

Streptococcal Collagen-Like Proteins: Gene Distribution, Expression, and Role in Pathogenesis

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Two related genes were identified in the human pathogen group A *Streptococcus* (GAS). The *scl1* and *scl2* genes encode extracellular proteins with similarity to human collagen. The Scl1 and Scl2 proteins contain a central region composed of Gly-X-X collagen-like motifs. Scl proteins in GAS have different numbers of GXX repeats. The amino-terminal part of mature Scl proteins is variable. V regions differ in length and primary sequence, and are M-serotype specific. The *scl1* and *scl2* genes were present in all 50 genetically-diverse GAS strains tested. The *scl1* and *scl2* genes were simultaneously transcribed in the exponential phase and the Scl proteins were also produced. Scl1 and Scl2 were identified in a cell-associated form and free in culture supernatants. Production of Scl1 is regulated by Mga, a positive transcriptional regulator that controls expression of several GAS virulence factors. In contrast, production of Scl2 is controlled at the level of translation by variation in the number of short-sequence pentanucleotide repeats (CAAAA) located immediately downstream of the GTG (Val) start codon. Control of protein production by this molecular mechanism has not been identified previously in GAS. The role of Scl proteins in GAS pathogenesis was studied using isogenic mutant strains. *scl* genes were inactivated by allelic replacement strategy. Isogenic GAS strains were compared in a mouse infection model. In addition, the Scl-protein deficient strains were tested for their ability to adhere to human cultured cells.