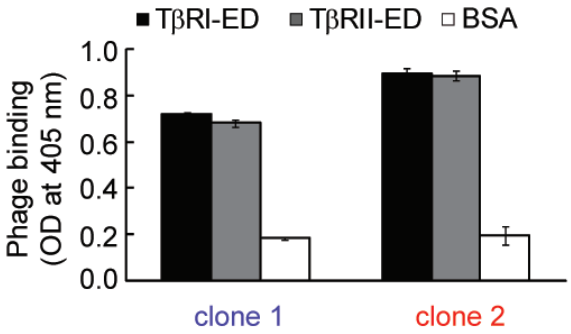
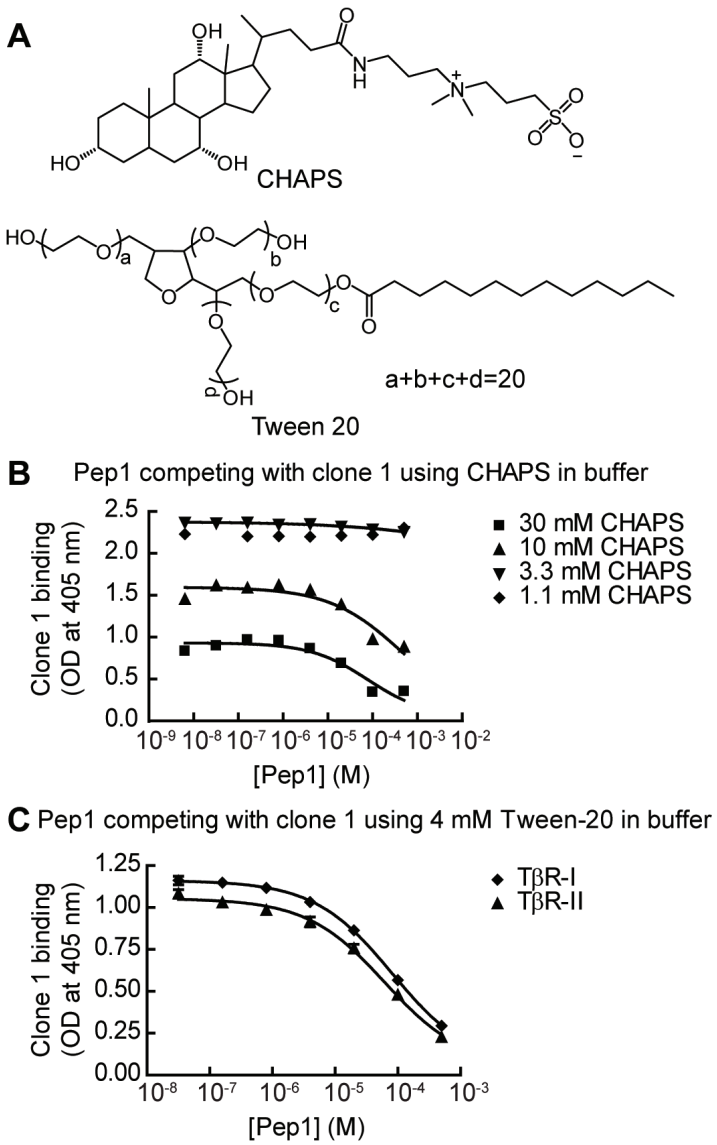


Supplementary Fig. S1 Phage clone 1 and clone 2 display specificity for TβRI-ED and TβRII-ED over BSA.



Supplementary Fig. S2 Optimization of detergent additives for phage ELISA. (A) Structures of CHAPS and Tween-20. (B) Phage binding signals decrease with increasing CHAPS concentrations, indicating this detergent disrupts phage aggregation. The ability of Pep1 to compete clone 1 is enhanced as the CHAPS concentration is raised. (C) TBST containing 4 mM Tween-20 (0.5%) is optimal for this competition ELISA. Error bars represent the mean ± the standard deviation in **(**B**)** and (C).

