Supporting Information

Table S1. ESI MS-identification of modified aptamers

Name[1]	Chemical Formula	Molecular Weight	Exact Mass [M]	Found [M]
Aptscl56-a	$C_{423}H_{540}N_{153}O_{263}P_{41}S$	13277.8	13271.3	13268.3
Aptscl56-b	$C_{425}H_{544}N_{153}O_{263}P_{41}S$	13305.8	13299.3	13296.1
Aptscl56-c	$C_{427}H_{548}N_{153}O_{263}P_{41}S$	13333.9	13327.3	13324.3
Aptscl56-d	$C_{427}H_{549}N_{154}O_{263}P_{41}S$	13348.9	13342.3	13339.5
Aptscl56-e	$C_{427}H_{549}N_{154}O_{263}P_{41}S$	13348.9	13342.3	13343.3
Aptscl56-f	$C_{424}H_{543}N_{154}O_{263}P_{41}S$	13306.8	13300.3	13299.7
Aptscl56-g	$C_{424}H_{543}N_{154}O_{263}P_{41}S$	13306.8	13300.3	13300.3
Aptscl56-h	$C_{425}H_{545}N_{154}O_{263}P_{41}S$	13320.8	13314.3	13314.2
Aptscl56-i	$C_{425}H_{545}N_{154}O_{263}P_{41}S$	13320.8	13314.3	13314.0
Aptscl56-j	$C_{426}H_{547}N_{154}O_{263}P_{41}S$	13334.9	13328.3	13328.1
Aptscl56-k	$C_{430}H_{547}N_{154}O_{263}P_{41}S$	13382.9	13376.3	13377.3
Aptscl56-l	$C_{430}H_{547}N_{154}O_{263}P_{41}S$	13382.9	13376.3	13376.3
Aptscl56-m	$C_{426}H_{545}N_{154}O_{263}P_{41}S$	13332.9	13326.3	13326.4

[1] Biotin labeled

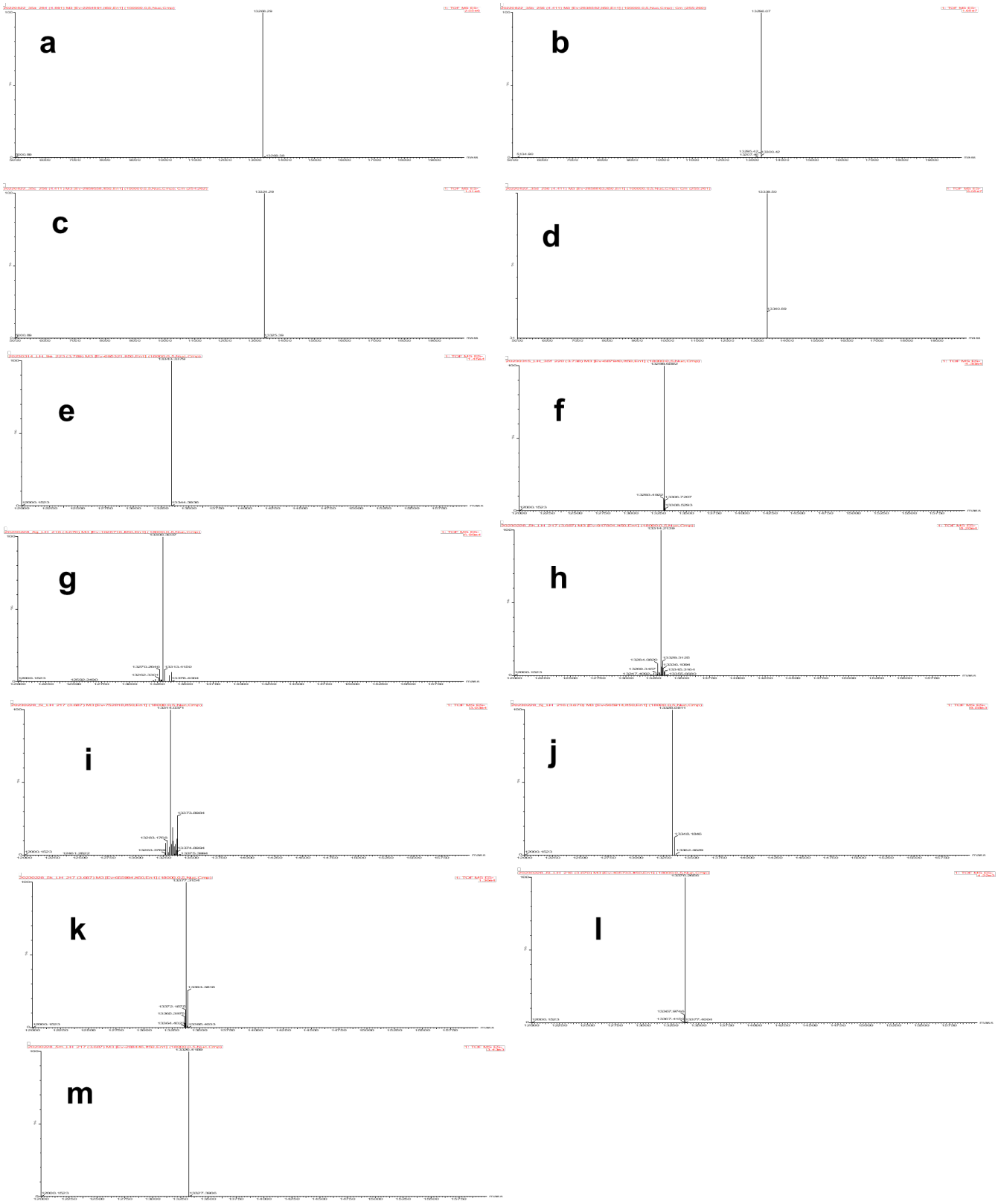

Figure S1. ESI-MS spectra of representative modified aptamers. (a-m) Aptscl56-a, Aptscl56-b, Aptscl56-c, Aptscl56-d, Aptscl56-e, Aptscl56-f, Aptscl56-g, Aptscl56-h, Aptscl56-i, Aptscl56-j, Aptscl56-k, Aptscl56-l, Aptscl56-m. *Notes*: Biotin labeled

