Electronic Supplementary Information

Increasing Bacterial Affinity and Cytocompatibility with Four-arm Star Glycopolymers and Antimicrobial *α*-Polylysine

Dicky Pranantyo[1], Li Qun Xu[1], Zheng Hou[2], En-Tang Kang[1]*, Mary B. Chan-Park[2]*

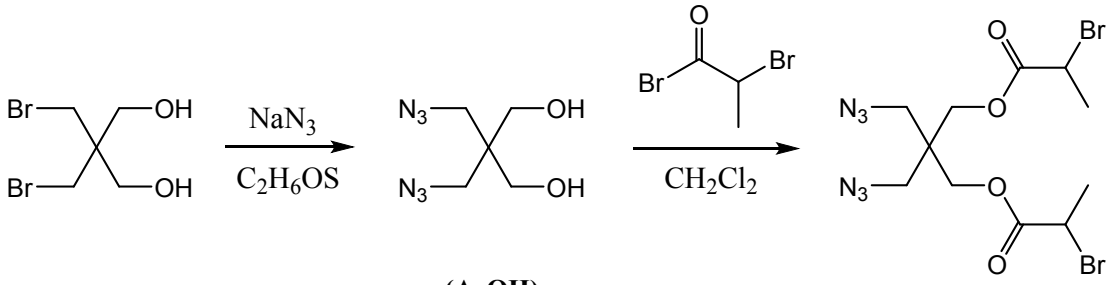
[1] Department of Chemical & Biomolecular Engineering
National University of Singapore
Kent Ridge, Singapore 119260

[2] Centre of Antimicrobial Bioengineering
School of Chemical and Biomedical Engineering
Nanyang Technological University
Singapore 637459

* Corresponding Authors
E-mail: cheket@nus.edu.sg (E.T.K)
mbechan@ntu.edu.sg (M.B.C.P)

* ORCID
En-Tang Kang: 0000-0003-0599-7834
Mary B. Chan-Park: 0000-0003-3761-7517

1. Synthesis and characterizations of the four-arm 'clickable' initiator (AzBr)



(AzOH) **(AzBr)**

2,2-Bis-(azidomethyl)-propane-1,3-diol (AzOH).[1] Due to the explosive nature, all reactions and purifications involving azide compounds were carried out with caution, following the standard safety rules. Briefly, 26.2 g (0.1 mol) of 2,2-bis(bromomethyl)propane-1,3-diol was dissolved in 100 mL of dimethyl sulfoxide, followed by adding 16.25 g (0.25 mol) of sodium azide. The suspension was stirred vigorously and heated to 100 °C with a reflux condenser overnight. After being cooled to room temperature, 50 mL of deionized water was added and the mixture was extracted thrice with 200 mL of ethyl acetate. The combined extract was washed thrice with 100 mL of saturated brine, and the organic phase was dried with magnesium sulfate overnight. After being filtered, the solution was concentrated using rotary evaporator and dried under reduced pressure to obtain AzOH (colourless oil, yield 95%).

Four-arm 'clickable' initiator (AzBr). Briefly, 7 g (37.6 mmol) of AzOH and 15.7 mL (112.8 mmol) of triethylamine were dissolved in 150 mL of dichloromethane (DCM). The solution was stirred vigorously and cooled down to 0 °C in an ice bath. Subsequently, 11.8 mL (112.8 mmol) of 2-bromopropionyl bromide in 50 mL of dichloromethane was introduced dropwise to the solution at 0 °C. After the addition, the reaction was allowed to proceed at room temperature for 24 h under stirring. The solution was concentrated in a rotary evaporator and purified through a silica column chromatography using hexane/ethyl acetate (4/1 volumetric ratio) as the spreading eluent. The desired fraction was concentrated in a rotary evaporator and dried under reduced pressure to obtain AzBr (light yellow oil, yield 72%).