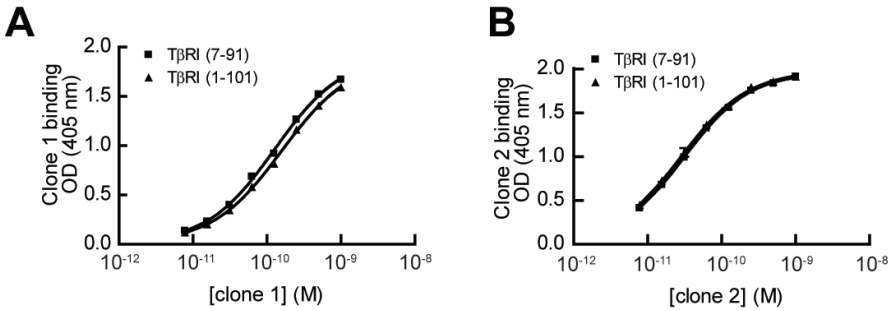
A

Phage clones	$K_{d\ phage}$ (pM)	
	TβRI-ED	TβRII-ED
Clone 1	298 ± 5	334 ± 8
Clone 2	45 ± 2	50 ± 2

B

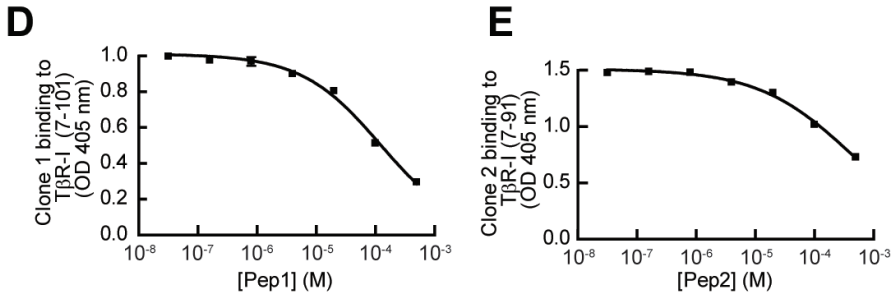
Synthetic peptides	IC_{50} (μM)		K_d (μM)	
	TβRI-ED	TβRII-ED	TβRI-ED	TβRII-ED
Pep1	82 ± 4	62 ± 6	40 ± 2	33 ± 3
Pep2	155 ± 15	141 ± 9	88 ± 10	83 ± 6

Supplementary Table S1 (A) Apparent dissociation constants for the interaction of phage clones ($K_{d\ phage}$) with the immobilized extracellular domains of TβRI and TβRII. (B) Pep1, derived from clone 1, and Pep2, derived from clone 2, inhibit phage clones from binding to immobilized receptors. The IC_{50} values of Pep1 and Pep2 were determined, and dissociation constants (K_d) were then derived using the Cheng-Prusoff equation: $K_d = IC_{50}/(1+[phage]/K_{d\ phage})$. Standard deviations from three experimental replicates are shown.



C

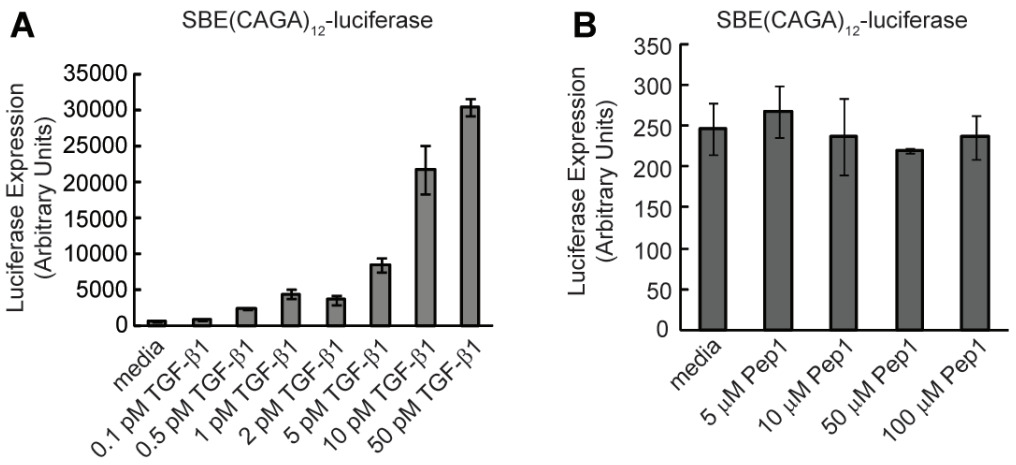
Phage clones	$K_{d\ phage}$ ± S.E. (n=3) pM phage	
	TβRI (7-91)	TβRI (1-101)
clone 1	127 ± 6.11	157 ± 7.97
clone 2	30.6 ± 0.652	27.7 ± 1.70



