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Genomic analysis of invasive streptococcus

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Wim D'Haeze

Abstract

The genome sequence of a *Streptococcus* group A strain that causes rheumatic fever has been determined

Significance and context

Invasive infection with *Streptococcus* group A strains can lead to acute rheumatic fever, a cause of childhood heart disease in which antibodies against components of the bacterium attack the heart. Although this disease has been intensively studied, the causal agents of the invasive infectionproduced by *Streptococcus* group A strains are not yet well known. This is because *Streptococcus* group A strains are not often isolated from infected patients, there is no animal model system, and thesestrains are genetically diverse. To tackle this problem, Smoot *et al*. determined the entire genome sequence of strain MGAS8232, a serotype M18 strain associated with acute rheumatic fever outbreaks in the US, and compared it with the published sequence of a serotype M1 strain SF370, which is not often associated with acute rheumatic fever. In addition, DNA microarrays were carried out on 36 serotype M18 strains.

Key results

The genome of strain MGAS8232 is 1,895,017 base-pairs (bp), contains 1,889 open reading frames, and has a G+C content of 38.6%. Comparison of the two genome sequences revealed 178 genes that are unique to MGAS8232, and 112 that are unique to SF370. The MGAS8232 genome contains many mobile elements, including phage DNA and insertion sequences: in contrast to the genome of SF370, it contains 11 copies of the IS*1239* transposase gene and 4 of IS*1239* transposase gene variants. Furthermore, a 13.8 kilobase-pair DNA 'island' was found in the MGAS8232 genome but not in that of SF370. This island carries an IS*1562*transposase gene inserted in another transposase gene, located in the middle of the island. Other genes present on the island encode ATP-binding cassette transporters and two-component regulatory systems. Unique MGAS8232 genes encoding putative virulence factors - a streptodornase, streptococcal protective antigen and streptococcal pyrogenic exotoxin A - were noted. Both strains have genes encoding 21 extracellular cell-surface-anchored proteins. One surface amidase and another conserved hypothetical protein were present in the MGAS8232 proteome but not in SF370. In addition, MGAS8232 is predicted to secrete eight proteins, possibly involved in pathogenicity. The production of virulence factors is controlled by a set of two-component regulatory systems and

transcription factors, many of which are shared by both strains. MGAS8232 contains in addition two genes encoding putative histidine kinases. The DNA microarray analysis carried out on 36 M18 strains obtained from different locations throughout the US revealed that the primary source of variation among these isolates was the presence of phages and phage-like elements, probably involving horizontal gene transfer events. Comparison of M18 strains obtained from two acute rheumatic fever outbreaks in Salt Lake City that happened 12 years apart demonstrated that these isolates were genetically nearly identical.

Links

Additional general information about invasive *Streptococcus* A strains can be found at the Group A Streptococcus (invasive) webpage.

Conclusions

This study shows that horizontal gene transfer events may contribute to the genetic variation among different serotype M18 strains. Analysis of the genome sequences of infective M18 strains obtained from a distinct location at two different time points demonstrated that these were nearly identical genetically and suggested that this must be the dominant serotype in this region. Comparison of these M18 genomes with that of the M1 strain revealed genetic elements that may be important for acute rheumatic fever outbreaks.

Reporter's comments

Smoot *et al*. studied differences between different *Streptococcus* group A strains in order to identify components that are required for disease development. Future work should include, for instance, the in-depth study of proteins that are produced by MGAS8232 and not by SF370, as well as the regulatory mechanism required for their production. Proteins involved in these regulatory mechanisms and/or new virulence proteins involved in the acute rheumatic fever outbreaks may form good candidates to develop new therapeutics that inhibit their function.

Table of links

Proceedings of the National Academy of Sciences of the United States of America

References

1. Smoot JC, Barbian KD, Gompel JJ Van, Smoot LM, Chaussee MS, Sylva GL, Sturdevant DE, Ricklefs SM, Porcella SF, Parkins LD: Genome sequence and comparative microarray analysis of serotypeM18 group A *Streptococcus* strains associated with acute rheumatic fever outbreaks. Proc Natl Acad Sci USA. 2002, 99: 4668-4673. 0027-8424