a

Name	Sequence (5′-3′)
Aptscl56	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCCT
Aptscl56-5alkyne	CGGG**G**$_{alkyne}$TGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCCT
Aptscl56-7alkyne	CGGGGT**G**$_{alkyne}$TGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCCT
Aptscl56-9alkyne	CGGGGTGT**G**$_{alkyne}$GGTTCGTCGTTAGCTTGATTTGGCAGCTGCCT
Aptscl56-10alkyne	CGGGGTGTG**G**$_{alkyne}$GTTCGTCGTTAGCTTGATTTGGCAGCTGCCT
Aptscl56-11alkyne	CGGGGTGTGG**G**$_{alkyne}$TTCGTCGTTAGCTTGATTTGGCAGCTGCCT
Aptscl56-15alkyne	CGGGGTGTGGGTTC**G**$_{alkyne}$TCGTTAGCTTGATTTGGCAGCTGCCT
Aptscl56-18alkyne	CGGGGTGTGGGTTCGTC**G**$_{alkyne}$TTAGCTTGATTTGGCAGCTGCCT
Aptscl56-22alkyne	CGGGGTGTGGGTTCGTCGTTA**G**$_{alkyne}$CTTGATTTGGCAGCTGCCT
Aptscl56-26alkyne	CGGGGTGTGGGTTCGTCGTTAGCTT**G**$_{alkyne}$ATTTGGCAGCTGCCT
Aptscl56-31alkyne	CGGGGTGTGGGTTCGTCGTTAGCTTGATTT**G**$_{alkyne}$GCAGCTGCCT
Aptscl56-32alkyne	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTG**G**$_{alkyne}$CAGCTGCCT
Aptscl56-35alkyne	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCA**G**$_{alkyne}$CTGCCT

b

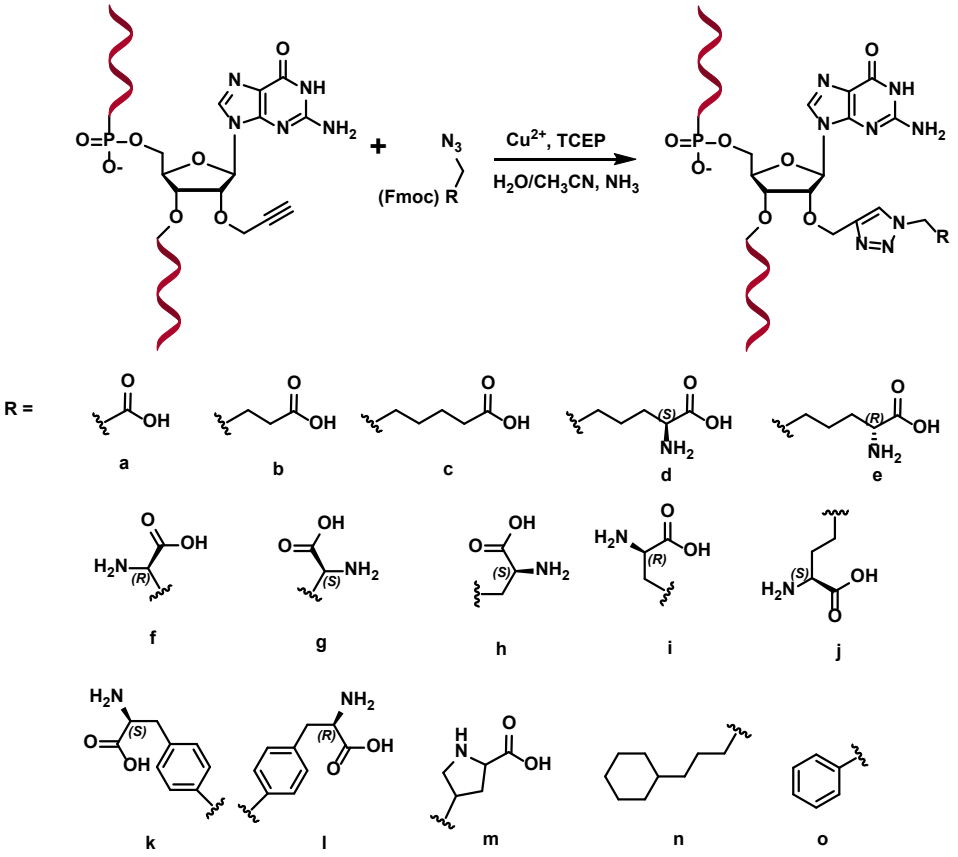

Figure S2. Design and synthesis of chemically modified aptamers through Copper (I)-Catalyzed Alkyne–Azide Cycloaddition (CuAAC). (**a**) The sequences of alkyne modified aptamer. The functional propargyl group was modified at the 2′-hydroxyl of guanosines (**G**$_{alkyne}$) in the sclerostin aptamer Aptscl56, including site 5, 7, 9, 10, 11, 15, 18, 22, 26, 31, 32, and 35. (**b**) The scheme of synthetic route of aptamer modification. The functional azide group was conjugated to the small modification molecules. The reaction was catalyzed by reduction product of Cu^{2+} by tris(2-carboxyethyl)phosphine (TCEP) in a mixed solvent of CH_3CN/H_2O (6%, v/v).

a

Name	Sequence (5′-3′)
Aptscl56-x1	**x**GGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-x2	C**x**GGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-x3	CG**x**GGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-x4	CGG**x**GTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-x5	CGGG**x**TGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-x6	CGGGG**x**GTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-x8	CGGGGTG**x**GGGTTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-x11	CGGGGTGTGG**x**TTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-x13	CGGGGTGTGGGT**x**CGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-x15	CGGGGTGTGGGTTC**x**TCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-x29	CGGGGTGTGGGTTCGTCGTTAGCTTGAT**x**TGGCAGCTGCC
Aptscl56-x30	CGGGGTGTGGGTTCGTCGTTAGCTTGATT**x**GGCAGCTGCC
Aptscl56-x31	CGGGGTGTGGGTTCGTCGTTAGCTTGATTT**x**GCAGCTGCC
Aptscl56-x32	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTG**x**CAGCTGCC
Aptscl56-x33	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGG**x**AGCTGCC
Aptscl56-x34	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGC**x**GCTGCC
Aptscl56-x35	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCA**x**CTGCC
Aptscl56-x36	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAG**x**TGCC
Aptscl56-x37	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGC**x**GCC
Aptscl56-x38	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCT**x**CC
Aptscl56-x39	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTG**x**C
Aptscl56-x40	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGC**x**

