboratories) and were non-enzymatically dissociated. Donors were a 64 year old female, 34 year old female, and a 30 year old male. All had HbA1c ≤ 5.5%. **(A)** Gating scheme and representative plots of human beta cells (live, single CD45$^-$ cells) or human IRMs (live, single CD45$^+$ HLA-DR$^+$ CD68$^+$). **(B)** gMFI intensities are relative to FMO (IRM Siglec expression) or human IgG secondary antibody (recombinant Siglec bound). A 1-way ANOVA with Tukey's multiple comparison tests were performed with error bars representing standard deviation.

Supplemental Figure 3



Quantification of geometric mean fluorescence intensity of bound recombinant Siglec-E.
(A) Recombinant Siglec-E bound to murine thymocytes. gMFI intensities are relative to human IgG secondary antibody bound. Thymocytes from C57BL/6J (n = 4) vs. ST8Sia6 KO (n = 4) mice were utilized. A 2-way ANOVA with Sidak's multiple comparison test was performed with error bars representing standard deviation. **(B)** Recombinant Siglec-E bound to murine thymocytes with or without 0.1 U/mL sialidase treatment. gMFI intensities are relative to untreated cells. Thymocytes from C57BL/6 (n = 5) mice were utilized. An unpaired T test was performed. **(C)** Recombinant Siglec-E bound to beta cells with or without 0.1 U/mL sialidase treatment. gMFI intensities are relative to untreated littermate cells. Beta cells from littermate (n = 3) vs. βST (n = 3) mice were utilized. A 1-way ANOVA with Tukey's multiple comparison test was performed with error bars representing standard deviation. For **(B)-(C)**, representative plots accompany each bar graph, with black histograms representing human IgG secondary antibody bound. Islets were nonenzymatically dissociated into single cells before exposure to 0.1 U/mL sialidase (Millipore Sigma) in Hank's Balanced Salt Solution at 37˚ C for 1 hour.

Supplemental Figure 4



Kinetic analysis of diabetes induction by MLD-STZ in RIP-cre$^+$ littermates (n = 12) vs. βST (n = 13) mice. A 2-way ANOVA with Geisser-Greenhouse correction was performed, with shaded regions representing standard deviations.