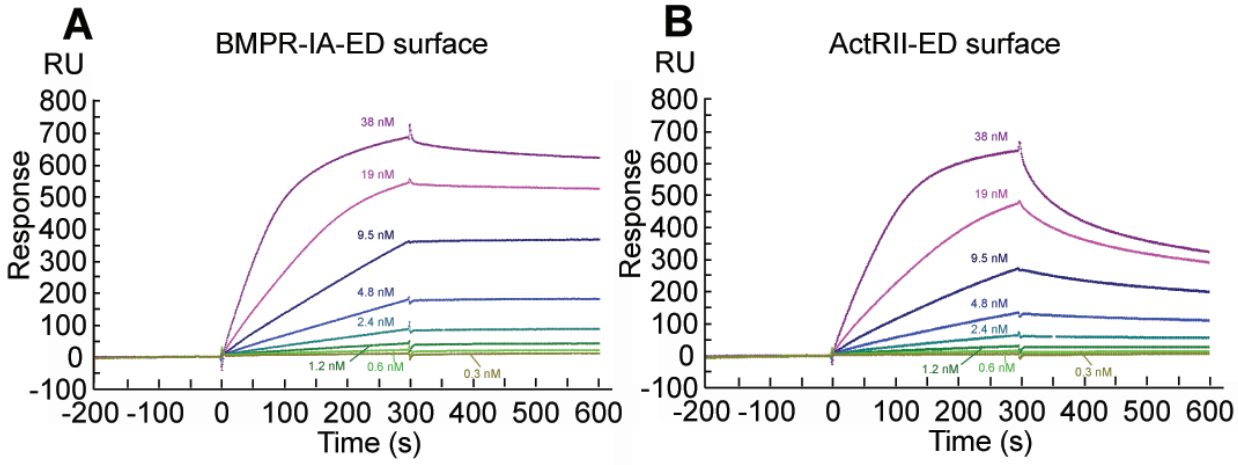
F

Synthetic peptides	IC_{50} ± S.E. (n=3) μM peptide	K_d ± S.E. (n=3) μM peptide	
	TβRI (7-91)	TβRI (7-91)	TβRI (1-101)
Pep1	120 ± 9.19	57.5 ± 5.29	40.5 ± 2.15
Pep2	420 ± 26.9	96.1 ± 6.69	87.5 ± 9.93

Supplementary Fig. S3 The abilities of (A) phage clone 1 and (B) clone 2 to bind immobilized TβRI-ED (residue 7-91) and TβRI-ED (residue 1-101) were tested using a phage based ELISA. (C) Apparent dissociation constants for the interaction of phage clones ($K_{d\ phage}$) with immobilized TβRI-ED (residue 7-91) and TβRI-ED (residue 1-101). (D) ELISA-based competition binding assay. Pep1 derived from clone 1 and (E) Pep2 derived from clone 2 inhibit phage clones from binding to immobilized TβRI-ED (residues 7-91). (F) The IC_{50} values of Pep1 and Pep2 were determined, and their dissociation constants (K_d) to TβRI-ED (residue 7-91) were derived using the Cheng-Prusoff equation: $K_d = IC_{50}/(1+[phage]/K_{d\ phage})$. Standard deviations from three experimental replicates are shown.



Supplementary Fig. S4 (A) TGF-β1 treatment upregulates the reporter gene expression with an EC_{50} value of ~10 pM. (B) Pep1 treatment alone does not initiate luciferase expression.



Supplementary Fig. S5 (A) Binding of BMP-4 to BMPR-IA and (B) ActRII were assessed by SPR. All proteins were immobilized through their lysine residues. A protein-free flow cell was used as control. BMP-4 was injected to all flow cells at concentrations ranging from 0.6 nM to 38 nM. The dose-dependent response curves indicate that both receptors are active when immobilized on the SPR sensor chip.