

Sweet and sticky: Synthetic mucins by NCA polymerization

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Mucins are glycoproteins that collectively form mucus gels on the surface of epithelial tissues and comprise the nanoscale glycocalyx on cell-surfaces. Despite essential roles in life, mucins are challenging to study and obtain in pure form due to heterogeneity in chain length, sequence, and glycosylation pattern. Glycopolymers have emerged as

useful tools to probe mucin biology. Glycosylated polypeptides are particularly attractive polymers since they can display glycans in their native form, naturally form complex secondary structures that drive self-assembly, and are biodegradable.

Here, we have produced a panel of carbohydrate functionalized mucin-like polypeptides via polymerization of N-carboxyanhydrides.¹ Molecular weight and glycan density can be controlled by polymerization reaction stoichiometry to give glycopolypeptides of biologically-relevant length and composition.² The glycopolypeptides are dual end-functionalized with chemical handles that allow conjugation to biological targets and probes. We examined the effect of glycosylation on mucin polymer physical properties such as secondary structure and persistence length. Glycosylation density, and glycan linkage stereochemistry, was found to have dramatic effects on these properties. We were able to efficiently display these synthetic mucins on live cell surfaces by conjugation to an engineered membrane protein, thus precisely engineering the glycocalyx. Overall, these synthetic mucins have broad applications in the study of epithelial cell biology and as lubricating and hydrating biomedical materials.

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References

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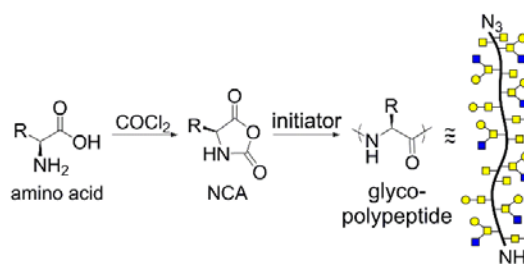


Figure 1. Synthesis of dual end-functional chemically tunable mucin glycopolypeptides by N-carboxyanhydride polymerization.