b

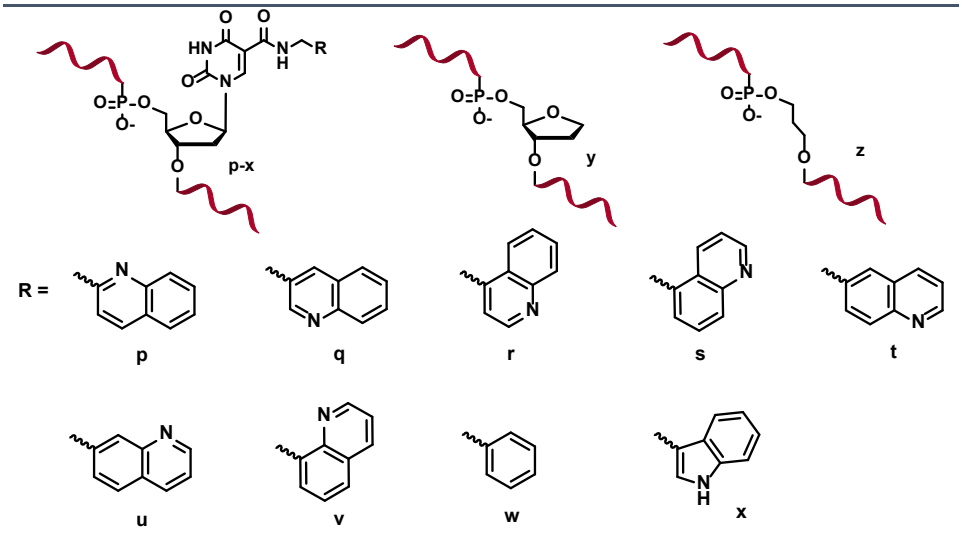

Figure S3. **Design of chemically modified aptamers through solid-phase phosphoramidite method.** (**a**) The sequences of chemically modified aptamer. The incorporated sites included 1, 2, 3, 4, 5, 6, 8, 11, 13, 15, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, and 40. (**b**) Substituting the key sites with chemical modifications.

Table S2. Model comparison of twenty regressors on modified aptamers' affinity estimation

Model	MAE	MSE	RMSE	R2	RMSLE	MAPE
CatBoost	0.3631	0.3118	0.5106	0.4711	0.1809	0.2697
Random Forest	0.3574	0.3039	0.506	0.4539	0.175	0.2572
Light Gradient Boosting Machine	0.4322	0.4447	0.6219	0.3528	0.1949	0.2774
Gradient Boosting	0.39661	0.3576	0.5501	0.3413	0.1954	0.2891
Extreme Gradient Boosting	0.40341	0.36821	0.5599	0.32991	0.2002	0.3244
K Neighbors	0.4272	0.45761	0.63301	0.29881	0.1982	0.2725
Huber	0.42961	0.44971	0.61955	0.2987	0.2032	0.27611
Bayesian Ridge	0.4533	0.4378	0.62071	0.2797	0.2055	0.3169
AdaBoost	0.49351	0.46751	0.6443	0.22735	0.2157	0.3671
Decision Tree	0.4284	0.5079	0.60401	0.1964	0.2107	0.3128
Ridge	0.4673	0.4423	0.6301	0.1932	0.2125	0.3262
Extra Trees	0.4351	0.5217	0.61741	0.1706	0.2162	0.3205
Orthogonal Matching Pursuit	0.48721	0.4513	0.6446	0.1282	0.2213	0.3486
Linear	0.48391	0.4595	0.64431	0.1162	0.2203	0.3382
Lasso	0.6525	0.8368	0.8562	-0.2095	0.301	0.5087
Elastic Net	0.6525	0.8368	0.8562	-0.2095	0.301	0.5087
Lasso Least Angle	0.6525	0.8368	0.8562	-0.2095	0.301	0.5087
Dummy	0.6525	0.8368	0.8562	-0.2095	0.301	0.5087
Passive Aggressive	0.6028	0.6333	0.7446	-0.2124	0.2824	0.4822
Least Angle	6.742×10^{10}	5.569×10^{22}	7.470×10^{10}	4.264×10^{22}	11.5441	5.854×10^{10}

a

Name	Sequence (5′-3′)
Aptscl56	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCCT
Aptscl56-5**sg**	CGGG**sg**TGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCCT
Aptscl56-7**sg**	CGGGGT**sg**TGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCCT
Aptscl56-9**sg**	CGGGGTGT**sg**GGTTCGTCGTTAGCTTGATTTGGCAGCTGCCT
Aptscl56-10**sg**	CGGGGTGTG**sg**GTTCGTCGTTAGCTTGATTTGGCAGCTGCCT
Aptscl56-11**sg**	CGGGGTGTGG**sg**TTCGTCGTTAGCTTGATTTGGCAGCTGCCT
Aptscl56-15**sg**	CGGGGTGTGGGTTC**sg**TCGTTAGCTTGATTTGGCAGCTGCCT
Aptscl56-18**sg**	CGGGGTGTGGGTTCGTC**sg**TTAGCTTGATTTGGCAGCTGCCT
Aptscl56-22**sg**	CGGGGTGTGGGTTCGTCGTTA**sg**CTTGATTTGGCAGCTGCCT
Aptscl56-26**sg**	CGGGGTGTGGGTTCGTCGTTAGCTT**sg**ATTTGGCAGCTGCCT
Aptscl56-31**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTT**sg**GCAGCTGCCT
Aptscl56-32**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTG**sg**CAGCTGCCT
Aptscl56-35**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCA**sg**CTGCCT

