Supplementary Figures and Legends

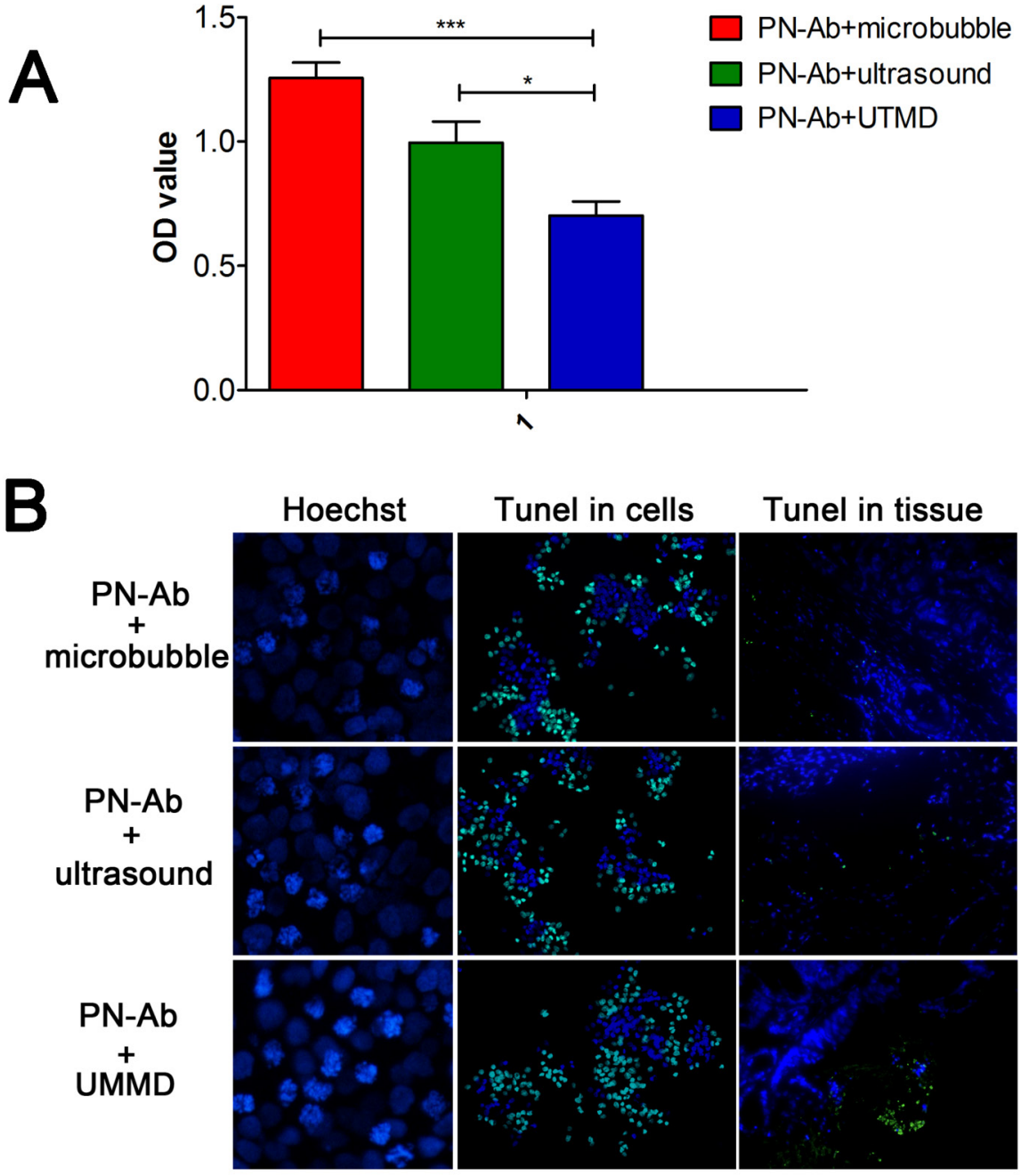

Figure S1. (A) CCK8 assay in the three groups of PN-Ab+microbubble, PN-Ab+ultrasound, and PN-Ab+UMMD at the same PTX dose of 5.0μg/ml and incubated for 24h. Cytotoxicity of PN-Ab+UMMD is significantly higher than the other two groups (* $p<0.05$, ** $p<0.01$, *** $p<0.001$ by One-way ANOVA and Tukey HSD statistical tests, n=6). (B) 24 h cell apoptosis assessed by Hoechst 33342 and TUNEL staining in groups of PN-Ab+microbubble, PN-Ab+ultrasound, and