## **Supporting Information**

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**Fig. S1.** Complementary prime boost provide protection from weight loss after airway challenge by recombinant vaccinia gag virus. Female CxB6  $F_1$  mice are vaccinated and challenged as described in the legend of Fig. 1. Weight loss was monitored daily for 7 days after challenge. (*A* and *B*) Body weight lost data for Fig. 1 with each group displayed in the corresponding color of its mean lung virus titer as shown in the bar graphs. (*C* and *D*) Weight lost data corresponding to Fig. 2.



**Fig. 52.** HIV gag and LCRV CD4-restricted peptides in combination with polyIC induce antigen-specific CD4<sup>+</sup> T cells. CxB6  $F_1$  mice received 100  $\mu$ g of either HIV gag or LCRV CD4-restricted peptides, or HIV gag CD8-restricted peptide, i.p. twice at 0 and 2 weeks in combination of 50  $\mu$ g of polyIC (*y* axis). Seven days after the last peptide vaccination, specific IFN- $\gamma$ -producing T cell responses were evaluated from bulk splenocytes by restimulation with peptides along the top + anti-CD28. Shown is one of three similar experiments. Red arrows indicate the immune response.



**Fig. S3.** DC-targeted protein vaccine requires CD40 to help DNA vaccines. Female wild-type and  $CD40^{-/-}$  mice were vaccinated as indicated on the *y* axis. Thirty days after the last DNA boost, bulk splenocytes were cultured for 4 days with or without gag p41 peptides and assessed for gag-specific T cell proliferation in CD4<sup>+</sup> and CD8<sup>+</sup> T cells by CFSE dilution. At the end of the cultures, cells were boosted with gag peptides and anti-CD28 for 6 h followed by intracellular staining for IFN- $\gamma$ .

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**Fig. S4.** Preparation of multifunctional HIV gag-specific CD4<sup>+</sup> T cells with DEC-p41 plus polyIC vaccination for use in adoptive transfer experiments (Fig. 6C). Female CxB6  $F_1$  mice were vaccinated with DEC-gag p41 protein or MHC II restricted gag peptides plus polyIC twice at 0 and 4 weeks. At 8 weeks, immune responses were determined by intracellular cytokine staining for IFN- $\gamma$ , IL-2, and TNF- $\alpha$ . The cells in the rows with red arrows were used for adoptive transfer in the experiments of Fig. 6C.

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