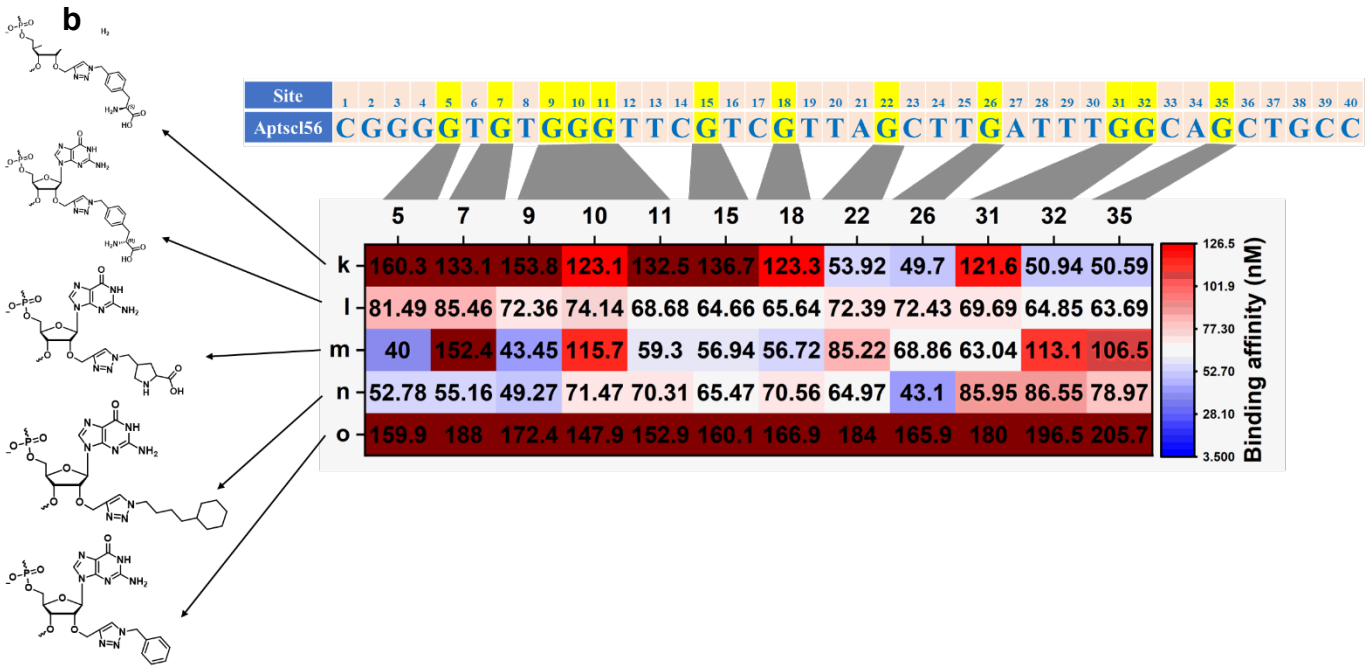

Figure S4. The first round of the modified aptamer-affinity dataset for AI model construction. 5 types of ring modifications at 12 sites, respectively. (**a**) The modified sequences of sclerostin aptamer Aptscl56. Note: substitutional group (**sg**) **= k, l, m, n, o.** (**b**) The measured binding affinity data of the modified aptamer to sclerostin by Biolayer interferometry.

a

Name	Sequence (5′-3′)
Aptscl56	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCCT
Aptscl56-5**sg**	CGGG**sg**TGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCCT
Aptscl56-7**sg**	CGGGGT**sg**TGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCCT
Aptscl56-9**sg**	CGGGGTGT**sg**GGTTCGTCGTTAGCTTGATTTGGCAGCTGCCT
Aptscl56-10**sg**	CGGGGTGTG**sg**GTTCGTCGTTAGCTTGATTTGGCAGCTGCCT
Aptscl56-11**sg**	CGGGGTGTGG**sg**TTCGTCGTTAGCTTGATTTGGCAGCTGCCT
Aptscl56-15**sg**	CGGGGTGTGGGTTC**sg**TCGTTAGCTTGATTTGGCAGCTGCCT
Aptscl56-18**sg**	CGGGGTGTGGGTTCGTC**sg**TTAGCTTGATTTGGCAGCTGCCT
Aptscl56-22**sg**	CGGGGTGTGGGTTCGTCGTTA**sg**CTTGATTTGGCAGCTGCCT
Aptscl56-26**sg**	CGGGGTGTGGGTTCGTCGTTAGCTT**sg**ATTTGGCAGCTGCCT
Aptscl56-31**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTT**sg**GCAGCTGCCT
Aptscl56-32**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTG**sg**CAGCTGCCT
Aptscl56-35**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCA**sg**CTGCCT

b

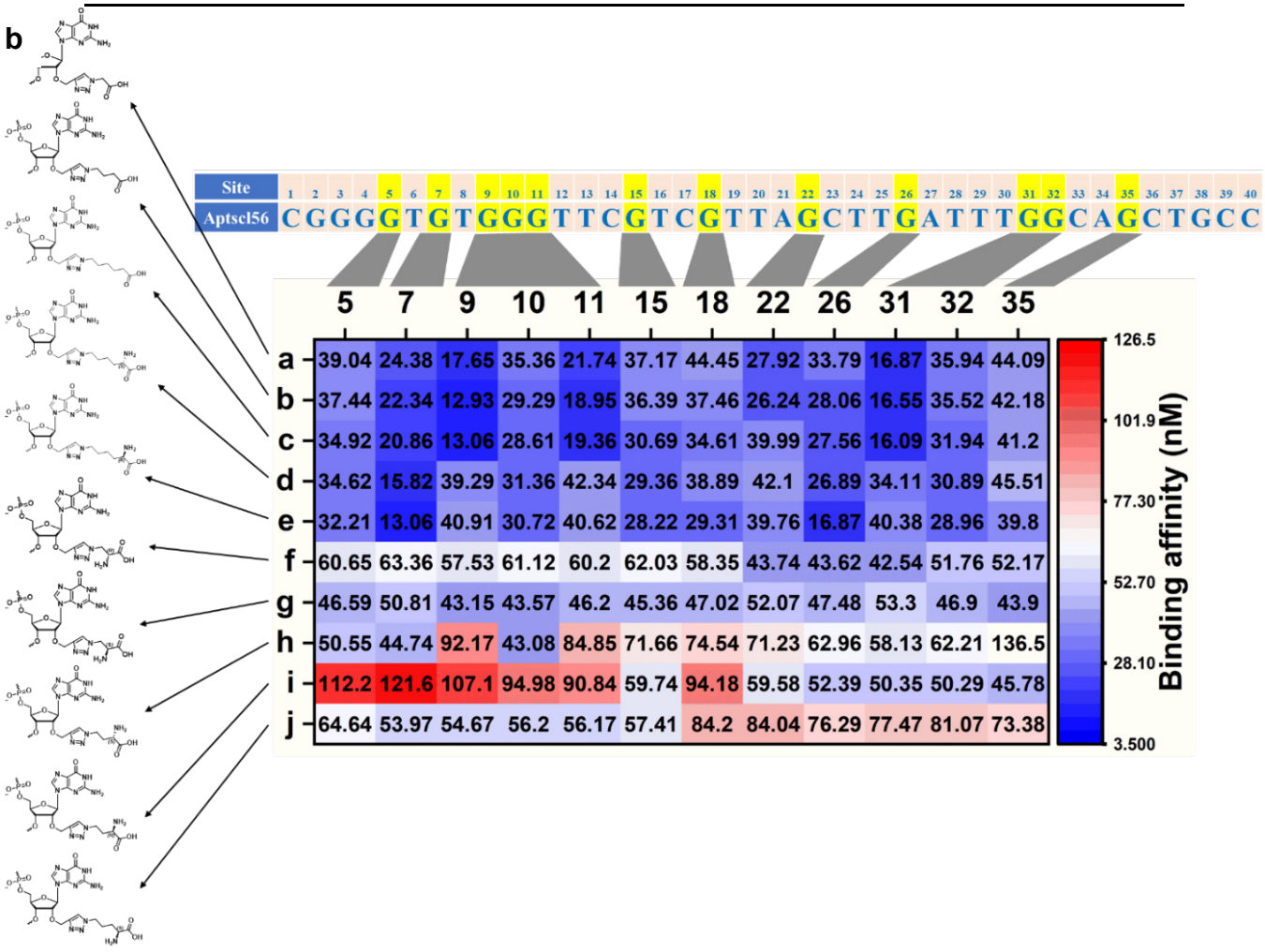

Figure S5. The second round of the modified aptamer-affinity dataset. 10 types of ring modifications at 12 sites, respectively. (**a**) The modified sequences of sclerostin aptamer Aptscl56. Note: substitutional group (**sg**) **= a, b, c, d, e, f, g, h, i, j.** (**b**) The measured binding affinity data of the modified aptamer to sclerostin by Biolayer interferometry.

