The genetic basis for susceptibility to childhood infections is poorly understood. The goal of the EU-funded project 'The genetic basis of meningococcal and other life threatening bacterial infections of childhood' (EUCLIDS) is to study the genetics of susceptibility and outcome for major childhood infections. The consortium of 14 institutional members uses meningococcal disease as a model for the investigation.

Consortium members successfully established patient recruitment in the clinical network of 143 centres across Europe and West Africa. They developed an online
database for patient enrolment and obtained all the necessary ethical approvals in all partner institutions.

Genomic analysis of the Spanish and central European meningococcal cohorts have been completed and analysis of the data is now underway by the bioinformatics teams. The phenotypic features of illness severity are being analysed in relation to genotype.

The most significant finding is confirmation of the role of factor H (FH), identified in all three cohorts. FH is a member of the regulators of the complement activation family and is a complement control protein. Its principal function is to prevent damage to host tissues by complement activation.

Bacteria subvert host immune responses by binding FH to specific FH proteins on the bacterial surface, preventing complement killing. Genetic differences in FH appear to alter the ability of the bacteria to evade host responses. At this stage, partners developed monoclonal antibodies against each of the FH-related proteins and complement FH that are required for analysis of genotype and phenotype.

Genotyping of an initial discovery cohort of recipients of meningococcal group C vaccine has now been completed together with functional phenotyping of vaccine responses. Another major effort has developed methodology for sequencing the FH region and other candidate regions. Genotyping has been completed and identified a number of novel variants that are currently under validation.

Functional studies of the mechanisms through which FH controls meningococcal susceptibility are likely to provide a new understanding of host–pathogen interactions during infection. The identification of genes controlling vaccine response will provide new information on improved vaccines and strategy for childhood vaccination.

**Keywords**

Bacterial infection, childhood infections, meningococcal, genomic analysis, factor H
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