

Supporting Information

Assessing the single-molecule interactions between targeted peptides and the receptors on living cell membrane

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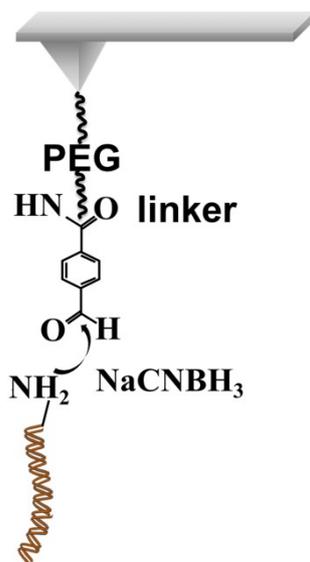


Figure S1. The peptide is covalently conjugated onto the AFM tip via heterobifunctional polyethylene glycol (aldehyde-PEG-NHS) linker.

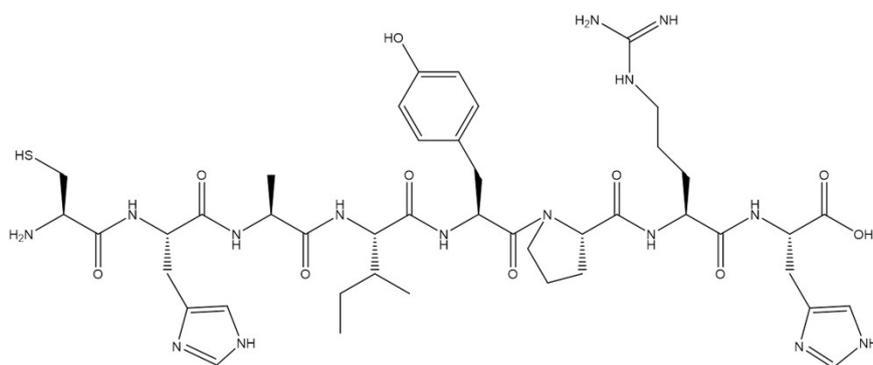


Figure S2. The chemical structure of T7.

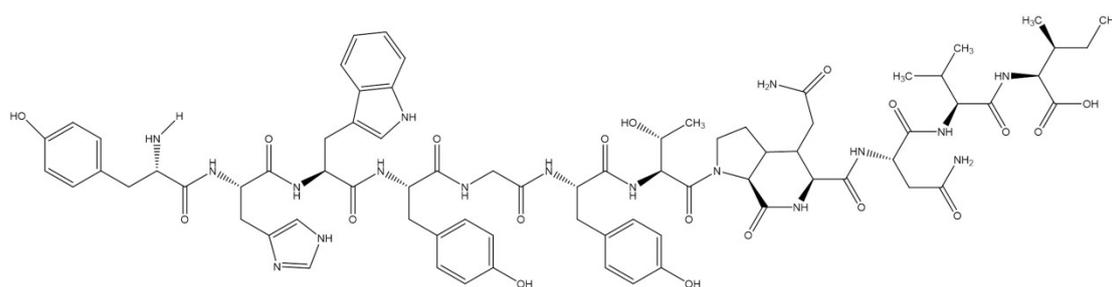


Figure S3. The chemical structure of GE11.

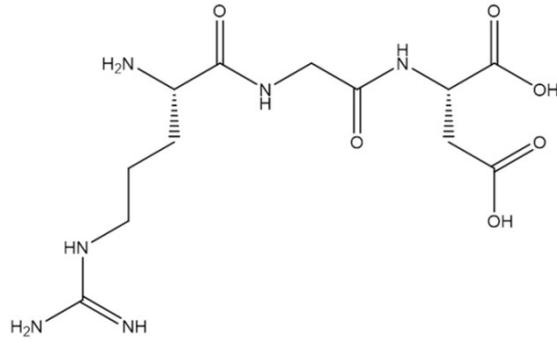


Figure S4. The chemical structure of RGD.

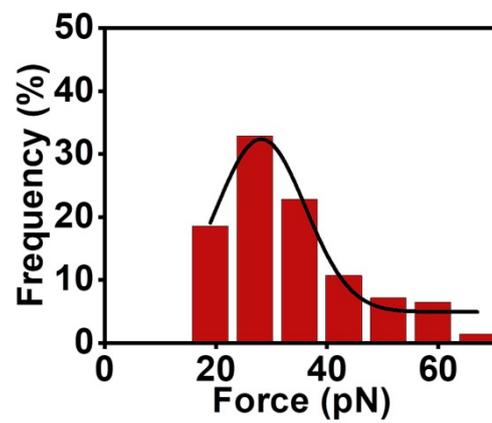


Figure S5. The histogram distribution of unbinding force for T7-TfR after coincubation A549 cells with ferristatin (final concentration 50 μ M) for 1 h. $N \approx 150$.

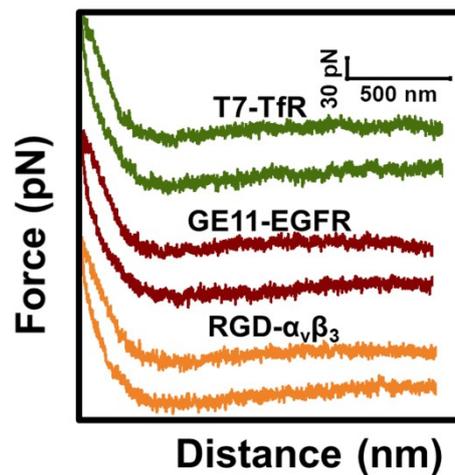


Figure S6. The typical force-distance curves acquired in cells after blocking with free peptides

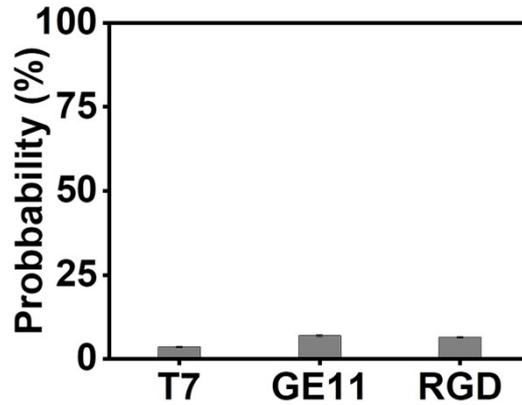


Figure S7. The probability of obtaining the unbinding force signal in cells after blocking with free peptides.