PN-Ab+UMMD, respectively. The figures in group of PN-Ab+UMMD refer to that in Fig. S6, Fig. 3 and Fig. S8, respectively. Increased apoptosis is seen in PN-Ab+UMMD than in other groups.

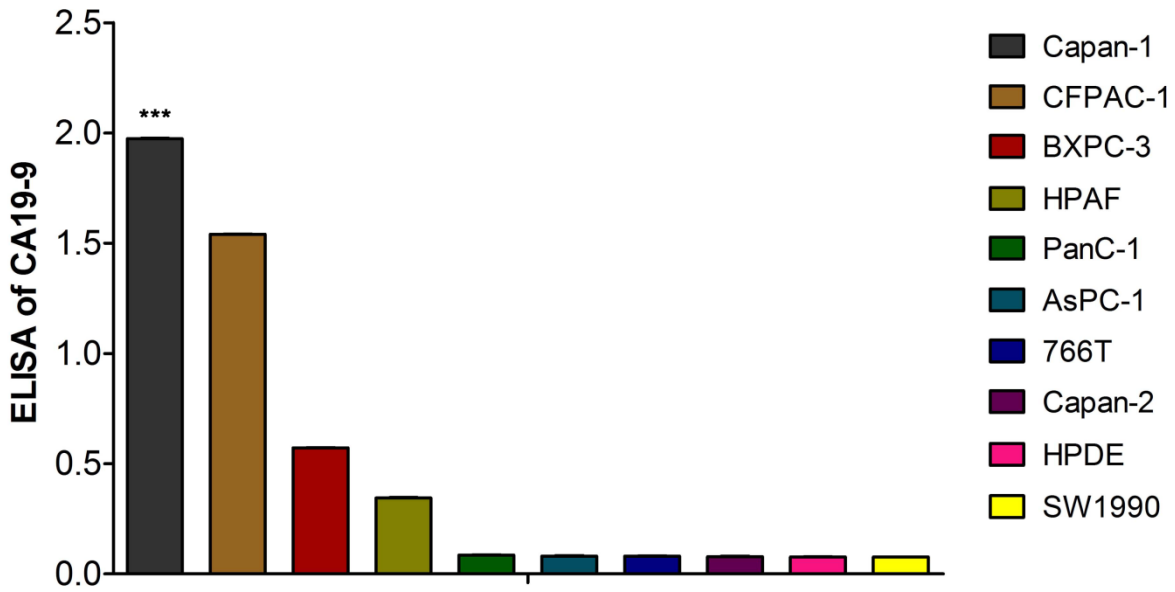

Figure S2. ELISA assay of CA19-9 in the supernatant of 10 pancreatic cancer cell lines Capan-1, CFPAC-1, BXPC-3, HPAF, PanC-1, AsPC-1, 766T, Capan-2, HPDE and SW1990: Capan-1 cells showed the highest expression of CA19-9 (*** $p<0.001$ compared with other cell lines by One-way ANOVA and Tukey HSD, n=4).