a

Name	Sequence (5′-3′)
Aptscl56-1**sg**	**sg**GGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-2**sg**	C**sg**GGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-3**sg**	CG**sg**GGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-4**sg**	CGG**sg**GTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-5**sg**	CGGG**sg**TGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-6**sg**	CGGGG**sg**GTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-8**sg**	CGGGGTG**sg**GGGTTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-11**sg**	CGGGGTGTGG**sg**TTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-13**sg**	CGGGGTGTGGGT**sg**CGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-15**sg**	CGGGGTGTGGGTTC**sg**TCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-29**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGAT**sg**TGGCAGCTGCC
Aptscl56-30**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATT**sg**GGCAGCTGCC
Aptscl56-31**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTT**sg**GCAGCTGCC
Aptscl56-32**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTG**sg**CAGCTGCC
Aptscl56-33**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGG**sg**AGCTGCC
Aptscl56-34**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGC**sg**GCTGCC
Aptscl56-35**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCA**sg**CTGCC
Aptscl56-36**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAG**sg**TGCC
Aptscl56-37**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGC**sg**GCC
Aptscl56-38**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCT**sg**CC
Aptscl56-39**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTG**sg**C
Aptscl56-40**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGC**sg**

b

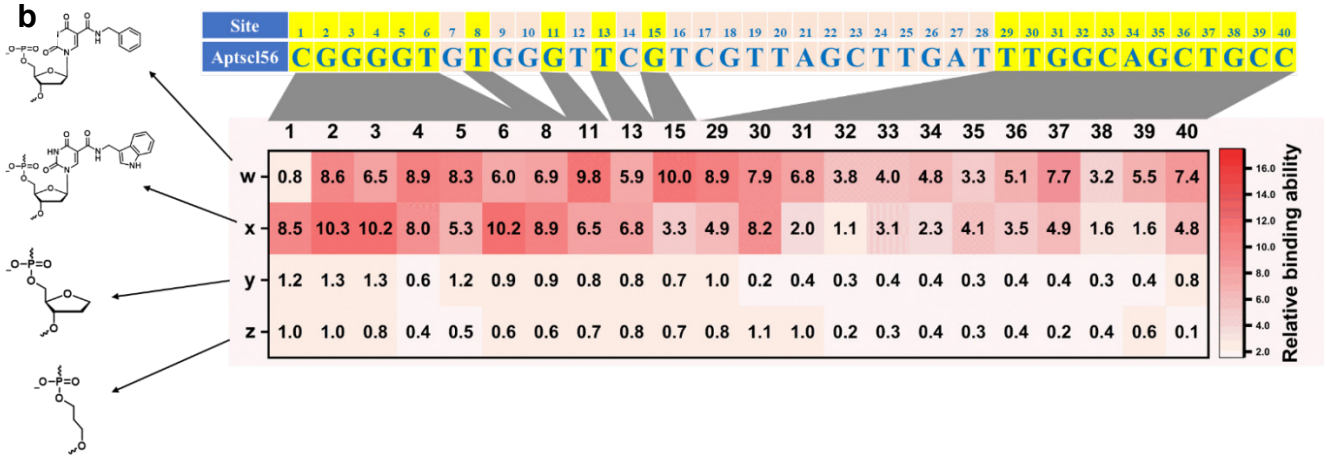

Figure S6. The third round of the modified aptamer-affinity dataset. 4 types of modifications at 22 sites, respectively. (**a**) The modified sequences of sclerostin aptamer Aptscl56. Note: substitutional group (**sg**) **= w, x, y, z.** (**b**) The measured binding ability data of the modified aptamer to sclerostin by Enzyme-Linked Oligonucleotide Assay (ELONA).

a

Name	Sequence (5′-3′)
Aptscl56-1**sg**	**sg**GGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-2**sg**	C**sg**GGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-3**sg**	CG**sg**GGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-4**sg**	CGG**sg**GTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-5**sg**	CGGG**sg**TGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-6**sg**	CGGGG**sg**GTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-8**sg**	CGGGGTG**sg**GGGTTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-11**sg**	CGGGGTGTGG**sg**TTCGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-13**sg**	CGGGGTGTGGGT**sg**CGTCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-15**sg**	CGGGGTGTGGGTTC**sg**TCGTTAGCTTGATTTGGCAGCTGCC
Aptscl56-29**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGAT**sg**TGGCAGCTGCC
Aptscl56-30**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATT**sg**GGCAGCTGCC
Aptscl56-31**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTT**sg**GCAGCTGCC
Aptscl56-32**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTG**sg**CAGCTGCC
Aptscl56-33**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGG**sg**AGCTGCC
Aptscl56-34**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGC**sg**GCTGCC
Aptscl56-35**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCA**sg**CTGCC
Aptscl56-36**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAG**sg**TGCC
Aptscl56-37**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGC**sg**GCC
Aptscl56-38**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCT**sg**CC
Aptscl56-39**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTG**sg**C
Aptscl56-40**sg**	CGGGGTGTGGGTTCGTCGTTAGCTTGATTTGGCAGCTGC**sg**

