Identification of a boron nitride nanosphere-binding peptide for the intracellular delivery of CpG oligodeoxynucleotides

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**Figure Legends**

**Supplementary Figure 1.** Yield (output phages /input phages) against the rounds of panning. The phages with higher affinity for BNNS had been successfully concentrated in the phage pool.

**Supplementary Figure 2.** Amino acid frequencies in the BNNS-binding peptide sequence, as compared to the original phage library.

**Supplementary Figure 3.** Fluorescence microscopy images of the FITC-labeled peptides binding to BNNS. In the control group, the BNNS were incubated without peptides.

**Supplementary Figure 4.** Fluorescence emission spectra of BNNS, BP7 and BNNS/BP7 complex in TBS buffer.

**Supplementary Figure 5.** Cytotoxicity, cell uptake of the BNNS/BP7 complexes to HEK293XL-null and Hela cells. (a) Viabilities of 293XL-null and Hela cells measured by a water-soluble tetrazolium salt assay against BNNS and BNNS/BP7 complexes. Concentrations of the nanospheres: 0 µg/mL (Red), 25µg/mL (Cyan), 50µg/mL (Blue), 75µg/mL (Olive), 100µg/mL (Yellow). (b) Confocal microscopy images of HEK293XL-null and Hela cells after 24 h of incubation with BNNS/BP7 complexes. Data presented as mean ± SD (n =5)

**Supplementary Figure 6.** Loading capacity of the BP7 mutants–CpG ODN conjugate on BNNS, denoted as µg CpG ODNs loaded on 1 mg BNNS. M1 (BP7-Y8A) and M2 (BP7-L10A) are mutants of BP7 whose tyrosine (Y8) and leucine (L10) at eighth and tenth positions from N-terminal were replaced by alanine (A), respectively. Loading capacity of the BP7–CpG ODN conjugate on BNNS is shown in Fig. 6a. Data presented as mean ± SD (n = 3).

**Supplementary Figure 7.** Zeta potentials of BNNS, BNNS/BP7, BNNS/CpG ODNs, BNNS/BP7-CpG ODNs complexes in TBS buffer (pH 7.4). Data presented as mean ± SD (n =6)

**Supplementary Figure 8.** IFN-α induction from PBMCs stimulated by CpG ODNs. M1 (BP7-Y8A), M2 (BP7-L10A). The concentration of the BNNS was about 87µg/mL. PTO-2216 is positive control. Data presented as mean ± SD (n =3). The symbol # means not detectable (below detection limit).

**Supplementary Figure 9.** Cytokine induction from PBMCs stimulated by BP7 mutants–CpG ODN conjugate–loaded BNNS. (a) IL-6 production. (b) TNF-α production. Loaded BNNS (87 µg/mL) was incubated with PBMCs for 8 h (TNF-α) and 24 h (IL-6) respectively, M1 (BP7-Y8A) and M2 (BP7-L10A) are mutants of BP7 whose tyrosine (Y8) and leucine (L10) at eighth and tenth positions from N-terminal were replaced by alanine (A), respectively. The levels of IL-6
and TNF-α induced by BNNS/BP7-CpG ODNs are shown in Fig. 7. Data are presented as mean ± SD (n = 3).
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