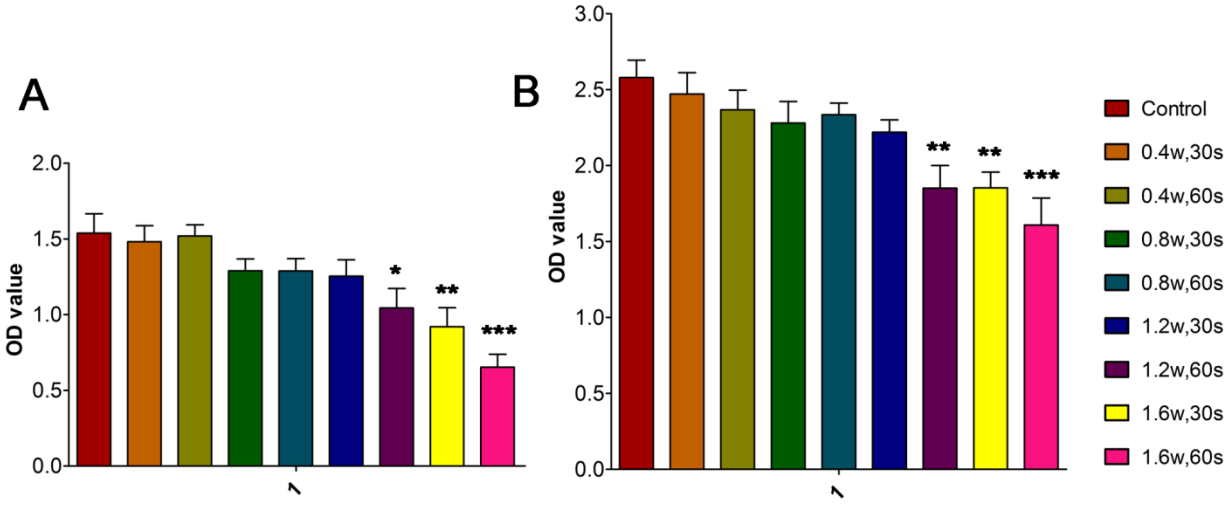

Figure S3. CCK8 assay of capan-1 cells (A) 24 h and (B) 48 h under different UMMD conditions including 0.4w, 30s; 0.4w, 60s; 0.8w, 30s; 0.8w, 60s; 1.2w, 30s; 1.2w, 60s; 1.6w, 30s; 1.6w, 60s. Cell viability decreased in the last three groups, * $p<0.05$, ** $p<0.01$, *** $p<0.001$ compared with the control group by One-way ANOVA and Tukey HSD, n=6. 0.8w, 60s and 1.2w, 30s were the proper conditions of UMMD.