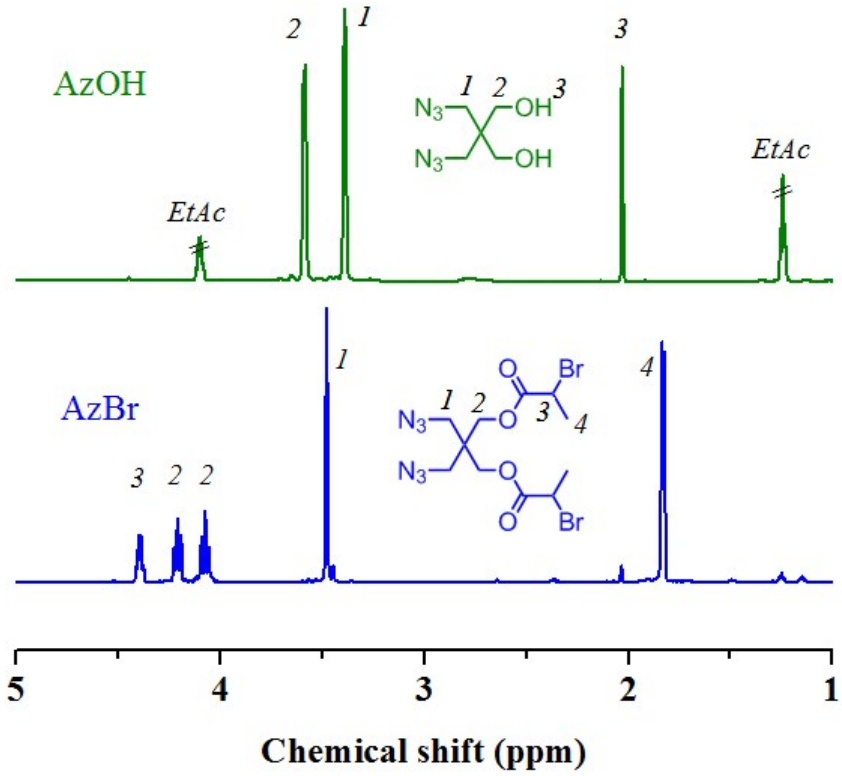
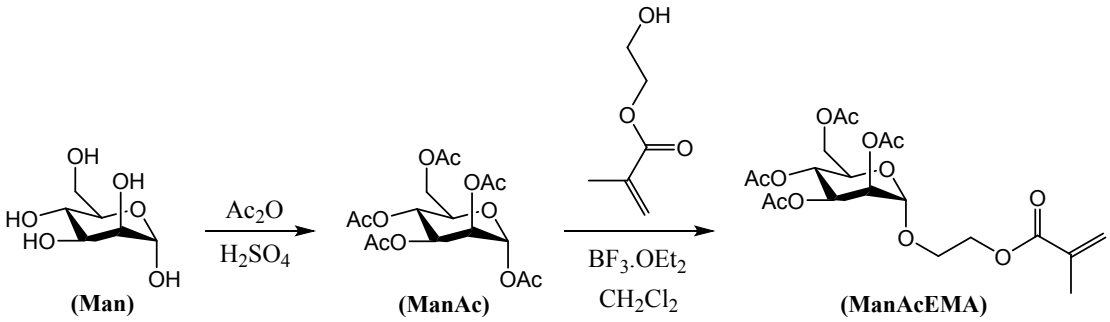


Figure S1. ^{1}H NMR spectra of the AzOH and AzBr initiator in $CDCl_3$.

2. Synthesis and characterization of the glycomonomers and glycopolymers



1,2,3,4,6-penta-*O*-acetyl-D-mannopyranoside (AcMan).[2] Briefly, 25 g (138.8 mmol) of D-(+)-mannose was dissolved in 150 mL of acetic anhydride. The solution was cooled down to 0 °C in an ice bath, and 8 drops of sulfuric acid was added slowly under vigorous stirring. After 10 min, the reaction was allowed to proceed at room temperature for 1 h. The solution was poured in a 1 L glass beaker containing 500 mL of icy water, and the top layer was decanted out. Then, 200 mL of ethyl acetate was poured into the bottom layer, and sodium bicarbonate was gradually added to the mixture under stirring until no more bubble was generated. After the mixture was

settled, the acetate layer was collected, washed thrice with 200 mL of deionized water, and dried with magnesium sulfate overnight. After being filtered, the solution was concentrated in a rotary evaporator and dried under reduced pressure to obtain AcMan (light yellow oil, yield 70%).

