SUPPLEMENTARY FIGURE LEGENDS

Supplementary Figure 1. Paraneoplastic autoimmune syndrome. (A) Images of representative staining patterns obtained in immunofluorescence assays of HEp-2 cells incubated with sera from tumor-bearing mice: a., Golgi-like; b., mitochondrial; c., nuclear membrane; d., gastric parietal cells; e., negative control. **(B)** Table shows both number of autoantibody-containing sera and sera distribution according to antibody titer in each condition.

Supplementary Figure 2. GC reaction in spleens from tumor-free mice (A) Upper panels, Immunofluorescence images of GC in spleen sections from tumor-bearing mice stained for PD-1 (green), CD4 (red) and DAPI (blue). Lower panels, Immunofluorescence images of GC in spleen sections from tumor-bearing mice stained for Ki67 (green), CD20 (red) and DAPI (blue). **(B)** Upper panels, immunohistochemical images of spleen sections from tumor-free mice, stained for either PD-1 (right) or Ki67 (left). Scale bars represent 500 μm. Lower panel, percentage of PD-1+ and Ki67+ GC in spleens from tumor-free mice (n=3).

Supplementary Figure 3. (A) TLS organization degree. Upper panel, hematoxylin and eosin staining of tumors showing TLSs with different organization degree. Scale bars represent 250 μm. Lower panel, percentage of grade I, II and III TLSs in tumors of anti-PD-1-and isotype-treated mice (n=22 and n=26, respectively). **(B)** Anti-PD-1 mediated effect on TLS-related chemokines and inflammatory factors. Graphs show quantification of expression of selected chemokines and inflammatory factors upon anti-PD-1 treatment, measured by qPCR in whole tumor sections from isotype and anti-PD-1-treated mice (n=7 and n=6, respectively).

Supplementary Figure 4. Gating strategy for Flow Cytometry assays. (A) Gating strategy for Tfh analysis. Lymphocytes were selected from a forward scatter-area vs side scatter-area dot plot, and single cells were subsequently selected in a forward scatter-area vs forward scatter height dot plot. Then, T cells were selected by CD3+ expression, and T helper cells were identified by CD4+ staining. Tfh were selected by double positive staining for CXCR5 and PD-1 inside T helper cells. This population was analyzed for CCR7, CXCR3 and CD38 expression. **(B)** Gating strategy for mouse Tfr. Tfh cells were selected as in (A), and then Tfr cells were identified as double CD25 and FoxP3 positive events within Tfh population. **(C)** In in vitro stimulation assays, previously purified Tfh cells T naive cells (see Methods) were evaluated for IL-21, IL-4, IFNγ and CD69 expression.

Supplementary Figure 5. Proposed novel mechanisms of action mediating anti-PD1 antineoplastic effects. Tfh cells originate from naïve CD4+ T cell precursors, upon interaction with APCs in T cell zone of SLOs in the presence of cytokines as IL-6 and IL-21. CD4+ T cells migrate to the T-B border zone due to changes in CCR7 and CXCR5 expression on their surface, where they interact as pre-Tfh committed cells with cognate B cells, and differentiate into fully mature Tfh cells that eventually enter GCs. Mature Tfh cells regulate somatic hypermutation processes and optimal clonal selection of GC B cells. Likewise, Tfh cells may exit from SLOs to circulation as memory cTfh cells. Anti-PD-1 may promote either Tfh differentiation or exiting to peripheral circulation, leading to an increment in cTfh population. This therapy may also act *in situ* at tumor location by increasing TLS number through induced CCL21 production, possibly in combination with other mechanisms. This chemokine would attract increased amounts of cTfh to tumor microenvironment, where Tfh cells would enhance B cell activation and maturation, thus triggering antibody-mediated immune response against tumor.