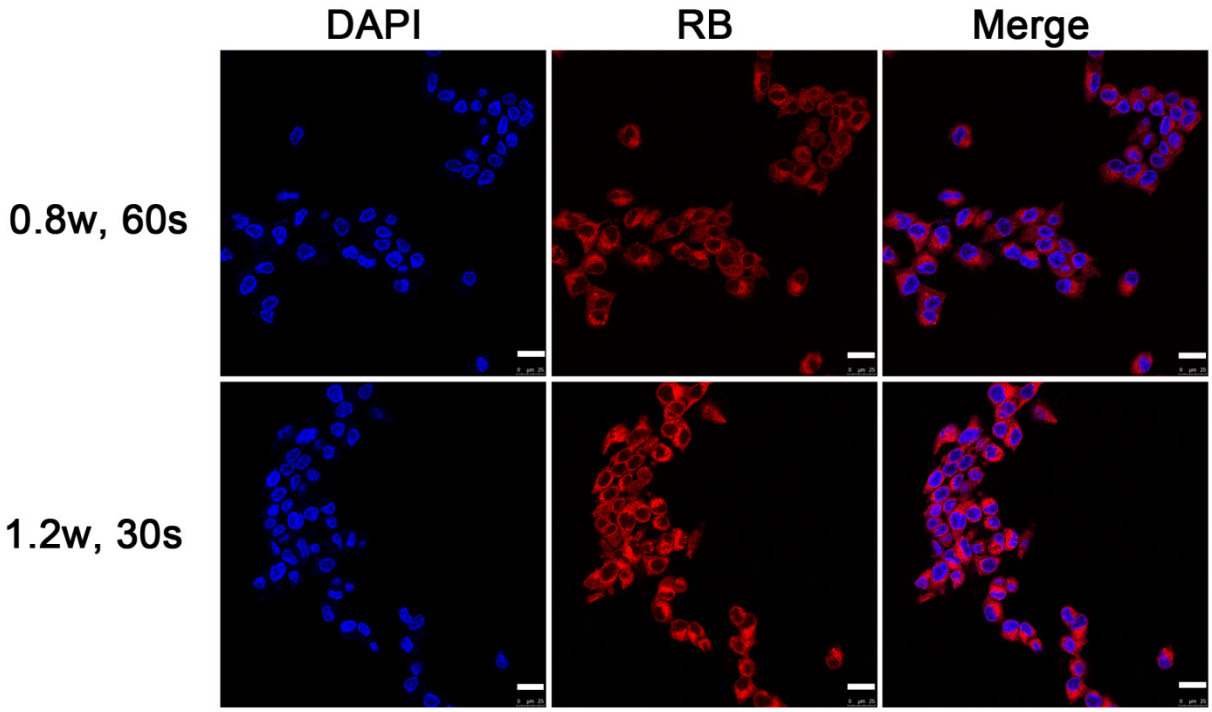

Figure S4. Cellular uptake of RB-NP 8 h after application of UMMD at 0.8w, 60s and 1.2w, 30s: The scale bars represent 25 μ m. A relatively brighter fluorescence was observed with 1.2w, 30s than with 0.8w, 60s. Therefore, we selected 1.2w,30s as the final UMMD condition *in vitro*.

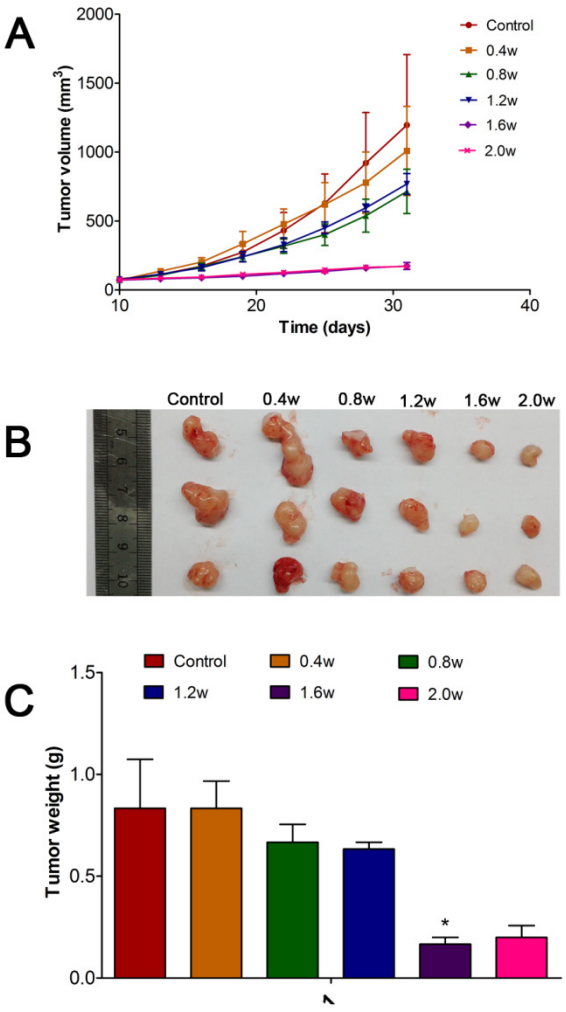

Figure S5. Determination of the appropriate UMMD conditions *in vivo*: The conditions tested were 0.4w, 0.8w, 1.2w, 1.6w and 2.0w for 5 minutes. (A) tumor growth curve, (B) tumor samples, and (C) tumor weight Data demonstrated that tumor progression was most inhibited at 1.6w and 2.0w. * $p < 0.05$ compared with the control group by Mann-Whitney U test, the p value of overall comparison was 0.029 by Kruskal-Wallis test. Thus, we chose 1.2w,5min as the final UMMD condition for t *in vivo* experiments.