2-(2',3',4',6'-tetra-*O*-acetyl-D-mannosyloxy)ethyl methacrylate (AcManEMA).[3] Briefly, 38 g (97.4 mmol) of ManAc was dissolved in 300 mL of anhydrous DCM, and 14.17 mL (116.9 mmol) of 2-hydroxyethyl methacrylate was added into the solution. The solution was cooled down to 0 °C in an ice bath, and 30 mL (243.5 mmol) of boron trifluoride diethyl etherate in 50 mL of anhydrous DCM was added dropwise under vigorous stirring. The reaction was allowed to proceed at room temperature for 36 h in a sealed flask to avoid contact with ambient moisture. The solution was washed thrice with 200 mL of saturated brine, and the organic phase was dried with magnesium sulfate overnight. After being filtered, the solution was concentrated in a rotary evaporator and purified through a silica column chromatography using hexane/ethyl acetate (4/1 volumetric ratio) as the spreading eluent. The desired fraction was concentrated in a rotary evaporator and dried under reduced pressure to obtain AcManEMA (pale yellowish oil, yield 71%).

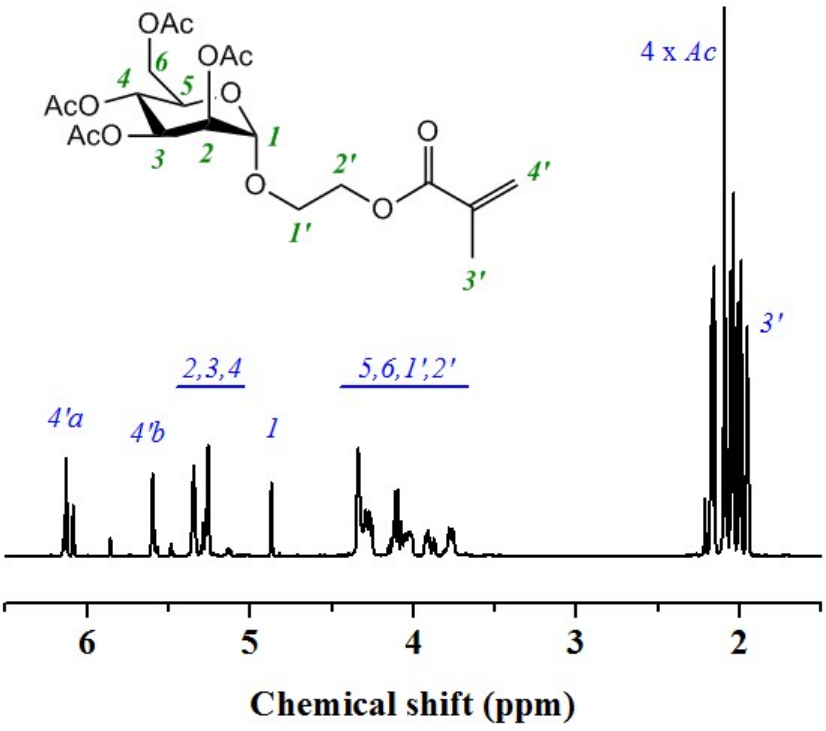


Figure S2. ^{1}H NMR spectrum of the AcManEMA monomer in $CDCl_3$.

2-(2',3',4',6'-tetra-*O*-acetyl-D-glucosyloxy)ethyl methacrylate (AcGluEMA) and 2-(2',3',4',6'-tetra-*O*-acetyl-D-galactosyloxy)ethyl methacrylate (AcGalEMA). The AcGluEMA and AcGalEMA monomers were prepared using similar procedures as that of AcManEMA, by replacing D-(+)-mannose starting material with D-(+)-glucose and D-(+)-galactose, respectively.