b

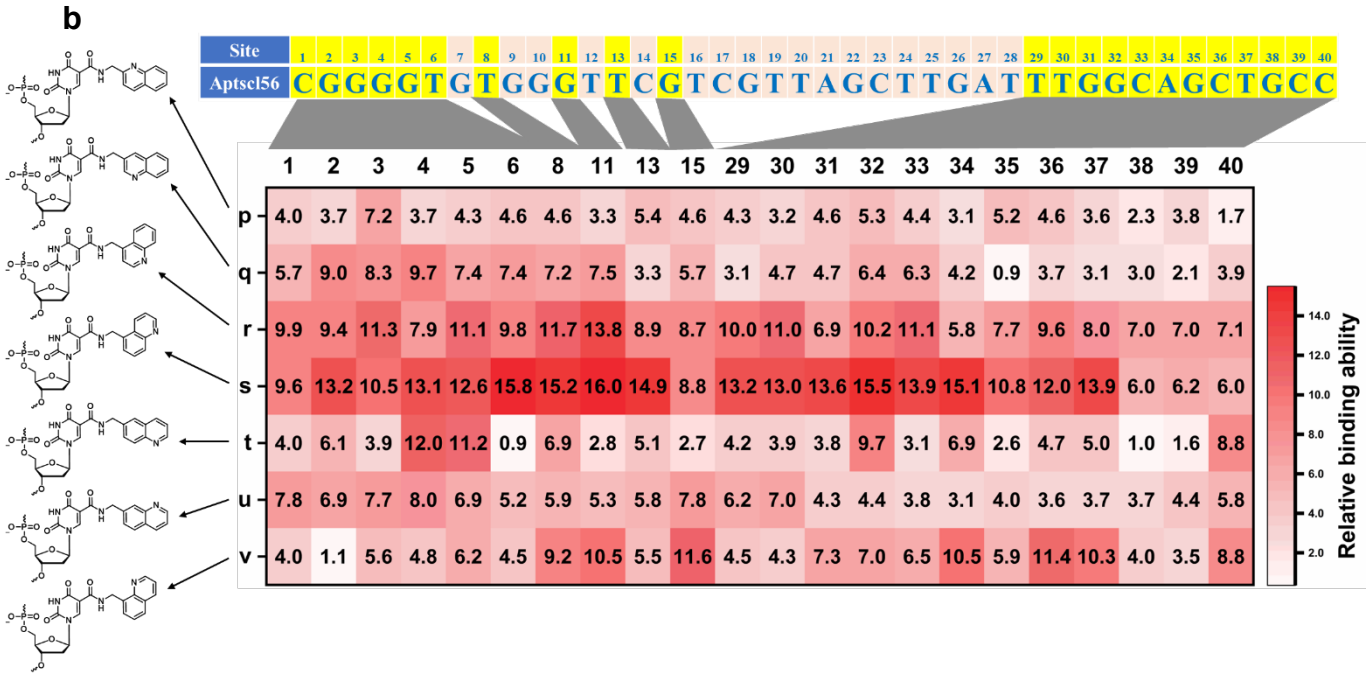

Figure S7. The third round of the modified aptamer-affinity dataset. 7 types of modifications at 22 sites, respectively. (**a**) The modified sequences of sclerostin aptamer Aptscl56. Note: substitutional group (**sg**) **= p, q, r, s, t, u, v.** (**b**) The measured binding ability data of the modified aptamer to sclerostin by Enzyme-Linked Oligonucleotide Assay (ELONA).

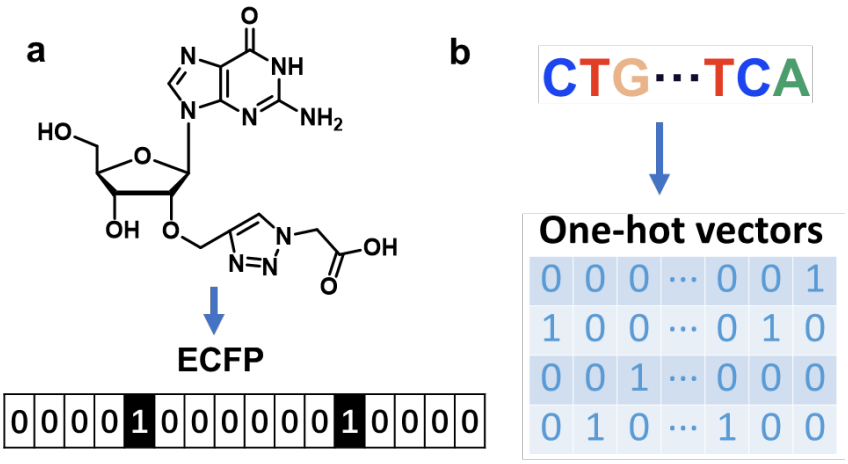

Figure S8. **The training data represented model.** (**a**) fingerprint for each candidate small molecule. (**b**) 40-bit one-hot vectors for modification sites**.**