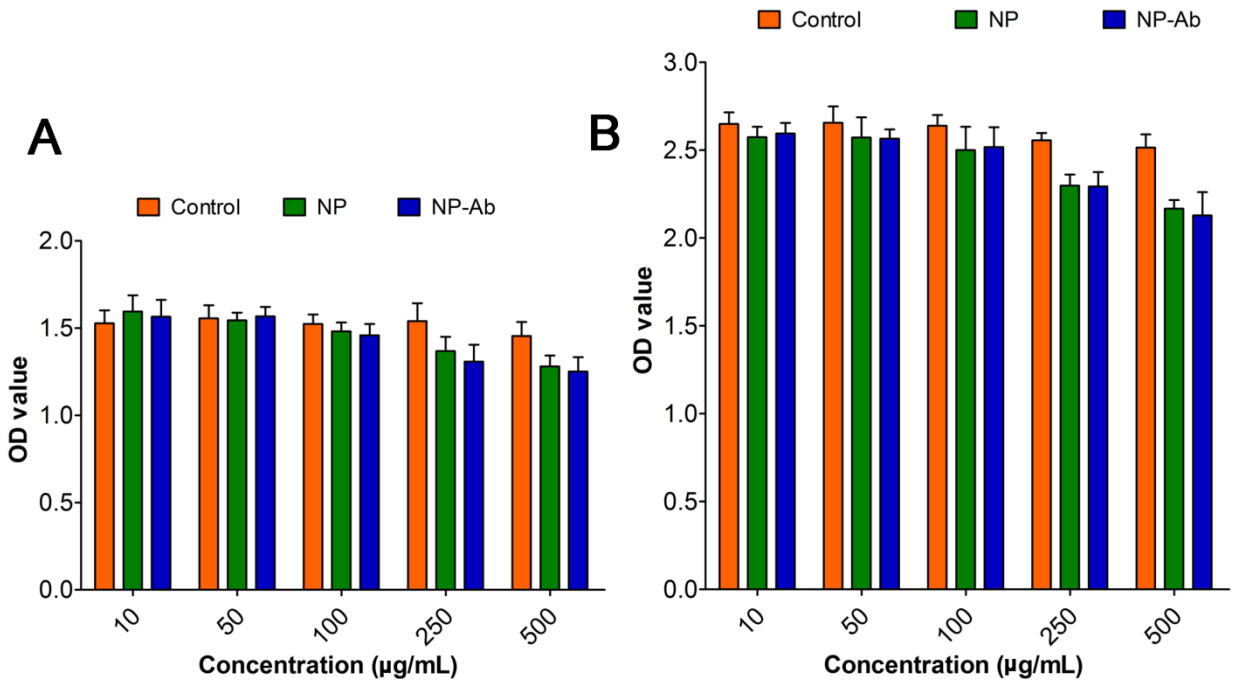

Figure S6. CCK8 assay of Capan-1 cells: (A) 24 h and (B) 48 h after incubation with different concentrations of blank NP and NP-Ab. One-way ANOVA and Tukey HSD were performed for statistical tests at every concentration. For 250 μ g/mL and 500 μ g/mL at 48 h, the overall p value was 0.045 and 0.048, respectively, but there was no significant difference in multiple comparison by Tukey HSD.