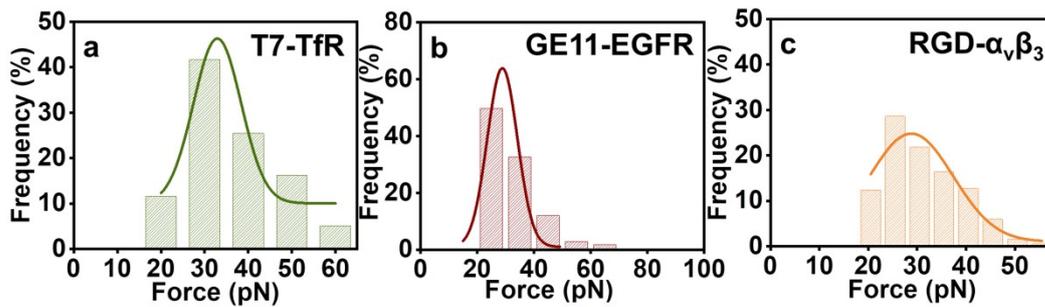


Figure S8. The histogram distribution of unbinding force after blocking with free peptides for T7-TfR, GE11-EGFR, and RGD- $\alpha_v\beta_3$ integrins, respectively. $N \approx 500$.

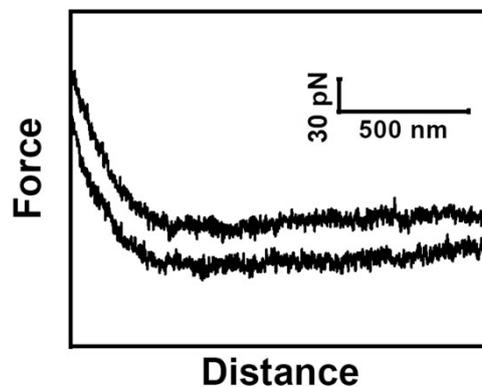


Figure S9. The typical force-distance curves recorded using a non-functionalized AFM tip in living cells.

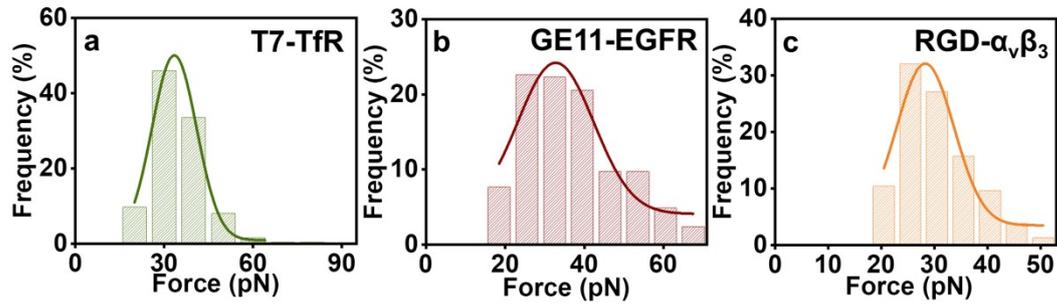


Figure S10. The histogram distribution of unbinding force obtained in A549 cells treated with DOX for a) T7-TfR, b) GE11-EGFR, and c) RGD- $\alpha_v\beta_3$ integrin, respectively.

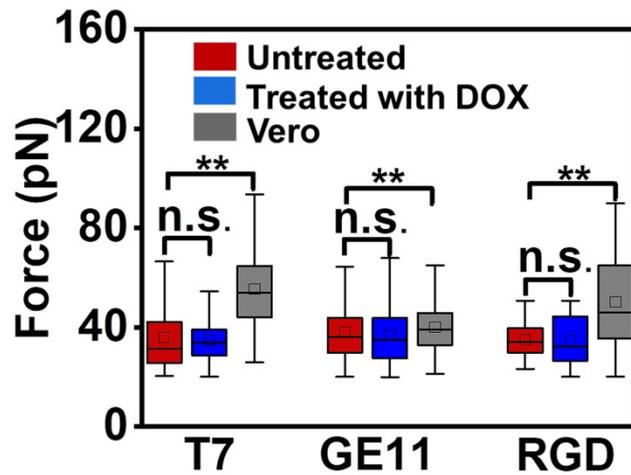


Figure S11. Box-Plot statistical analysis of interaction force for different peptides and the corresponding receptors in Vero cells and A549 cells (before and after treatment with DOX). Boxes represent the data distribution (50%), the vertical lines through the boxes represent the distribution of 95% of all data, the horizontal lines in every box represent the median, and the squares in each box represent the average values. Two-tailed Student's t-test: n.s. $P > 0.05$, $**P < 0.01$.

Table S1. The fluorescence intensity of cancer cells (A549), cancer cells treated with DOX (Treatment), and normal cells (Vero) after coincubation with T7-Cy5, GE11-Cy5, and RGD-Cy5, respectively.

	T7-Cy5	GE11-Cy5	RGD-Cy5
A549	13.47	12.19	7.30
Treatment	2.67	2.17	1.52
t			
Vero	0.63	0.57	0.51