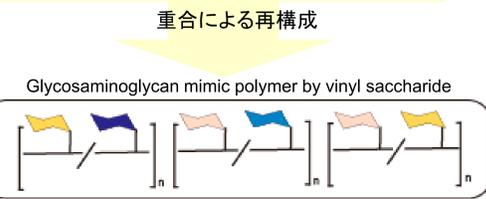
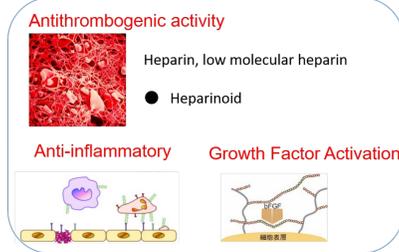
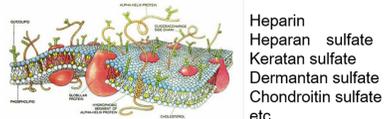
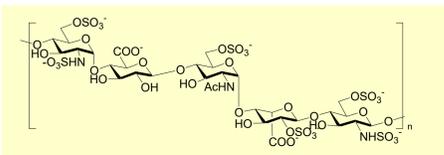


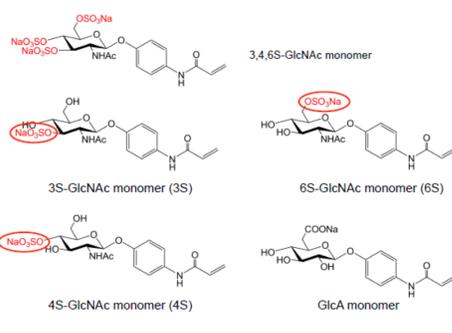
生理活性オリゴ糖は重要なリガンドであり、生命活動で重要な役割を果たしている。オリゴ糖は保護基の化学を含む、困難な合成が伴うため、糖鎖をモジュールとして分解し、重合によって再組織化する、糖モジュール法を駆使して生理活性糖鎖ミミックの創製を検討した。

1. 重合性硫酸化糖によるグリコサミノグリカンミミック

グリコサミノグリカン (GAGs) はヘパリン、ヘパランなどの重要な生理活性多糖を含む相称である。硫酸化糖モノマーの重合によって、GAGsミミックを創製した。VEGFに特異的な結合を示し、GAGsミミックの投与によって、腫瘍成長の抑制効果が見られた。



Structure of heparin mimic monomer



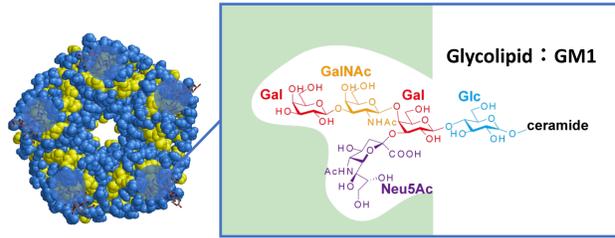
NPs including heparin mimic monomer

	NIPAm	3,4,6S	TBAAm	Bis
0% 3,4,6S	58	0	40	2
5/3% 3,4,6S	53+10/3	53	40	2
5% 3,4,6S	53	5	40	2
10% 3,4,6S	58	10	40	2

	Size (nm)	PDI	ζ-potential (mV)
0% 3,4,6S	79.9	0.014	-28.1
5/3% 3,4,6S	85.91	0.017	-38.1
5% 3,4,6S	87.66	0.026	-31.1
10% 3,4,6S	74.77	0.044	-29.7

2. 糖モジュール法によるGM1ミミックの創製

Cholera Toxin B subunit(CTB)



Cholera toxin recognizes penta saccharide of GM1.

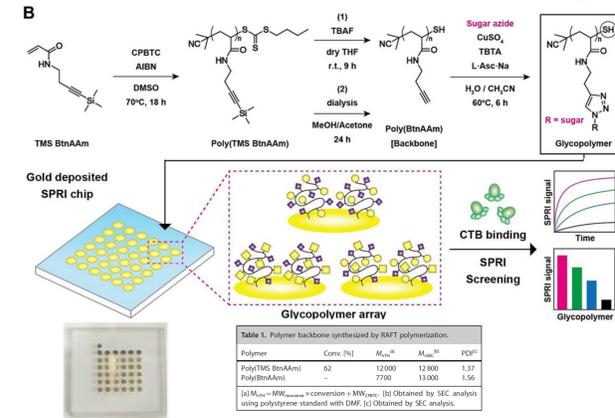


Table 2. Glycopolymers synthesized by the carbohydrate module method.