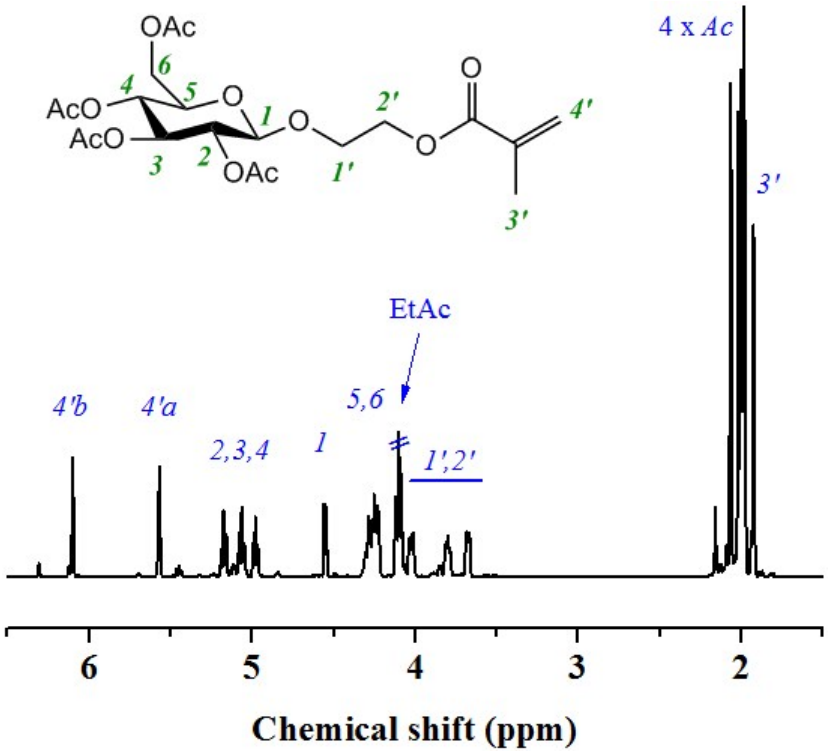


Figure S3. ^{1}H NMR spectrum of the AcGluEMA monomer in $CDCl_3$.

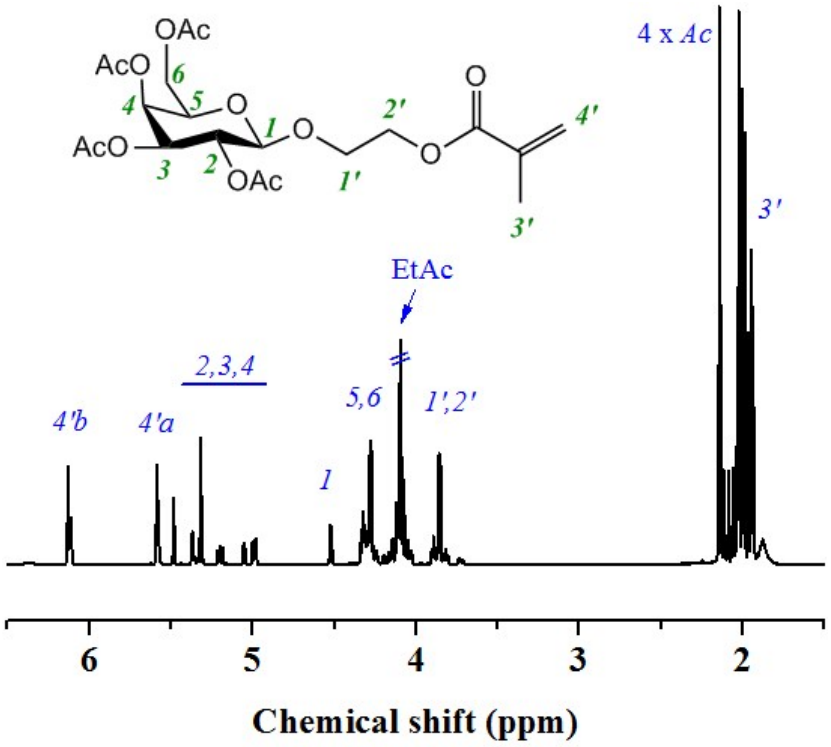


Figure S4. ^{1}H NMR spectrum of the AcGalEMA monomer in $CDCl_3$.

