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***In situ* Extension as a Protocol for Identifying Novel Alpha-Amylase Inhibitors.** G.D. Brayer, C. Li, A. Begum, S.G. Withers, Dept. of Biochemistry and Molecular Biology, and Chemistry, Univ. of British Columbia, Vancouver, British Columbia, Canada.

Human pancreatic alpha-amylase (HPA) is responsible for cleaving large malto-oligosaccharides, such as starch, to maltose and cross-linked junction points. Post-prandial blood glucose levels are correlated to this digestive process and therefore alpha-amylase inhibitors have the potential to be therapeutic agents in the treatment of diabetes and obesity. Despite considerable interest, it has proven difficult to develop inhibitors for HPA that are both specific and of high affinity. Recently we have designed and refined a new high-throughput approach for the discovery and subsequent structural elucidation of oligosaccharide-based inhibitors for HPA, based upon auto-glycosylation. This approach has demonstrated the ability to transform poor HPA inhibitors into significantly improved inhibitors with enhanced specificity and binding affinity profiles. Application of our multi-step high-throughput screening approach has identified a number of new classes of potential HPA inhibitors. Supported by the Canadian Institutes of Health Research.