Polymer	Incorporated carbohydrate module 1	module 2	module 3	M _n ^(a)	M _w ^(a)	PDI ^(c)
P1	Gal	-	-	21500	10000	1.57
P2	Man	-	-	21500	9000	1.50
P3	Glc	-	-	21500	9000	1.51
P4	GalNAc	-	-	24000	6000	1.52
P5	GlcNAc	-	-	24000	9000	1.73
P6	Neu5Ac	-	-	30000	15000	1.44
P7	3'SALac	-	-	50000	18000	1.47
P8	6'SALac	-	-	50000	19000	1.33
P9	Gal	GalNAc	-	23000	6000	1.65
P10	Gal	Neu5Ac	-	24000	16000	1.48
P11	Gal	GalNAc	Neu5Ac	25000	8000	1.60
P12	Gal	3'SALac	-	36000	26000	1.44

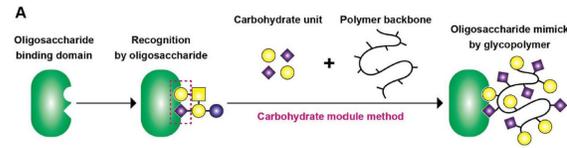
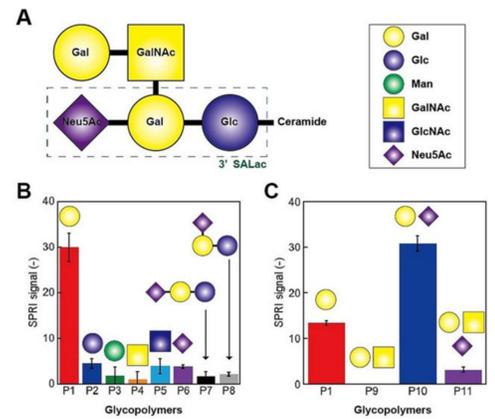


Table 3. Kinetic analysis results of CTB binding to glycopolymers obtained by SPRI measurements.

Polymer	k _{on} [M ⁻¹ s ⁻¹]	k _{off} [s ⁻¹]	K _D [M]
P1	5.2 × 10 ³	2.4 × 10 ⁻³	4.6 × 10 ⁻⁷
P10	9.9 × 10 ⁴	3.6 × 10 ⁻⁶	3.7 × 10 ⁻¹⁰

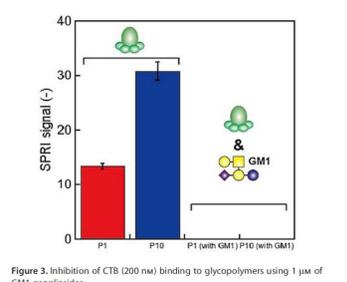
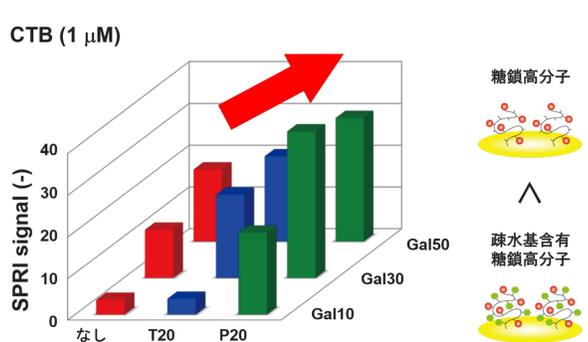
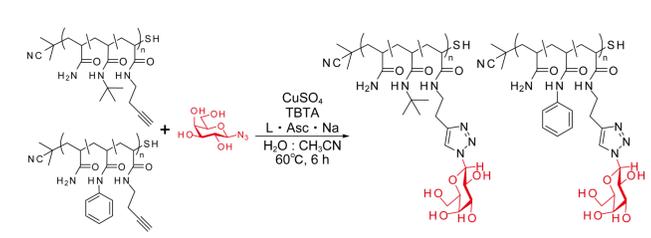
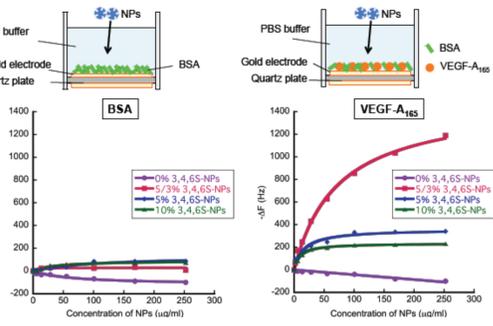


Figure 3. Inhibition of CTB (200 nM) binding to glycopolymers using 1 μM of GM1 gangliosides.

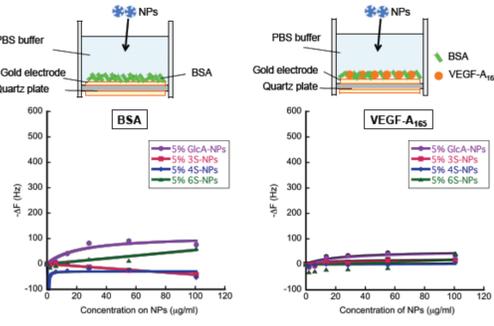
2. 糖モジュール法によるGM1ミミックライブラリー



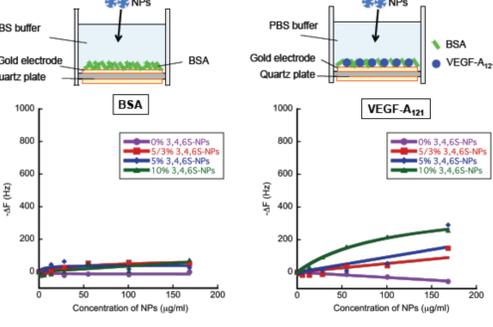
High affinity of 3,4,6S NPs to VEGF-A₁₆₅



No binding affinity of 5% mono sulfate heparin mimic monomer-containing NPs to VEGF-A₁₆₅



Binding affinity of 3,4,6S NPs to VEGF-A₁₂₁



Inhibition of VEGF binding to heparin by 3,4,6S NPs