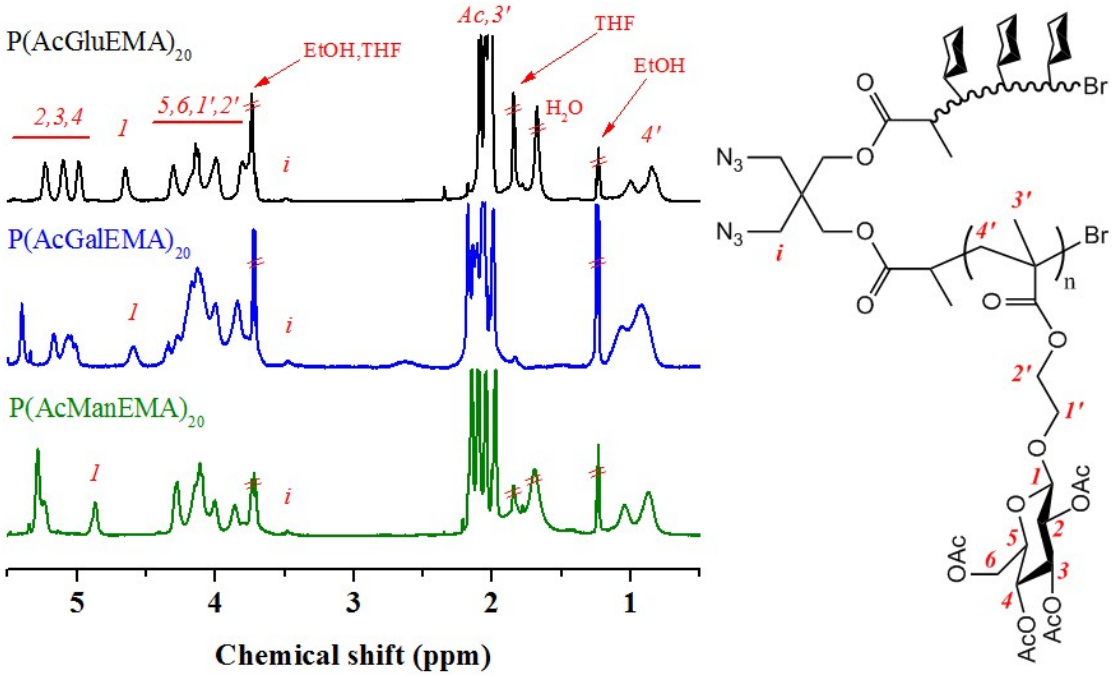


Figure S5. ^{1}H NMR spectra of the $P(AcManEMA)_{20}$, $P(AcGluEMA)_{20}$, and $P(AcGalEMA)_{20}$ polymers in $CDCl_3$.

