

TITLE: *IN SILICO* CONSTRUCTION OF A MULTI-EPITOPE VACCINE BASED ON PAN-EXOPROTEOME OF *Neisseria gonorrhoeae* THROUGH AN SUBTRACTIVE GENOMICS AND REVERSE VACCINOLOGY APPROACH.

AUTORS: NOGUEIRA, W. G. ¹; TOSTA, S. F. O. ¹; CAVALCANTE, A. L. Q. ²; PINHEIRO, K. C. ²; AZEVEDO, V. A. C. ¹; SILVA, A. L. C. ²; RAMOS, R. T. J. ²

INSTITUTION: 1. DEPARTMENT OF GENETICS, ECOLOGY AND EVOLUTION, FEDERAL UNIVERSITY OF MINAS GERAIS, BELO HORIZONTE, MINAS GERAIS, BRAZIL; 2. LABORATORY OF GENOMIC AND BIOINFORMATICS, CENTER OF GENOMICS AND SYSTEM BIOLOGY, FEDERAL UNIVERSITY OF PARÁ, BELÉM, PARÁ, BRAZIL

ABSTRACT

Gonorrhea is a sexually transmitted infection (STI) involving inflammatory discharge from the urethra or vagina caused by *Neisseria gonorrhoeae*. Based on the increasing number of cases due to inconsistent safe-sex practices and the rise of drug-resistant *N. gonorrhoeae*, it is of major importance to have an effective vaccine that can control the progression of the gonorrhea disease at an early stage. The present work aims to perform the *in silico* prediction and selection of vaccine candidates by Density of Mature Epitopes (MED) of *Neisseria gonorrhoeae*'s core-exoproteoma as potential universal targets in the future manufacture of a multi- epitope vaccine against this pathogen. The WP_003688359.1, WP_095071216.1, WP_003692059.1, WP_003689818.1 and WP_003694816.1 proteins of *N. gonorrhoeae* were predicted *in silico* from the core-exoproteome of 33 complete genomes by MED analysis. Core genes (1431) were identified from 72.917 total genes at the pangenome, by PGAP 1.2.1. For the remaining candidates, subcellular localization was predicted and the 271 proteins identified as potentially membrane exposed (PSE) or extracellular (SEC) proceeded further. Pathogenic Islands (PAIs) analyses and Essential Genes Assessment were carried out also as strategies to reduce the number of best antigenic targets, by GIPSy (Genomic Island Prediction Software) and Database of Essential Genes (DEG), respectively. Final proteins were submitted to epitope binding prediction tools, NetCTL 1.2 (0.75), IEDB(0.8) and BcPred(0.8) for TH cell, TC cell and B-cell, respectively. The MED analysis had a MED Score range of 48.16 to 20.00 nM/mer for the top candidates. The value of α found, according to the Heap Law, suggests that the pangenoma of *N. gonorrhoeae* with 33 sequences is open ($\alpha = 0.88$), inferring in a core genome representative for the species but still in expansion involving Genetic Mobile Elements (GME) through mechanisms of Horizontal Gene Transfer (HGT). A multi-epitope based vaccine was constructed merging selected epitopes with peptide linkers and a peptide adjuvant at N-terminal end. Further studies should be performed to ascertain immunogenic *in silico* features of the final construct and verify cross-reaction potential between homologous proteins and the specificity of the alleles used in the prediction of MHC I and II.

Keywords: *Neisseria gonorrhoeae*; Reverse vaccinology; Core pan-genome; Multi-epitope vaccine.

Development Agencies: CNPq, CAPES