**Regioselective synthesis of polysaccharide–amino acid ester conjugates**

Yang Zhou1, Kevin J. Edgar1,2\*

*1 Department of Sustainable Biomaterials, Virginia Tech, Blacksburg, VA 24061, United States*

*2 Macromolecules Innovation Institute, Virginia Tech, Blacksburg, VA 24061, United States*

Site-specific conjugation of polysaccharides with proteins is very challenging. Creating the ability to control chemo- and regioselective reaction between polysaccharides and amino acid derivatives can not only create potentially useful and bioactive natural polymer constructs, but should also provide useful guidance for the principles of polysaccharide**–**protein conjugate synthesis. In this work, we exploited regioselective bromination of the non-reducing end primary dextran hydroxyl using *N*-bromosuccinimide (NBS) and triphenylphosphine (Ph3P) in the dimethylacetamide (DMAc) and lithium bromide solvent system, thereby enabling a regio- and chemoselective synthetic strategic approach to a variety of polysaccharide-amino acid ester adducts. We demonstrated selective condensation of the α- amino groups of esters of the amino acids tyrosine and proline, displacing the single, terminal C6 bromides of 6-BrCA320S and 6-BrDextran with high conversion (71-96%). Histidine ester side group amines were found to react with 6-BrCA320S, while those of tryptophan ester did not. These results provide useful access to polysaccharide**–**amino acid ester adducts of various architectures, and guide us in designing new pathways to polysaccharide**–**protein copolymers.

