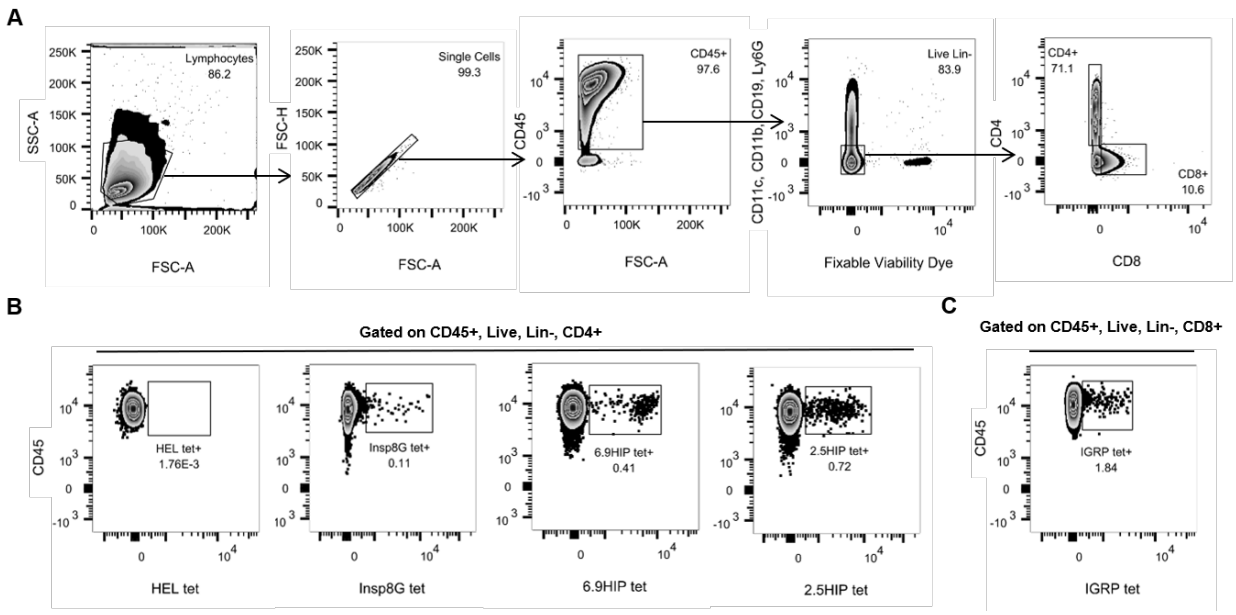
| Peptide | Mean (µg/mg) | Std Dev | Total (µg/2.5 mg) |
|---|---|---|---|
| HEL | 24.1 | 4.7 | 60.4 |
| InsB:9-23 | 69.7 | 17.0 | 174.3 |
| 2.5HIP | 36.4 | 8.3 | 91.0 |

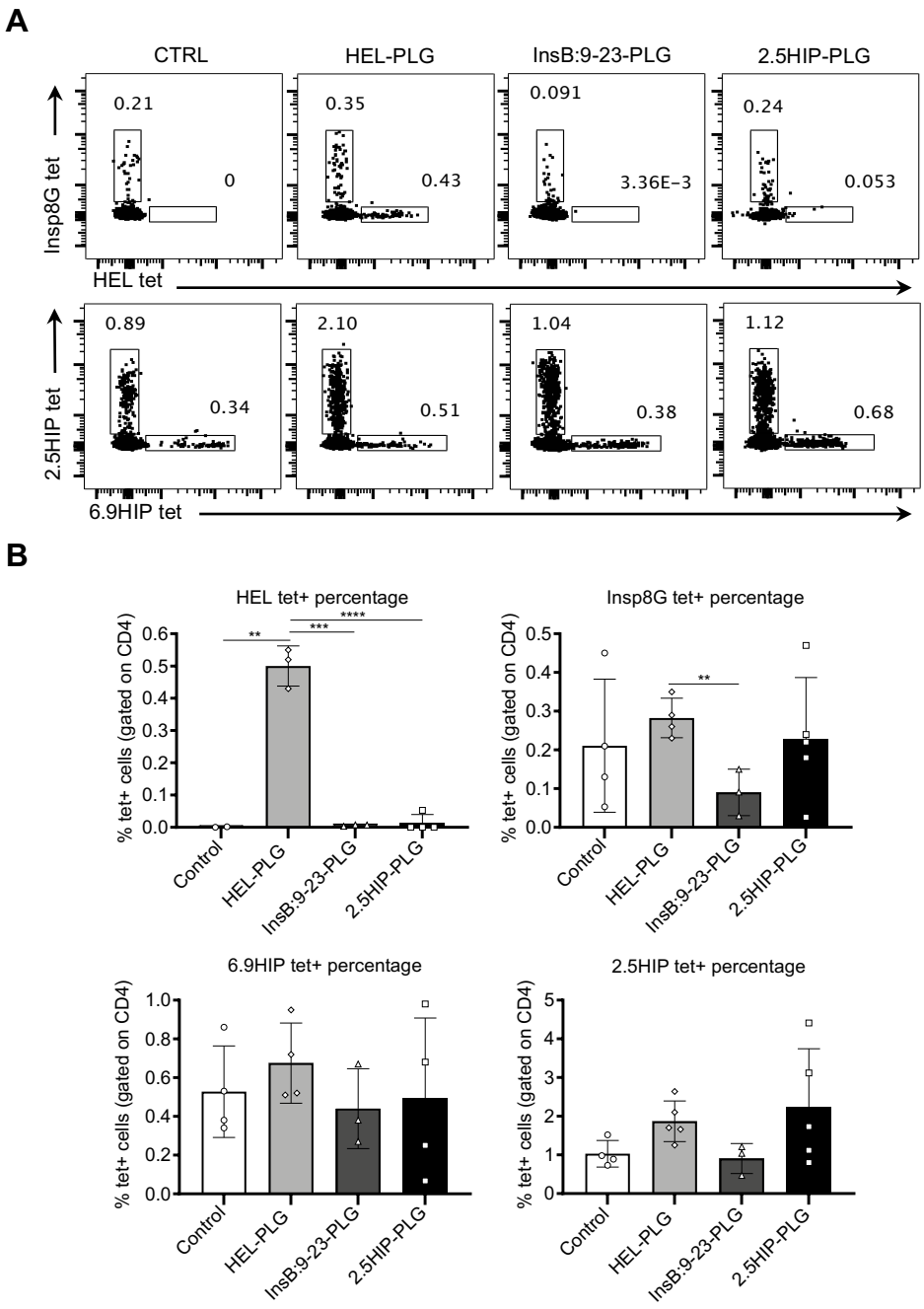
**Supplementary Table 1. Quantification of Ag-coupling to PLG-NPs.** Peptide was coupled to single emulsion NPs in 5 separate reactions and 0.5 mg from each reaction was dissolved in DMSO. Solutions were analyzed using a 3-(4carboxybenzoyl) quinoline-2-carboxaldehyde (CBQCA) assay, read on a fluorescent microplate reader, and the mean and standard deviation were determined. The total amount of antigen administered per mouse per NP dose is also shown.

