Synthesis of Glycoconjugate Vaccines on Clustered Modes against Candida Albicans Using the Novel Methodology

Xiangyang Wu, Tomasz Lipinski, J. James Bailey, Frédéric Carrel and David R. Bundle*
Department of Chemistry, University of Alberta, Edmonton, Alberta, Canada T6G 2G2

Introduction

The cell wall phosphomannan of Candida species is a glycoprotein containing predominantly α-linked mannose residues. A minor β-mannan component constitutes the protective epitope of the glycoprotein and occurs in different forms linked to the α-mannan backbone via a phosphodiester bond (acid labile β-mannan) or directly via a glycosidic bond.1 Protective monovalent antibodies that recognize the (1→2)-β-mannan disaccharide or trisaccharide sequences are highly effective immunogens in rabbits, the same antigen is less effective in mice. In a search for a better method to present the Candida epitope to mice we have investigated clustering of oligosaccharide motifs. We report the synthesis of (1→2)-β-mannan disaccharides clustered on a glucose core, the conjugation of these clustered epitopes with proteins and preliminary immunization data.

Synthesis of Building block 7

Glucosyl trichloroacetimidate donor was employed to establish a β-glucopyranosyl linkage. Subsequent Swern oxidation and selective reduction facilitated an efficient approach to the β-mannopyranoses which was transformed to compound 7 by Birch reaction and photochemical addition of thioacetic acid.

Conjugation Chemistry

Cluster 11 containing the (1→2)-β-D-mannopyranan epitope of the Candida albicans cell wall has been synthesized and coupled to BSA or tetanus toxoid via a homobifunctional adipate linker. In Balb/c mice the glycoconjugate 12 gave an antibody response similar to those obtained with simple trisaccharide tetanus toxoid conjugates. Similar vaccination experiments are being pursued in outbred mice.

Summary

Cluster 11 was synthesized from the (1→2)-β-D-mannopyranan epitope of the Candida albicans cell wall and coupled to BSA or tetanus toxoid via a homobifunctional adipate linker. In Balb/c mice the glycoconjugate 12 gave an antibody response similar to those obtained with simple trisaccharide tetanus toxoid conjugates. Similar vaccination experiments are being pursued in outbred mice.

References
3. Xiangyang Wu, Tomasz Lipinski and David R. Bundle*. Unpublished result.

Acknowledgements

Financial support for this work was provided by research grants from the Alberta Ingenuity Centre for Carbohydrate Science and the Canadian Institutes of Health Research (CIHR).