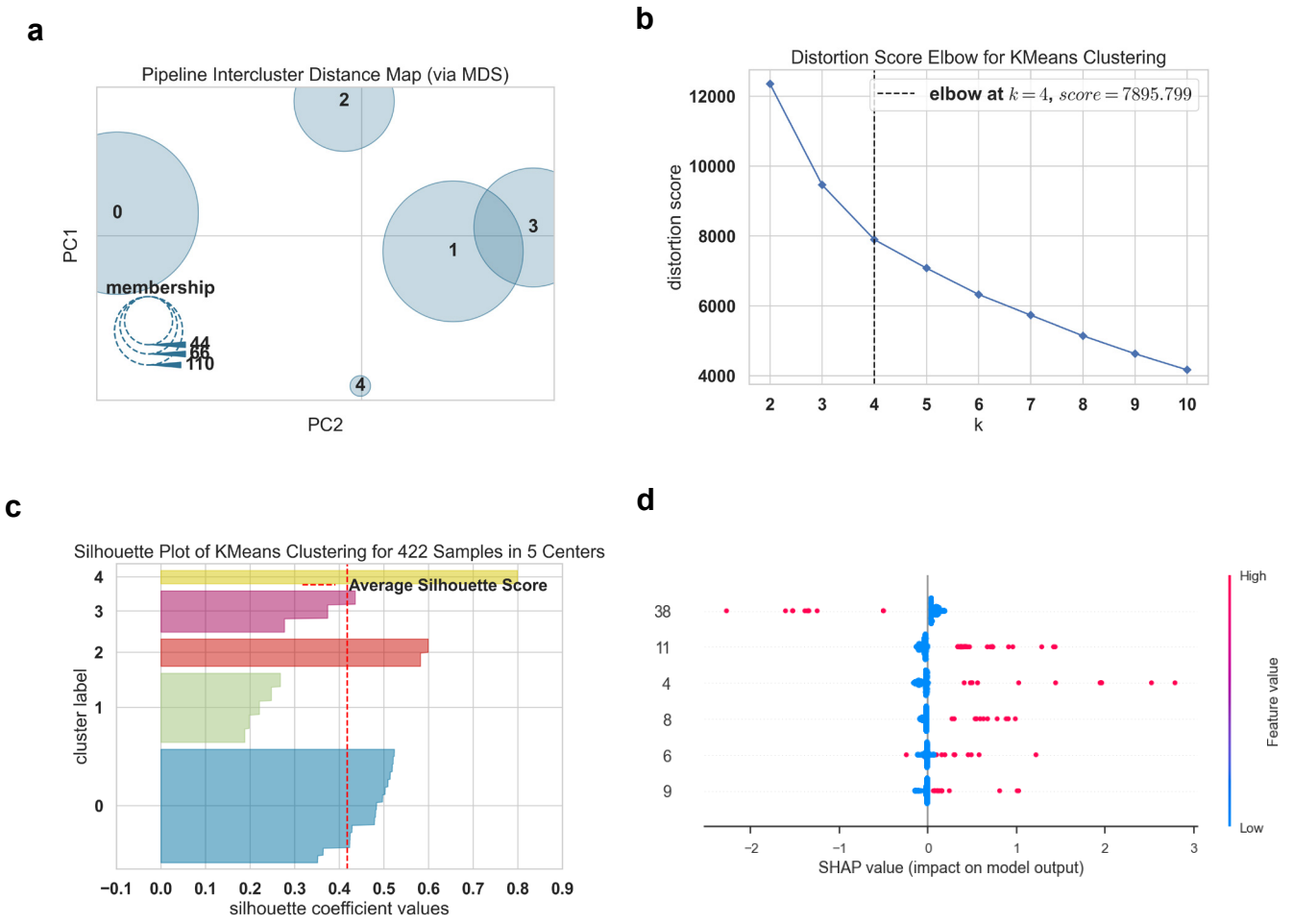

Figure S9. Model interpretability analysis. (**a**) Distances between classes in clustering results. (**b**) Distortion Score Elbow for K-Means. (**c**) Silhouette score Elbow for K-Means. (**d**) The importance of the modified sites for the results was assessed by the shap value on model output.

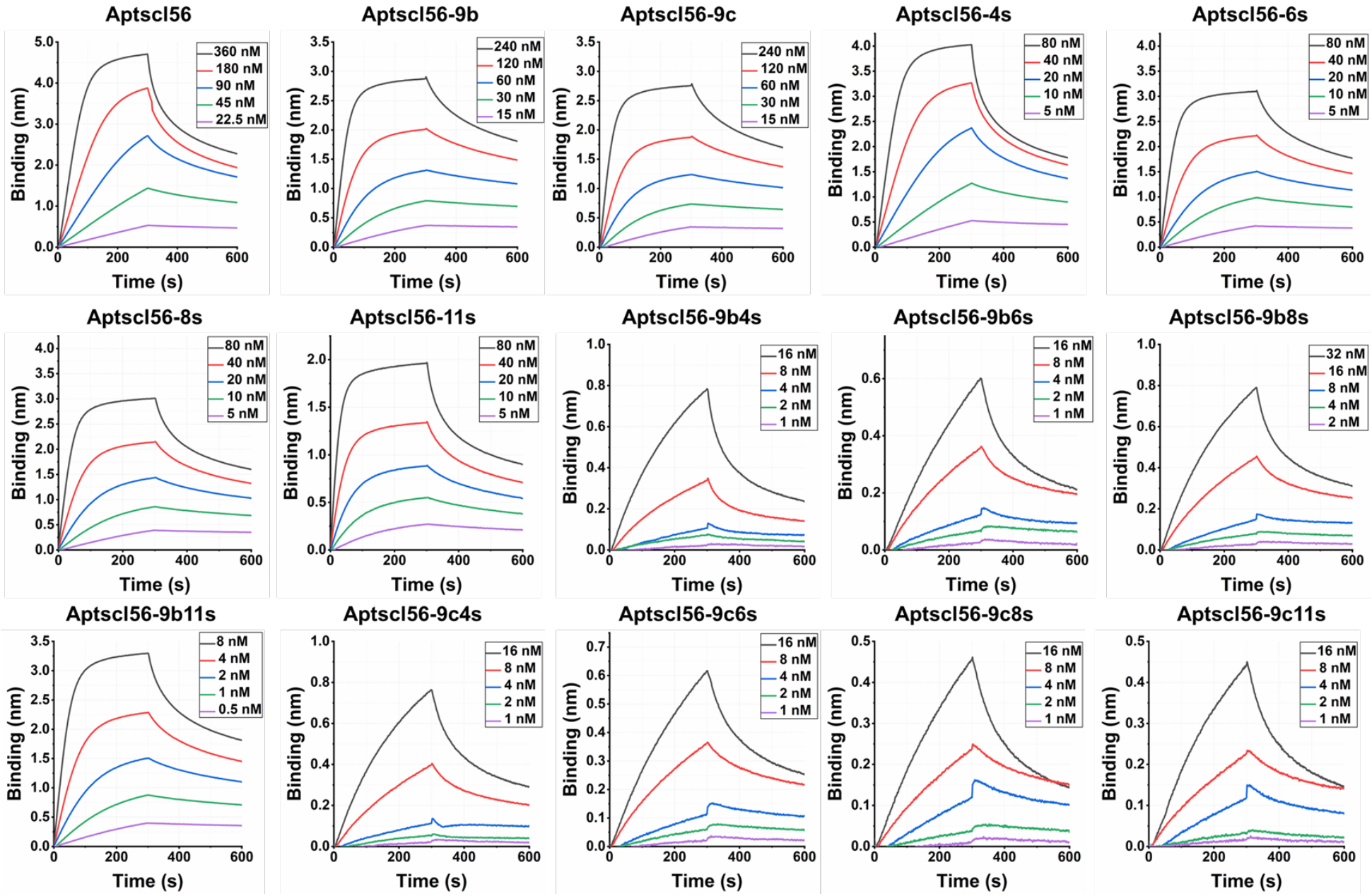

Figure S10. The association and dissociation curves of the naturally unmodified Aptscl56 and the selected aptamers with chemical modification.

