Carbohydrates as Vaccine Candidates

[Identification of Immunogenic Sugar Moieties of Anthrax Spores (B. Anthracis)]

Description of Technology:

This technology relates to the first identification of the highly specific immunogenic sugar moieties of B. anthracis spores. Since these carbohydrate structures are displayed on the outermost surfaces of anthrax spores and are highly specific for B. anthracis, they are novel immunological targets for pathogen identification, diagnosis and vaccine development against anthrax infection.

Gram negative pathogenic bacteria get both their virulence factors and protective antigens from their surface carbohydrates. Antibodies to these pathogens work by recognizing these sugars on the bacteria's surface. While it is possible to raise antibodies to polysaccharides, the immune response is weak because sugars are poor immunogens. Chemically linking carbohydrates to proteins makes them into stronger antigens, widens the spectrum of antibodies and gives rise to greatly increased antibody titers. When this is done with carbohydrates characteristic of different pathogens, both antigens to and means of detecting the pathogens to which the carbohydrates belong are created. This technology is generally applicable to all gram negative pathogens. It has been demonstrated for anthrax and cholerae.

Applications:

- Creation of antibodies to gram negative pathogenic bacteria
- Detection of gram negative pathogenic bacteria
- Development of diagnostic tools for presence of anthrax spores or infections by Bacillus anthracis
- Development of vaccines

Advantages:

The identification of the specific immunogenic sugar moieties of B. anthracis provides an opportunity to develop vaccine candidates which can be substituted for traditional vaccines that are often pyrogenic or have other undesirable effects.

Development Status:

- The di-, tri-, tetra- and higher oligosaccharides characteristic of the coats of several pathogenic bacteria, such as V. cholerae and B. anthracis, have been synthesized.
- These oligosaccharides have been linked to proteins, such as bovine serum albumin and recombinant anthrax protective antigen.

Inventors:

Dr. Paul Kovac (NIDDK) et.al.

Publications:

1. Saksena, R., Adamo, R., Kováč, P., Immunogens related to the synthetic tetrasaccharide side chain of the *Bacillus anthracis* exosporium, *Bioorg. Med. Chem*. (2007), doi:10.1016/j.bmc.2007.03.057.

2. Wang, D., Carroll, G.T., Turro, N.J., Koberstein, J.T., Kovac, P., Saksena, R., Adamo, R., Herzenberg, L.A., Herzenberg, L.A., Steinman, L. Photogenerated glycan arrays identify immunogenic sugar moieties of Bacillus anthracis exosporium. Proteomics. 2007 Jan;7(2):180-4. [Pubmed reference]

Patent Status:

DHHS Reference No. E-153-2006, a provisional patent application has been filed

Licensing Status:

Available for exclusive or non-exclusive licensing

Licensing Contact:

Dr. Peter Soukas, 301-435-4646, soukasp@od.nih.gov

Collaborative Research Opportunity:

The National Institute of Diabetes and Digestive and Kidney Diseases, Laboratory of Medicinal Chemistry is seeking parties interested in collaborative research to further develop, evaluate, or commercialize conjugate vaccines from synthetic carbohydrates. Please contact Rochelle S. Blaustein at 301-451-3636, Rochelle.Blaustein@nih.gov for more information.

Research Focus and Selected Publications for Principal Investigator –
Paul Kovac, Ph.D, Laboratory of Medicinal Chemistry

The primary focus of Dr. Kovac's laboratory is to further the development of conjugate vaccines from synthetic carbohydrate antigens. Ultimately, he would like to develop reliable protocols for the preparation of neoglycoconjugates which could become substitutes for traditional cellular antigen-based vaccines: Such vaccines are often pyrogenic or have other undesirable effects. Synthetic oligosaccharides that mimic the structure of polysaccharides present on surface of bacterial pathogens are used as antigens of immunogens. Since there is virtually an infinite number of choices of architectonic details a synthetic neoglycoconjugate can incorporate, part of his research involves studying the effects of variables such as size of the carbohydrate antigen, type of linker, linking chemistry, type of carrier, etc., on immunogenicity and protective capacity. In addition to obtaining potent immunogens, it is expected that the studies will result in findings of general utility in synthetic vaccine preparation.

1. Provenzano, D., Kováč P., Wade, W. F., The ABCs (Antibody, B Cells, and Carbohydrate Epitopes) of Cholera Immunity: Considerations for an Improved Vaccine, *Microbiol. Immunol*., **50** (2006) 899–927.

2. Taylor, R. K., Kirn, T. J., Bose, N., Stonehouse, E., Tripathi, S. A., Kováč, P., Wade, W. F., Progress towards development of a cholera subunit vaccine, *Chemistry & Biodiversity*, **1** (2004) 2036-2057.

3. Chernyak, A., Kondo, S., Wade, T., Meeks, M., Alzari, P. M., Fournier, J,-M., Taylor, R. K., Kováč, P., Wade, W. F., Induction of protective immunity by synthetic *Vibrio Cholerae* Hexasaccharide derived from *Vibrio cholerae* O:1 Ogawa lipopolysaccharide bound to a protein carrier, *J. Inf. Dis.*, **185** (2002) 950-962.

4. Saksena, R., Zhang, J., Kovác, P. Immunogens from a synthetic hexasaccharide fragment of the O-SP of Vibrio cholerae O:1, serotype Ogawa *Tetrahedron Asymmetry*(16): 187-197, 2005. [Pubmed reference]

5. Ruttens, B., Kovác, P., A facile synthesis of armed and disarmed colitose thioglycosides *Synthesis*: 2005-2008, 2004.

6. Taylor, R. K., Kirn, T. J., Bose, N., Stonehouse, E., Tripathi, S. A., Kovác, P., Wade, W. F. Progress towards development of a cholera subunit vaccine *Chemistry & Biodiversity*(1): 2036-2057, 2004. [Pubmed reference]