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Towards the Synthesis of an Acetyl Free TF Antigen

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Abstract

In the past two decades the central role of carbohydrates in biology has become more widely acknowledged. Many biological processes including bacterial and viral infections (notably HIV and the flu), immunogenic responses, and cancer pathogenesis/metastasis are mediated by carbohydrate interactions. Treatment and understanding of these conditions can be probed by using carbohydrate vaccines, enzyme inhibitors and anti-tumour compounds. However, a key drawback to all of these compounds is the inherent low in vivo half-lives of carbohydrate containing materials. The TF antigen is particularly interesting as it shows up in a large number of different cancer cells including stomach, pancreas, lung, and breast, while it is never found in healthy cells. If the immune system could be trained to target this molecule, then the immune system could be used to help cure cancer.

As a result, great synthetic effort is carried out to prepare complicated polysaccharides that are rapidly metabolized by the body before they can fully fulfill their therapeutic roles. This Trant Team project aims to remove the unstable acetal functionality in carbohydrates by replacing the exocyclic anomeric oxygen with a methylene (C-glycoside) to make new acetal-free *C*-glycoside analogues of the TF antigen for biological evaluation. Removing the labile functionality should result in greatly enhanced lifetime, and bioavailability relative to the native system with no loss of activity as the exocyclic oxygen is not involved in the vast majority of molecular recognition events. These molecules are being made by total synthesis for their incorporation into new anti-cancer vaccines.