

Glycoprotein mimetic materials - synthetic methods and study of viral inhibition properties

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The human body houses some of the most unique materials on the planet and is a promising source of bioinspiration. The high molecular weight and glycosylation of mucin-type glycopeptides make them challenging to produce or even mimic. This material production challenge is one of the key limiting factors for the study and design of biological materials such as mucus and cartilage.

The first section of this thesis develops two approaches for creating high molecular weight heavily modified protein brushes. The first uses a combination of cysteine and diazo coupling reactions, while the second uses combination of global amino acid substitution and copper(I)-catalyzed alkyne-azide cycloaddition (CuAAC). The tyrosine enrichment required to prepare elastin-like-polypeptides (ELP) proteins for diazo coupling reactions prevented protein expression at 96 pentapeptide repeats and above, but maintained yields comparable to other work at 48 repeats and below. Homopropargylglycine (HPG) incorporation through global amino acid substitution in a 50 pentapeptide repeat ELP backbone was found to achieve an average methionine replacement of 93%. Tyrosine was demonstrated as an attractive target for mass bioconjugation for protein because of the high specificity and efficiency of diazonium coupling reaction. The technique was performed in reducing and denaturing conditions as well as shown to couple chemical functionalities in sufficient quantities to affect the protein solubility as well as orthogonal to cysteine coupling. Sensitive chemical groups such as saccharides were conjugated to the protein through CuAAC. The structure-reactivity relationship for functionalizing the ELP backbone with CuAAC was further studied using the HPG substituted ELPs with a series of protected and deprotected mono-, di-, and tri-saccharides.

The second part of this thesis utilizes both the protein backbone-based mimics developed in the first part and a synthetic polymer-based mucin mimic to investigate the antiviral properties of sialic acid functionalized glycoprotein mimics. The potential of using these adhesion-decoy based polymers as countermeasures against viruses was explored and aerosol formulations of these polymer countermeasures were developed as a delivery method to address respiratory system infections. These formulations balanced the mist suppression properties of polymers with reasonable polymer loadings.

This thesis developed synthetic toolboxes to create glycoprotein-mimetic materials and utilize the mucin mimics to create a deeper understanding of mucin's viral inhibition properties. The tools developed to create protein-backbone based glycoprotein-mimetic materials allow for the creation of materials that both allow for the study of structure-property relationships of complex biological molecules, but also the design of materials with tailorable bioactivity.

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