Table S3. The predicted interactions between Aptscl56 and sclerostin protein

Index	Residue Number in Protein	Residue Type	Nucleoside Number in Aptamer	Nucleoside Type	Distance	Interaction Type
1	112	PRO	25	U	1.66	Hydrogen Bonds
2	114	ARG	17	C	2.62	Hydrogen Bonds
3	114	ARG	22	G	3.72	Hydrogen Bonds
4	114	ARG	16	U	1.1	Hydrogen Bonds
5	114	ARG	23	C	2.16	Hydrogen Bonds
6	114	ARG	23	C	3.51	Hydrogen Bonds
7	114	ARG	24	U	2.37	Hydrogen Bonds
8	115	TYR	23	C	2.98	Hydrogen Bonds
9	119	ARG	20	U	3.26	Hydrogen Bonds
10	116	ARG	19	U	3.25	Salt Bridges
11	134	LYS	22	G	4.54	Salt Bridges
12	136	ARG	23	C	4.44	Salt Bridges

Table S4. The predicted interactions between Aptscl56-9b and sclerostin protein

Index	Residue Number in Protein	Residue Type	Nucleoside Number in Aptamer	Nucleoside Type	Distance	Interaction Type
1	119	ARG	3	G	3.27	Hydrophobic Interactions
2	121	GLN	4	G	3.91	Hydrophobic Interactions
3	122	LEU	31	G	3.84	Hydrophobic Interactions
4	135	VAL	33	C	3.51	Hydrophobic Interactions
5	137	LEU	34	A	2.95	Hydrophobic Interactions
6	116	ARG	38	G	2.07	Hydrogen Bonds
7	117	ALA	2	G	3.13	Hydrogen Bonds
8	118	GLN	36	C	2.51	Hydrogen Bonds
9	118	GLN	34	A	3.15	Hydrogen Bonds
10	121	GLN	5	G	2.21	Hydrogen Bonds
11	116	ARG	2	G	5.37	Salt Bridges
12	119	ARG	3	G	5.43	Salt Bridges
13	133	ARG	32	G	5.43	Salt Bridges
14	133	ARG	33	C	3.87	Salt Bridges
15	134	LYS	3	G	5.13	Salt Bridges

Table S5. The predicted interactions between Aptscl56-11s and sclerostin protein

Index	Residue Number in Protein	Residue Type	Nucleoside Number in Aptamer	Nucleoside Type	Distance	Interaction Type
1	121	GLN	37	U	3.09	Hydrophobic Interactions
2	122	LEU	1	C	3.34	Hydrophobic Interactions
3	123	LEU	37	U	3.75	Hydrophobic Interactions
4	135	VAL	2	G	3.96	Hydrophobic Interactions
5	116	ARG	31	G	3.17	Hydrogen Bonds
6	116	ARG	31	G	3.03	Hydrogen Bonds
7	117	ALA	33	C	2.71	Hydrogen Bonds
8	118	GLN	4	G	1.9	Hydrogen Bonds
9	119	ARG	36	C	2.24	Hydrogen Bonds
10	121	GLN	37	U	1.94	Hydrogen Bonds
11	121	GLN	36	C	2.46	Hydrogen Bonds
12	116	ARG	32	G	5.22	Salt Bridges
13	119	ARG	35	G	4.86	Salt Bridges
14	133	ARG	2	G	4.28	Salt Bridges
15	134	LYS	34	A	5.09	Salt Bridges

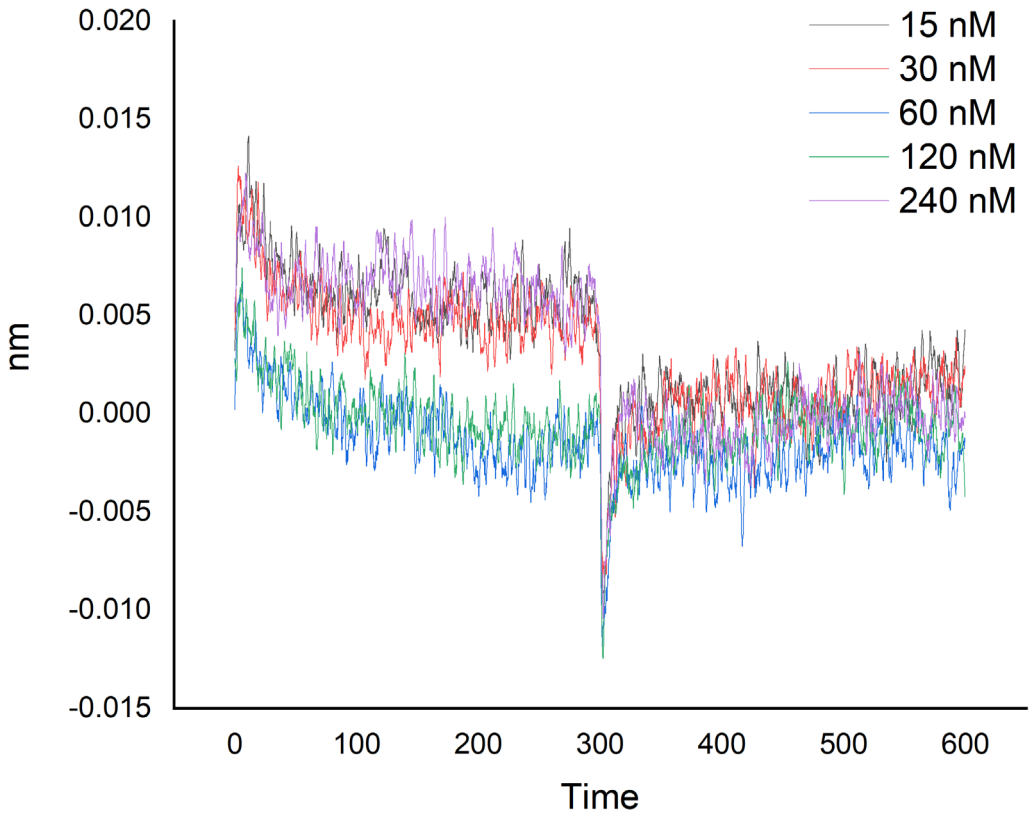

Figure S11. The association and dissociation curves of Aptscl56-9b11s to HSA protein.

Table S6. The predicted interactions between Aptscl56-9b11s and sclerostin protein

Index	Residue Number in Protein	Residue Type	Nucleoside Number in Aptamer	Nucleoside Type	Distance	Interaction Type
1	121	GLN	37	U	3.14	Hydrophobic Interactions
2	122	LEU	1	C	3.08	Hydrophobic Interactions
3	123	LEU	37	U	3.84	Hydrophobic Interactions
4	114	ARG	11	G	3.08	Hydrogen Bonds
5	116	ARG	33	C	2.89	Hydrogen Bonds
6	116	ARG	34	A	2.92	Hydrogen Bonds
7	118	GLN	4	G	2.11	Hydrogen Bonds
8	118	GLN	34	A	2.2	Hydrogen Bonds
9	119	ARG	36	C	2.33	Hydrogen Bonds
10	119	ARG	34	A	2.83	Hydrogen Bonds
11	121	GLN	37	U	1.99	Hydrogen Bonds
12	121	GLN	36	C	2.25	Hydrogen Bonds
13	114	ARG	32	G	4.28	Salt Bridges
14	119	ARG	35	G	3.99	Salt Bridges
15	133	ARG	2	G	4.29	Salt Bridges