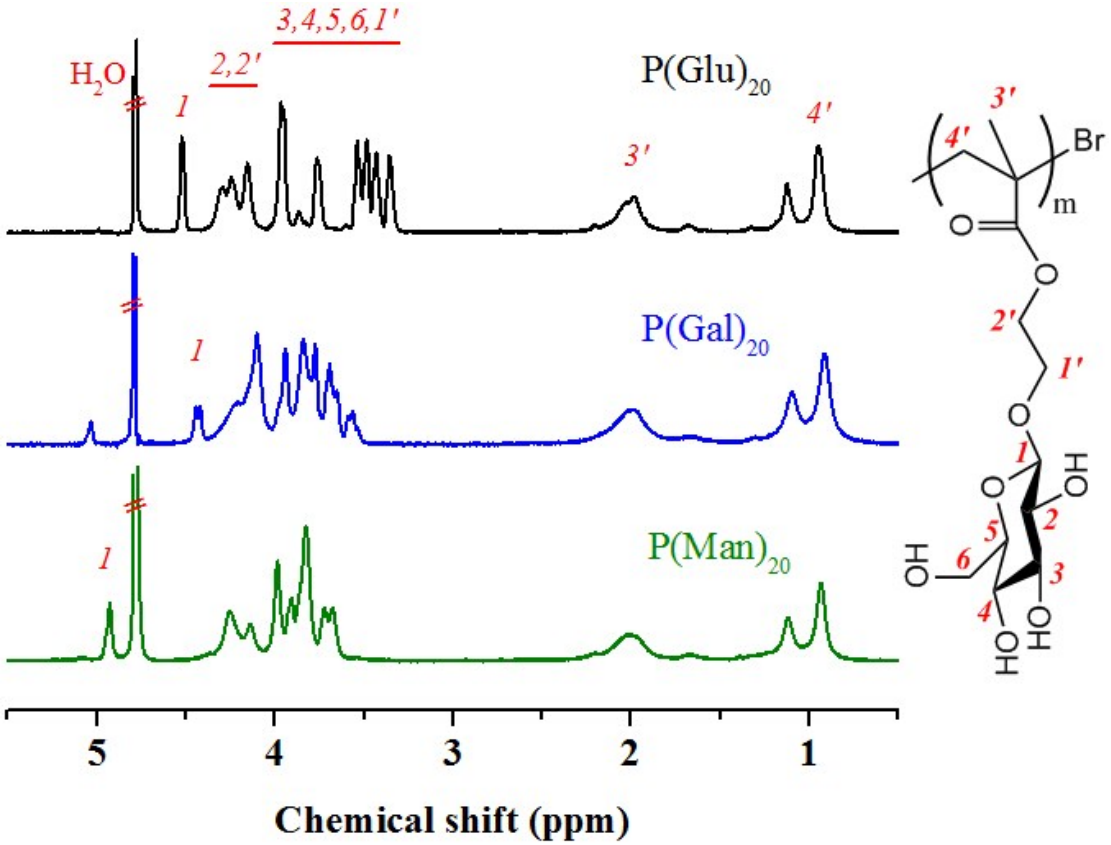


Figure S6. ^{1}H NMR spectra of the P(ManEMA)$_{20}$, P(GluEMA)$_{20}$, and P(GalEMA)$_{20}$ polymers in D_2O.

3. Synthesis of the peptide NCA monomer

***N*ε-carbobenzoxy-L-lysine *N*-carboxyanhydride (CbzLys-NCA).**[4] Briefly, 5 g (18 mmol) of *N*ε-carbobenzoxy-L-lysine (CbzLys) was suspended in 80 mL of anhydrous tetrahydrofuran (THF) and heated to 50 °C. A solution containing 2.4 g (8 mmol) of triphosgene in 20 mL of anhydrous THF was added to the CbzLys suspension under vigorous stirring. The reaction was allowed to proceed at 50 °C in a sealed flask until the solution became clear. The solution was cooled down to room temperature and precipitated into 400 mL of anhydrous hexane. The precipitate was washed thrice with 80 mL of anhydrous pentane and dried under reduced pressure to obtain CbzLys-NCA (white solid, yield 80%).

