TRANSFERRIN-BINDING PROTEINS AS CANDIDATES FOR A BROADLY CROSS-REACTIVE VACCINE AGAINST SEROGROUP B MENINGOCOCCAL DISEASE

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Introduction

Meningococcal disease caused by serogroup S meningococci remains an important health problem in many parts of the world. Because group B polysaccharide is poorly immunogenic in humans, several vaccine approaches bases on non-capsular antigens are being developed; transferrin-binding proteins (Tbp) have been proposed as a candidate antigen. Tbps have several attributes of good vaccine candidates: (i) they are surface-exposed molecules (1); (ii) they are expressed *in vivo* during infection (2, 3); (iii) they elicit protective and bactericidal antibodies in laboratory animals (4, 5); and (iv) as of today, no one has reported the occurence of natural mutants lacking Tbps. Among the two subunits, the lipoprotein TbpB has shown to induce more bactericidal antibodies than TbpA and has further been investigated. TbpS is produced as a recombinant protein, the gene encoding TbpB (67 kDa) has been cloned and sequenced (6) and recombinant lipidated TbpB is produced in *E. coli* using the arabinose-inducible expression vector (7). Recombinant TbpB from both strains B16B6 (67 kDa) and M982 (88 kDa) were purified from the membranes of *E. coli* and the purified protein retained its ability to bind human transferrin. Mice were immunized with various doses of the two recombinant TbpB on days 0, 21 and 35 and bled at regular intervals after immunization. The animals developed high IgG titers and bactericidal antibodies against both strains. To address the key question of broad cross-reactivity among different isolates, representative strains of serogroup S *N. meningitidis* were collected based on their different multilocus genotypes (8); the ability of polyclonal rabbit antisera raised to recombinant TbpB to kill meningococci in the presence of complement was evaluated. Full length recombinant TbpB from strain M982 elicited the most cross-reactive antisera which reacted with 98 % of the strains tested in a dot blot assay and killed 80 % of the strains in a bactericidal assay (9). Because antisera raised to the full length TbpB were more reactive than antisera specific of the N-terminal half defined as the minimal transferrin-binding domain, the relative role of antibodies specific of the N and C-terminal domains of TbpB were investigated; the results showed that the C-terminal half contributed both to transferrin- binding and to the induction of bactericidal antibodies (10).

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