Supporting information:

Peptide Synthesis

All buffers and salts were purchased from Fisher Scientific. Protected amino acids were purchased from Peptides International, and maleimidohexanoic acid from Sigma-Aldrich. SPv and SPv-NLS were synthesized using *t*-boc solid-phase peptide synthesis as described[11] and confirmed by MALDI TOF MS.

GFP conjugation:

GFP was expressed using *E. coli* BL-21 DE3 harboring the plasmid coding for GFP with a 6-his tag, induced by 1 mM IPTG at 0.6 OD600nm at 22°C overnight. The protein was purified by Ni-NTA affinity chromatography and dialyzed into labeling buffer (20 mM MOPS, 150 mM NaCl, pH 6.9). SPDP (Thermo-Fisher) dissolved in DMSO was added in a 10-fold molar excess to the protein, incubated for 1 hr at room temp, then the protein-SPDP conjugate was purified by gel filtration using a 10-DG column (biorad). A 50-fold molar excess of SPv dissolved in DMSO was added to the GFP-SPDP conjugate in the presence of 1 mM TCEP, incubated for 1 hr at room temp, then purified using gel filtration.

DNA conjugation:

The DNA fragment was generated by PCR using 5'-modified primers (see text) from IDT and isolated from a 1.5% agarose gel (Qiagen). The fragment was conjugated to SPv-NLS as described for GFP conjugation. The concentration of the final product was determined using the extinction coefficient ε_{650nm} = 237,000 $M^{-1}cm^{-1}$.

Phage Conjugation:

XL1-Blue *E. coli* cells were transformed with peGFP-N1, and a single colony was picked and grown in 1 mL 2XYT/kanamycin media for 8 hrs, infected with M13 KO7 bacteriophage (10^{10} phage/mL) for 30 min, then transferred to 30 mL 2XYT/kanamycin overnight. The culture was centrifuged for 10 minutes at 4000g and the phage was precipitated by mixing the supernatant with 6 mL of 20% w/v PEG 8000, 2.5 M NaCl incubated for 30 min on ice, followed by centrifugation for 10 minutes at 4000g. The phage pallet was resuspended in 1 mL of PBS (137 mM NaCl, 2.7 mM KCl, 4.3 mM Na_2HPO_4, 1.47 mM KH_2PO_4, pH 7.5). SPDP and Cy5-NHS ester (GE Healthcare) were added at 100-fold excess over phage particles. After 1.5 hour shaking at RT, precipitation with 20% PEG 8000/2.5 M NaCl was carried twice to clean up the reaction from the unattached fluorophore and crosslinkers. The resuspended phage was incubated with 100-fold excess of SPv in the presence of 1 mM TCEP at RT with shaking for 1.5 hour. The final conjugate was purified by 2 rounds of precipitation and resuspention in PBS.

Bead conjugation:

1 µm amine modified beads (Bangs laboratories, Inc) were centrifuged and resuspended in PBS. Cy5-NHS and SPDP (dissolved in DMSO) were added at 0.1 mM final concentration to 1 mL of resuspended beads for 1 hr at room temp. Excess Cy5 and SPDP were removed from the beads and SPv was added to the resusoended beads at 1 mM final concentration, incubated for 1 hr at room temp, then the supernatant was removed and the conjugated beads were resuspended in PBS.

Tissue culture

HeLa cells were transfected with the pNK1R (in pCDNA 3.1) using lipofectamine 2000 (Invitrogen) according to manufacturer's instructions. Lysates of transfected and untransfected were loaded (20 µg total protein/well) on 15% SDS polyacrylamide gel and used for western blot using polyclonal anti-NK1R antibodies (Abcam). Cells (U87 or HeLa) were plated on glass coverslips in 24-well plates in DMEM supplemented with 10% FBS. Cells were treated with the SPv conjugates (100 nM GFP-SPv, 200 pM DNA-SPv-NLS, 10^{10} phage-SPv/mL). After incubation with the conjugate, the cells were washed with PBS and fixed with 4% *p*-formaldehyde for 20 minutes, then washed with PBS + 0.1% Tween. DAPI was used for nuclear staining. Confocal imaging was carried out on a Leica AB2 microscope. Images were overlaid and processed using ImageJ software.

Supporting Figure 1: Trasfection of HeLa cells with the NK1R. Lane 1: untransfected HeLa cells, lane 2: HeLa cells transfected with the NK1R showing the expression of the receptor (red box).