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SYNTHESIS AND CHARACTERIZATION OF CLICKABLE POLY-PROLINE BASED MATERIALS

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Mucus, collagen, and proteoglycans serve crucial roles in the human body, yet current research on these structures is largely limited. Mucus is the interface and first line of defense to the world around us. Mucus serves a variety of purposes, including lubricating and hydrating epithelial surfaces, housing the microbiome, and diffusion of drugs and nutrients while trapping pathogens by acting as a selectively permeable membrane. Mucus is a hydrogel made primarily of water and ions and is 5-9 weight percent glycoproteins, known as mucins. These mucins are characterized by high molecular weight repeat domains rich in proline and O-glycosylated serine and threonine (PTS Domain). Proline, an amino acid that contributes to the rigidity of mucins and an important component in the formation of hydrogels, possesses unique properties in mucus, collagen, and proteoglycans. Despite polyproline-based materials having additional applications including surface coatings, hydrogels, antithrombotics, as ordered materials, and in probing protein structure, current mucin research is limited to reconstituted farm-animal derived mucins and synthetic structures that are either of low molecular weight or are comprised of unnatural backbones, non-native glycans, or non-native glycan linkages. These reconstituted mucins are often from intestinal scrapings of farm animals, which vary largely from samples in both structure and chemistry due to inherent heterogeneity in mucins as they differ between species, tissues, and pathologies. In response, we have synthesized the building blocks of proline-based mucin, collagen, and proteoglycan mimics leading towards a tool that will allow for modeling of mucins and mucus, structure-function relationships, related diseases, and novel

lubricating therapeutics. Through N-Carboxyanhydride polymerization, we have synthesized three proline analog based polypeptide materials: hydroxy-proline, azido-proline and azido-ethoxy proline. Creating these analogs supports the exploration of simpler materials to create a synthetic PTS Domain and capture hydrophilic PPII structure. We characterized each proline analog through nuclear magnetic resonance, infrared spectroscopy, thin layer chromatography, and circular dichroism. Through circular dichroism we characterized the secondary structure of the proline analogs confirming the transition in confirmation for conversion from PPI to PPII helices. These findings will be advantageous in next steps exploring click reactions of these proline analogs with sugars in exploring structure-function relationships, the contributions of individual amino acid residues, and sugar and glycan patterns.