VATUB

Study of new carbohydrate-based vaccines against tuberculosis

Main partners involved

Coordinator: Drug Science department; University of Pavia; responsible:

prof. Marco Terreni.

Collaborations:
1) Drug Science department; University of Milano; responsible:

prof. Paola Conti

2) Infective disease department; "IRCCS-Policlinico San Matteo" of Pavia; responsible:

prof. Gaetano Felice

3) Department of Biomedicine and Prevention; university of Rome Tor Vergata; Responsible:

Dr. Massimo Amicosante

4) Department of Molecular Chemistry; University of Pierre et Marie Curie Sorbonne (UPCM); Paris VI (France). Responsible:

Dr. Yongminn Zhang

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Goals

The main task of the study is the synthesis, characterization and biological evaluation of glyco-conjugates as potential vaccines against tuberculosis, rationally designed on the basis of defined antigens, suitable to stimulate both an adequate antigenic and antibody and cell-mediated response.

New vaccine will be designed combining recombinant antigenic protein from *Mycobacterium tuberculosis* (MTB), rationally designed in order to avoid the depression of the immune response after glycosylation, with immunogenic oligosaccharides chemically related to the lipoarabinomannan (LAM), the main sugar antigen of the MTB.

The second goal is the preparation of polymeric nanoparticles loaded with oligosaccharides or glycoproteins as adjuvants to enhance the immunogenicity of vaccines.

All products prepared will be tested by ex-vivo and in-vivo immunological assays.

Research phases

1) **Chemoenzymatic synthesis and production of antigenic oligosaccharides and glycoproteins**

The research activity will be devoted to the study and development of efficient strategies for the synthesis of complex oligosaccharides correlated to the structure of LAM by an integrated approach between chemistry and biotechnology. The prepared oligosaccharides will be conjugated with antigenic proteins obtained by site directed mutagenesis designed in order to address the glycosylation

towards sites not included in the epitopic sequences of the protein.

2) **Characterizations of oligosaccharides and glycoproteins**

All the experimental activities will be constantly supported by analytical studies aimed to a rapid and complete characterization of the prepared glyco-conjugates.

3) **Biological evaluation of the oligosaccharides and glycoproteins**

Set up of immunogenic assays of based on *in vitro* techniques (ELISA) in order to compare the antigenic properties of the oligosaccharides and glycoproteins prepared. Set up of assays e*x vivo* of the most promising glycoproteins by ELISA, for evaluation of antibody response using antibodies obtained from patients infected.

Achievements

Recombinant AG85B and TB10.4 have been produced and the epitopes of these MTB protein characterized Mutant proteins have been designed and prepared in order to avoid glycosylation of the epitopes.