4. Characterization of the polypeptide and the Janus four-arm glycopolymer-polypeptide conjugates

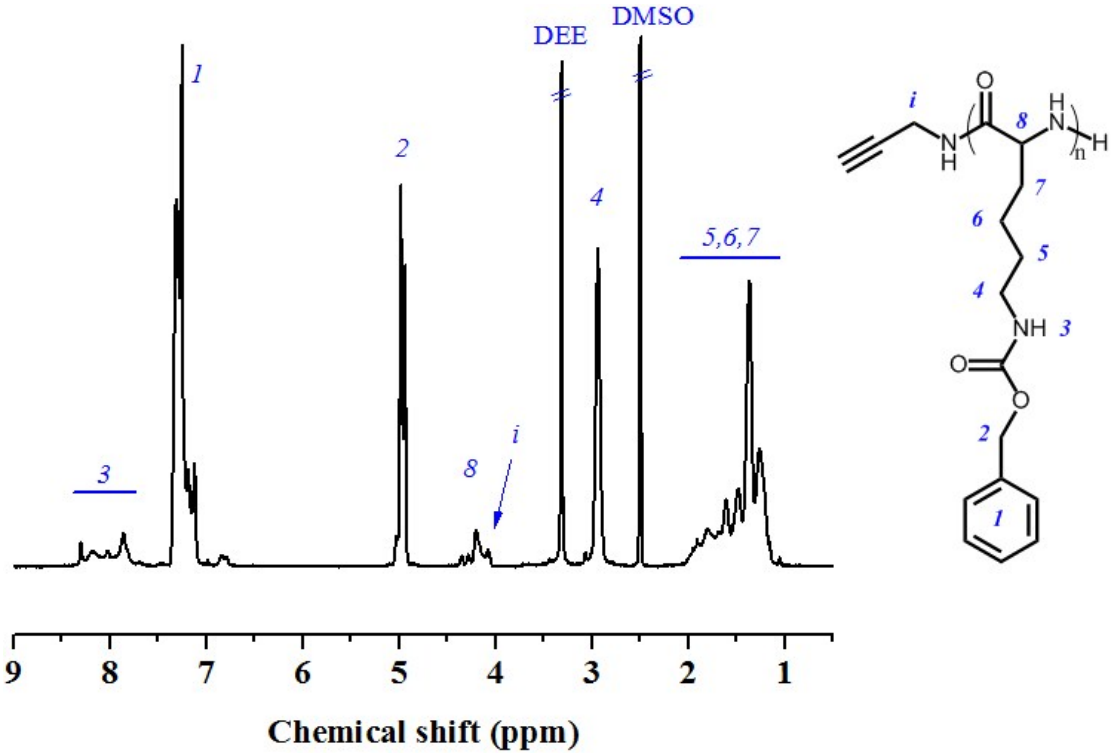


Figure S7. ^{1}H NMR spectrum of the CbzLys polymer (P(CbzLys)) in DMSO-d_6.

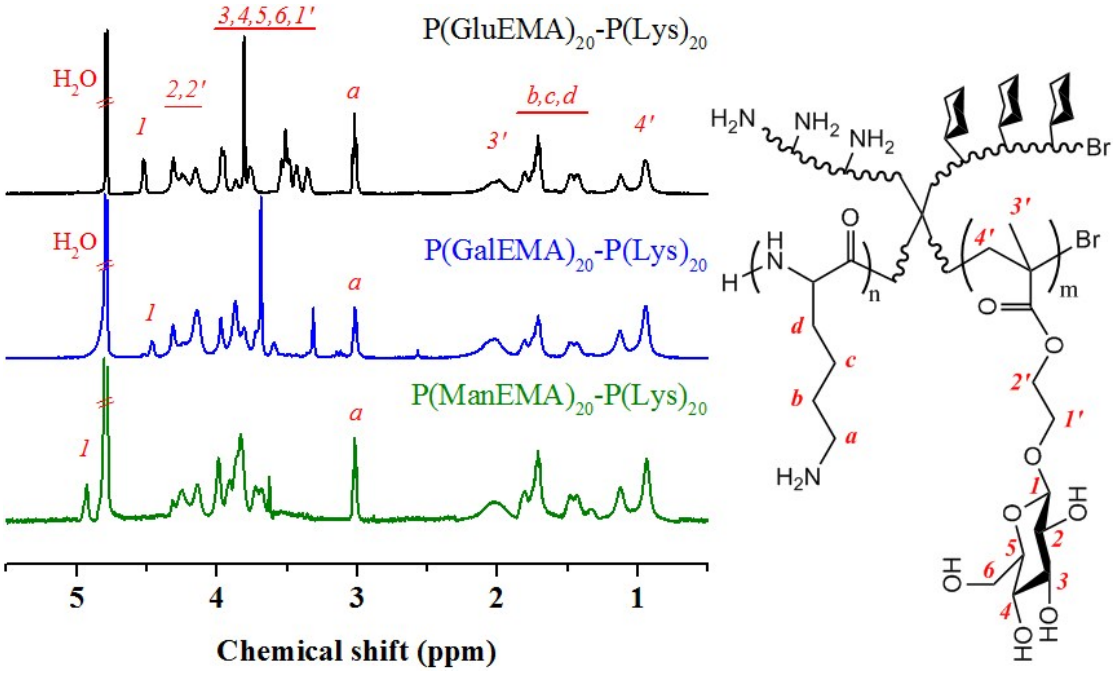


Figure S8. ^{1}H NMR spectra of the P(ManEMA)$_{20}$-P(Lys), P(GluEMA)$_{20}$-P(Lys), and P(GalEMA)$_{20}$-P(Lys) conjugates in D_2O.

References

1. Y. Shi, R. W. Graff, X. Cao, X. Wang and H. Gao, *Angew. Chem. Int. Ed.*, 2015, **54**, 7631-7635.
2. S. Zhang and Y. Zhao, *Macromolecules*, 2010, **43**, 4020-4022.
3. S. G. Spain, L. Albertin and N. R. Cameron, *Chem. Commun.*, 2006, 4198-4200.
4. C. Zhou, X. Qi, P. Li, W. N. Chen, L. Mouad, M. W. Chang, S. S. J. Leong and M. B. Chan-Park, *Biomacromolecules*, 2010, **11**, 60-67.