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Frequent Phase Variation of Five Outer Membrane Proteins During Persistent Meningococcal Carriage

M. Alamro[1], F. Bidmos[1], K. Neal[2], D. Turner[3], D. Ala'Aldeen3 [3], C. Bayliss[1]

[1]University of Leicester, Department of Genetics, Leicester, United Kingdom

[2]University of Nottingham, School of Community Health Sciences, Nottingham, United Kingdom

[3]University of Nottingham, Molecular Bacteriology and Immunology Group, Nottingham, United Kingdom

Introduction: Meningococcal carriage rates are in the range of 10-15% but can increase in closed and semi-closed populations. Meningococci can persist in a carrier for 6-9 months and this persistence may be enabled by antigenic or phase variation of outer membrane antigens. Phase variation of the five surface proteins, FetA, Opc, NadA , HpuA and PorA, are associated with changes in repeat tract lengths. The genesfetA,opcandporAhave polyG tracts located in the core promoter whilst thenadArepeats (TAAAs) are located upstream of the core promoter.ThehpuApolyG repeats are in the open reading frame. The aim of this study is to determine whether these five genes exhibit frequent alterations in repeat length during persistent carriage.

Methods: Multiple colonies were isolated of persistent nasopharyngeal meningococcal carriage strains obtained from university students over a 6 month period at three/four time points. PCR and sequencing methodologies were using to characterise the capsular group, fetA, porAand MLST types. DNA was extracted from 6 colonies for each time point. Length variation of the repeat tract was measured by GeneScan analysis and direct DNA sequencing.

Results: Five different meningococcal strains (CC174, CC167, CC23, CC60, CC32) from 21 volunteers were examined for changes in repeat tract length of 5 genes in 368 isolates. Tract lengths ranged between 8-13, 8->15,9-14, 9-14 and 10-20 forfetA, opc, nadA, hpuA, and porA, respectively. The CC60 strain did not exhibit changes in thefetArepeat length (6G) during carriage. The nadAgene was absent in CC60, CC167 and CC23 strains but exhibited an ON-to-OFF switch in 4 of 8 CC174 carriers. A 9G tract was observed for fetAat the first time point in all carriers of strains CC174 and CC32 and exhibited switches to other lengths in 6 of 9 of these carriers. Overall phase variation occurred in 11/21, 13/21, 4/9, 11/21 and 11/21 of volunteers for fetA, opc, nadA, hpuA and porA, respectively.

Conclusion: This study indicates that high frequencies of phase variation occur during persistent meningococcal carriage. We are currently investigating the expression status of these phase variants but speculate that the phase variable changes in the proteins encoded by these genes are affected by different conditions in each individual and may be mediating avoidance of host immune responses.