| | Control | HEL-PLG | InsB:9-23-PLG | 2.5HIP-PLG |
|---|---|---|---|---|
| Blood glucose values (mg/dL) – day 0 | 282 | 600 | 512 | 600 |
| | 561 | 600 | 600 | 562 |
| | 541 | 500 | 541 | 512 |
| | 600 | 450 | 540 | 600 |
| | 420 | 588 | 580 | 600 |
| | 477 | 485 | 585 | 600 |
| | 538 | 575 | | 581 |
| | | 600 | | 360 |
| | | 452 | | |
| | | 272 | | |
| **Average ± Std Dev** | 488.4 ± 116.2 | 512.2 ± 104.8 | 559.7 ± 44.8 | 551.9 ± 83.3 |

**Supplementary Table 2. Initial blood glucose of islet transplant recipients.** Individual blood glucose levels from mice on the day of transplantation (day 0) are shown followed by the average of mice in each treatment group. The majority of mice are far above the cutoff for hyperglycemia (250 mg/dL).




**Supplementary Figure 1. Gating strategy for tetramer-positive cells. A-C:** A single-cell suspension from an islet graft of an untreated control mouse euthanized upon disease recurrence was stained with HEL/I-$A^{g7}$, Insulin $B_{9\text{-}23}$-mimotope (Insp8G)/I-$A^{g7}$, 6.9HIP/I-$A^{g7}$, 2.5HIP/I-$A^{g7}$ or $IGRP_{206\text{-}214}$/H-$2K^{(d)}$ tetramers and antibodies. The HEL tetramer was used as a disease-irrelevant control. **A:** Gates were set on $FSC^{int}$ $SSC^{int}$ (lymphocytes), single cells (FSC-H/FSC-A), $CD45^{+}$, live (fixable viability $dye^{-}$), $lineage^{-}$ (CD11c, CD11b, CD19, Ly6G), and $CD4^{+}$ or $CD8^{+}$ cells. The bottom panel shows the percentage of $tetramer^{+}$ cells gated on $CD4^{+}$ (**B**) or $CD8^{+}$ (**C**) cells.




**Supplementary Figure 2. 2.5HIP NPs do not alter the frequency of graft-infiltrating CD4+ tet+ T cells. A&B:** Single-cell suspensions from islet grafts of mice euthanized upon disease recurrence were stained with HEL/I-$A^{g7}$, Insulin $B_{9\text{-}23}$-mimotope (Insp8G)/I-$A^{g7}$, 6.9HIP/I-$A^{g7}$, or 2.5HIP/I-$A^{g7}$ tetramers and antibodies. Gates were set on $CD4^+$ cells. **A:** Representative example of tetramer staining is shown. Each column corresponds to a PLG-NP treatment group which is listed overhead. **B:** Summary of $tet^+$ T cell percentages. Each graph shows a different tetramer which is listed overhead. The labels on the x-axis correspond to PLG-NP treatment groups. Each symbol represents an individual mouse. $^{**}P < 0.01$, $^{***}P < 0.001$, $^{****}P < 0.00$