

C-disaccharide glycopeptides as potential anti-cancer vaccines

Pierre Vogel

Swiss Federal Institute of Technology Lausanne, Switzerland

Abstract

Cancer-associated mucin glycoprotein MUC1 is characterized by the presence of altered carbohydrates such as Tn (α -N-acetylgalactosamine), sTn (sialyl-1-6-Tn) and the Thomsen-Friedenreich (TF: β -D-Galp-1-3- α -D-GalNAcp) antigen (tumor associated carbohydrate antigens: TACAs) that are conjugated to proteins via O- α -galactosylation of serine or/threonine. Patients immunized with synthetic TF conjugated with KLH (keyhole limpet hemocyanin) + QS21 adjuvant can generate IgM and IgG antibodies.¹ Because the disaccharide TF is hydrolyzed rapidly in the body, strong immune response requires longer lived disaccharides. Fluorinated TACAs have been proposed which elicit IgG antibodies found to cross-react with native TF epitopes.^{2,3} We have found that the C-linked disaccharide analogue 1 (constructed applying Danishesky's method for the conjugation with KLH 4) + QS21 adjuvant induces a strong immune response in mice. Interestingly, much weaker immune response was observed with a stereoisomeric antigen constructed with the α -C-galactoside analogue of TF disaccharide (α -D-Galp-1-CH₂-3- α -D-GalNAc-O-Ser).⁵ Several strategies and methods have been developed for the synthesis of C-linked disaccharides including disaccharide mimetics incorporating iminosugars C-linked to sugars and sugar mimetics such as conduritols and cyclitols. The latter work was motivated by the search for specific glycosidase and glycosyltransferase inhibitors that are potential drugs against cancers and other diseases.

Received date : July 14,2022 Accepted Date: July 21,2022 Published Date : July 28 ,2022

Biography

Born in Cully, VD, Switzerland, on October 23, 1944, Pierre Vogel attended elementary school in Grandvaux, then secondary school in Lausanne. In 1966 he graduated from the EPUL (Ecole Polytechnique de l'Université de Lausanne) as a chemical engineer, with the A3E2PL prize. In 1969 he obtained a PhD from the University of Lausanne with a thesis in organic photochemistry under the supervision of Prof. Horst Prinzbach, University Prize. A grant from the Basel industry allowed him to join the

group of Prof. Martin Saunders at Yale University (New Haven, USA) for a year of post-doctoral work. He was then hired by Yale University to collaborate with Prof. Jerome A. Berson, Prof. Kenneth Wiberg (Yale) and Prof. Paul v. R. Schleyer (Princeton) in the field of nuclear magnetic resonance of carbocations, which allowed him to establish, among other things, the mechanisms of reactions involved in petrochemistry.