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Disaccharide mimics as drugs against cancer and epitopes for anti-cancer vaccine candidates

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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/and threonine. Patients immunized with synthetic TF conjugated with KLH (keyhole limpet hemocyanin) + QS21 adjuvant can generate IgM and IgG antibodies. 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. We have found that a C-linked disaccharide analogue constructed from β-D-Galp-1-CH2-3-α-D-GalNAcp (applying Danishesky's method for the conjugation with KLH+QS21 adjuvant induces a strong immune response in mice. Interestingly, much weaker immune response was observed with a stereoisomeric antigen constructed from the α-C-galactoside analogue of TF disaccharide (α-D-Galp-1-CH2-3-α-D-GalNAc-O-Ser. Several strategies and methods have been developed for the synthesis of C-linked disaccharides including disaccharide mimics incorporating iminosugars C-linked to sugars and sugar mimics 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.

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Development of a monoclonal antibody based indirect competitive enzyme-linked immunosorbent assay for nitroimidazoles in edible animal tissues and feeds

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Nitroimidazoles (NDZs) are a well-known group of antiprotozoal and bactericidal agents in medicine and veterinary medicine. They are also used for the growth promotion and improvement of feed efficiency in the livestock industry. However, the misuse of nitroimidazoles (NDZs) can lead to NDZs residues in edible animal tissues, which would be harmful to consumer health. To quickly monitor NDZs residues in edible animal tissues and feed, a monoclonal antibody-based indirect competitive enzyme-linked immunosorbent assay (IC-ELISA) with a simple sample preparation method and clean-up was developed in the present study. At first, a broad-specificity monoclonal antibody, 1D5, against NDZs has been produced, which the IC50 values of the NDZs, dimetridazole, ipronidazole, ronidazole hydroxydimetridazole and hydroxyipronidazole were 4.79 μg L-1, 0.47 μg L-1, 5.97 μg L-1, 23.48 μg L-1 and 15.03 μg L-1, respectively. The limit of detection of the method for the NDZ matrix calibration ranged from 4.2-50.3 μg kg-1 in the feed matrices and from 0.11-4.11 μg kg-1 in the edible animal tissues matrices. The recoveries of the NDZs were in the range of 75.5-111.8%. The CVs were less than 14.4%. A good correlation (r=0.9905) between the ELISA and HPLC-MS results of the tissues demonstrated the reliability of the developed IC-ELISA. In a word, this simple method reduced the time required for sample preparation, ensured greater throughput and met the requirements for nitroimidazoles residues analyses. It can be used as a useful tool for screening of NDZs in animal edible tissue and feed.

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