

**Fig S1: mGPRC5D vaccine and PD1 Ab inhibit tumor growth in murine MM models (related to Fig. 2).** (A) Image showing the individual tumors. (B) Graphs showing the individual tumor growth curves. (C) Representative H&E staining images (×20) of major organs from treated mice.

Liver

Heart



Fig. S2. Analysis of prophylactic efficacy of the Nano-hGPRC5D vaccine in the MC38 mouse colon cancer model. (A) Individual mouse tumor growth curves. (B) Tumor weights at the endpoint. (C) TNF $\alpha$  and IFN $\gamma$  double color ELISpot analysis of splenocytes from treated mice. Splenocytes were stimulated with overlapping peptide pools spanning the full-length hGPRC5D protein for 24 hours. Blue spots represent TNF $\alpha$ , and red spots represent IFN $\gamma$ .



**Fig. S3. Analysis of preventive efficacy of the Nano-hGPRC5D vaccine against B16-F10 cells expressing hGPRC5D.** (A) Timeline of the vaccination and tumor inoculation (created using biorender.com). (B-C) Tumor growth curves as two groups or as individual tumors from mice prophylactically vaccinated with Nano-hGPRC5D. (D) Tumor weights at the endpoint. (E) hGPRC5D-specific antibody titers measured by ELISA using hGPRC5D recombinant protein as a coating antigen.



**Fig. S4. Analysis of preventive efficacy of the Nano-hGPRC5D vaccine against CT26 cells expressing hGPRC5D.** (A) Timeline of the vaccination and tumor inoculation (created using biorender.com). (B-C) Tumor growth curves as two groups or as individual tumors from mice prophylactically vaccinated with Nano-hGPRC5D. (D) Tumor weights at the endpoint. (E) hGPRC5D-specific antibody titers measured by ELISA using hGPRC5D recombinant protein as a coating antigen.



**Fig S5: Nano-hGPRC5D, in combination with anti-PD-1 Ab, suppresses tumor growth in the MC38 mouse model.** (A) Image showing the tumors. (B) graphs showing the individual tumor growth curves. (C) Representative H&E staining images (×20) of tumors and major organs from treated mice.



**Fig S6: Nano-hGPRC5D, in combination with anti-PD-1 Ab, suppresses tumor growth in the B16F10 melanoma model.** (A) Timeline of the vaccination and tumor inoculation (created using biorender.com). (B) Image showing the individual tumors. (C-D) Graphs showing the tumor growth curves as groups or individually. (E) Bar graph showing the tumor weights. (F) Graph showing animal body weights of mice by group.



**Fig S7: Nano-hGPRC5D, in combination with anti-PD-1 Ab, suppresses tumor growth in CT26 syngeneic mice.** (A) Timeline of the vaccination and tumor inoculation (created using biorender.com). (B) Image showing the individual tumors. (C-D) Graphs showing the tumor growth curves as groups or individually. (E) Bar graph showing the tumor weights. (F) Graph showing the body weights of mice.







**Fig S8: uncropped and unprocessed scans of all blots . (A)** Blots for Figure 1A. (B) Blots for Figure 4C. (C) Blot for Figure 4D.