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A naturally occurring single amino acid replacement in multiple gene regulator of group a streptococcus significantly increases virulence (Article) (Open Access)

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Abstract

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Single-nucleotide polymorphisms (SNPs) are the most common source of genetic variation within a species; however, few investigations demonstrate how naturally occurring SNPs may increase strain virulence. We recently used group A Streptococcus as a model pathogen to study bacteria strain genotype-patient disease phenotype relationships. Whole-genome sequencing of approximately 800 serotype M59 group A Streptococcus strains, recovered during an outbreak of severe invasive infections across North America, identified a disproportionate number of SNPs in the gene encoding multiple gene regulator of group A Streptococcus (mga). Herein, we report results of studies designed to test the hypothesis that the most commonly occurring SNP, encoding a replacement of arginine for histidine at codon 201 of Mga (H201R), significantly increases virulence. Whole transcriptome analysis revealed that the H201R replacement significantly increased expression of mga and 54 other genes, including many proven virulence factors. Compared to the wild-type strain, a H201R isogenic mutant strain caused significantly larger skin lesions in mice. Serial quantitative bacterial culture and noninvasive magnetic resonance imaging also demonstrated that the isogenic H201R strain was significantly more virulent in a nonhuman primate model of joint infection. These findings show that the H201R replacement in Mga increases the virulence of M59 group A Streptococcus and provide new insight to how a naturally occurring SNP in bacteria contributes to human disease phenotypes.

SciVal Topic Prominence

Topic: Streptococcus pyogenes | Streptococcal Infections | invasive GAS

Prominence percentile: 93.638

Indexed keywords

EMTREE drug terms:

amino acid | arginine | bacterial protein | histidine | protein Mga | transcriptome | unclassified drug | virulence factor | bacterial protein | mry protein, Streptococcus pyogenes

EMTREE medical terms:

amino acid substitution | animal experiment | animal model | Article | bacterial gene | bacterial genome | bacterial strain | bacterial virulence | bacterium culture | codon | controlled study | gene expression | gene sequence | human | human cell | infectious arthritis | Macaca fascicularis | mga gene | mouse | nonhuman | nuclear magnetic resonance imaging | phenotype | priority journal | regulator gene | single nucleotide polymorphism | skin infection | soft tissue infection | Streptococcus group A | amino acid substitution | animal | arthropathy | cell line | female | genetics | hairless mouse | metabolism | microbiology | missense mutation | pathogenicity | pathology | single nucleotide polymorphism | Streptococcus infection | Streptococcus pyogenes

MeSH:

Amino Acid Substitution | Animals | Bacterial Proteins | Cell Line | Female | Genome, Bacterial | Humans | Joint Diseases | Mice | Mice, Hairless | Mutation, Missense | Polymorphism, Single Nucleotide | Streptococcal Infections | Streptococcus pyogenes

Chemicals and CAS Registry Numbers:

amino acid, 65072-01-7; arginine, 1119-34-2, 15595-35-4, 7004-12-8, 74-79-3; histidine, 645-35-2, 7006-35-1, 71-00-1;

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