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SUGAR MIMETICS TOWARD AN ANTI-CANCER THERAPEUTIC VACCINE

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Cancer-associated mucin glycoprotein MUC1 is characterized by the presence of altered carbohydrates such as Tn (-N-acetylgalactosamine), sTn (sialyl-1-6-Tn) and the Thomsen-Friedenreich (TF: -D-Galp-1-3 -D-GalNAcp) antigen (tumor associated carbohydrate antigens: TACAs) that are conjugated to proteins via O- -galactosylation of serine or/and 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 -C-galactoside analogue of TF disaccharide (-D-Galp-1-CH₂-3- -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.

Biography

P. Vogel was born in Cully (Switzerland) Oct. 23, 1944. In 1969, he did his Ph.D under supervision of Prof. H. Prinzbach at the Institute of Organic Chemistry, University of Lausanne. He spent two years at Yale University, New Haven, Connecticut, USA with Prof. Martin Saunders, Prof. J. A. Berson, K. A. Wiberg and P.v.R. Schleyer (Princeton University). He worked then as a Research chemist at Syntex S.A., in Mexico with Prof. P. Crabbé before the return to the University of Lausanne in 1973. As of 1977 he became Professor of organic chemistry at the University of Lausanne. In 1991 he was Vice-Chairman of the Institute of organic Chemistry, University of Lausanne until 2001. He was also part-time grad.school teacher at the Universities of Rouen and Caen from 1991 to 1993 and Part-time professor at Ecole Polytechnique de Palaiseau from 1993-2000. Since 2001 he is Professor of organic chemistry at the EPFL.

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