Progress Towards the Synthesis of Acetal-Free TF Antigens Anti-Cancer Vaccine Candidate

Emma J. Flynn
Univeristy of Windsor, flynn116@uwindsor.ca

Title: progress towards the synthesis of acetal-free TF antigens anti-cancer vaccine candidate, TACA disaccharides containing no labile glycosidic linkages

Abstract

Many biological processes including bacterial and viral infections (notably HIV and the flu), immunogenic responses, and cancer pathogenesis/metastasis are mediated by carbohydrate interactions. Epithelial carcinomas continue to be a leading cause of death in all over the world and include some of the very high fatality cancers such as stomach, pancreas, lung, and breast. These cancer cells express unique carbohydrate signatures on their surface, tumor associated carbohydrate antigens (TACAs) that are not found on healthy non-foetal tissue. Treatment and understanding of these conditions can be probed by using carbohydrate vaccines, enzyme inhibitors and anti-tumor compounds. If the immune system could be trained to target this molecule, then the immune system could be used to help cure cancer. Unfortunately, carbohydrates are notoriously difficult immunotherapeutic targets, and no such treatments exist to date. This is partially because glycoconjugates are enzymatically-sensitive, and this has limited their therapeutic utility. This project aims to remove the unstable acetal functionality in carbohydrates by replacing the exocyclic anomeric oxygen with a methylene (C-glycoside) to make the first fully-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 likely loss in recognition specificity as the exocyclic oxygen is not generally involved in molecular recognition events. This presentation will discuss the importance of acetal-free carbohydrates, and our significant progress towards the synthesis of these promising but challenging molecules.

Authors: Emma Flynn; Seyed Iraj Sadraei; Advait Desai; Greg Yousif; Abdul Aljoudi; John F. Trant;