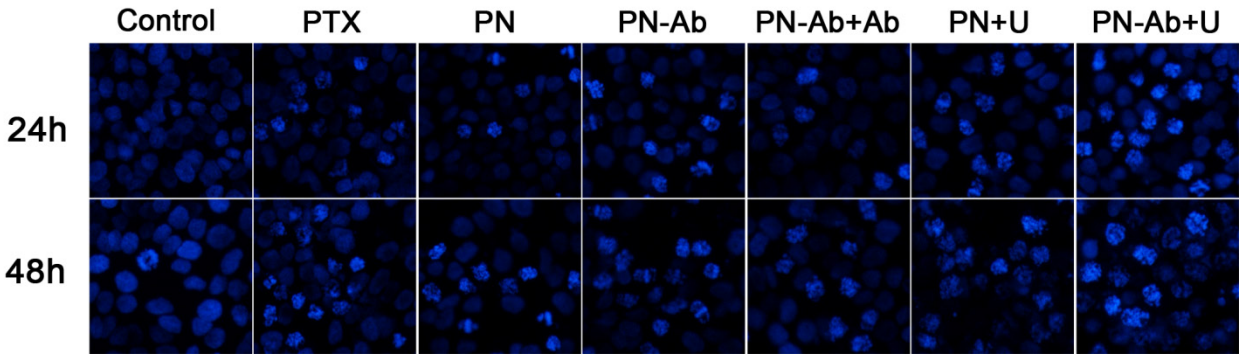

Figure S7. Cell apoptosis as assessed by Hoechst 33342 staining for (C) 24 h and (D) 48 h (×400) in the PTX, PN, PN-Ab, PN-Ab+Ab, PN+U, and PN-Ab+U groups.

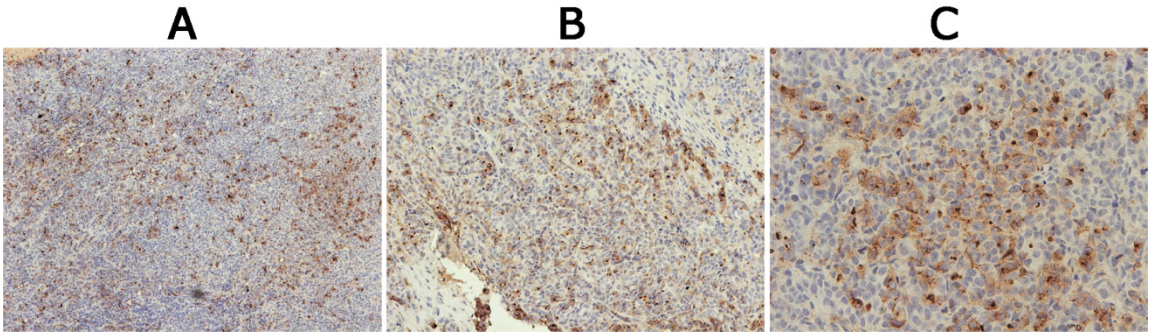

Figure S8. Immunohistochemistry of CA19-9 in the tumor tissue (A ×100，B ×200，C×400).

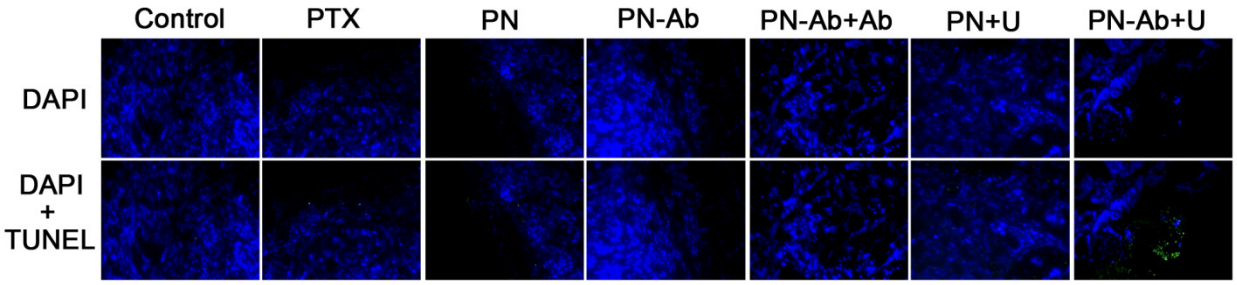

Figure S9. TUNEL staining of tumor tissue in PTX, PN, PN-Ab, PN-Ab+Ab, PN+U, and PN-Ab+U groups (×200): Apoptosis is evident only in PN-Ab+U group but not in other groups.