TITLE: DISTRIBUTION OF 4CMENB VACCINE ANTIGENS AMONG BRAZILIAN MENINGOCOCCAL ISOLATES

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ABSTRACT:

Neisseria meningitidis (Nm), which colonizes the human upper respiratory tract, is the etiologic agent of Meningococcal Disease (DM). Nm is classified into 12 serogroups based on the antigenic variation of the capsular polysaccharide, of which six serogroups (A, B, C, W-135, X and Y) are responsible for most DM worldwide. In recent years, studies aimed at the development of a non-polysaccharide vaccine to cover these 6 serogroups mainly due to serogroup B, which polysaccharide shows similarity with structures of human neural cells. With the aid of reverse vaccinology, three potentially immunogenic proteins were selected for the establishment of a vaccine against serogroup B meningococcus. After a series of studies, the 4CMenB vaccine (Bexsero, GSK Vaccines), composed of factor H binding protein (fHbp), Neisseria adhesin A (NadA) and Neisseria heparin-binding antigen (NHBA) antigens was formulated including the outer membrane vesicle of strain NZ98/254 used in a vaccine against an outbreak in New Zealand, containing PorA P1.4. The objective of the present study is to analyze the genetic variability of *nadA*, *fHbp*, *NHBA* and *porA* genes in Nm samples isolated from Brazilian states from 2010 to 2015, comparing with the variants present in 4CMenB vaccine. Gene amplification was performed using the primers described in the PubMLST database. Sequencing was performed on the PDTIS/FIOCRUZ Sequencing Platform, on the ABI PRISM3730 automatic sequencer. The sequences were submitted to the Neisseria Sequence Typing Home Page (http://pubmlst.org/neisseria/) for the definition of the variable regions. A total of 140 isolates of DM cases from four Brazilian states were included: Pernambuco (76.4%), Rio de Janeiro (21.4%), São Paulo (1.4%) and Pará (0.7%) belonging to serogroups B (25%), C (67%), W-135 (5%) and undetermined (3%). From the 35 (25%) samples analyzed to date, the following variants were observed: alleles 1 and 2 of fHbp, allele 1 of nadA, alleles 4, 7, 13, 15, 22, 32, 68, 85, 87, alleles 144 and 334 of NHBA, alleles 7, 18, 19 and 22 of PorA variable region 1 and alleles 1, 14, 15 and 34 of PorA variable region 2. The results obtained so far suggest that among the 4CMenB vaccine antigens only the fHbp protein variant is present in the strains studied.

Keywords: Neisseria meningitidis; 4CMenB antigens; Molecular epidemiology

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