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Resumo	The common pathogen Group A Streptococcus (GAS, Streptococcus pyogenes) is an extracellular bacterium that is associated with a multitude of infectious syndromes spanning a wide range of severity. The surface-exposed M protein is a major GAS virulence factor that is also target for protective antibody responses. In this study, we use a murine immunization model to investigate aspects of the cellular and molecular foundation for protective adaptive immune responses generated against GAS. We show that a wild type M1 GAS strain induces a nonprotective antibody response, while an isogenic strain carrying the immunodominant 2W T helper cell epitope within the M protein elicits an immune response that is protective against the parental non-recombinant M1 GAS strain. Although the two strains induce total anti-GAS IgG levels of similar magnitude, only the 2W-carrying strain promotes elevated titers of the complement-fixing IgG2c subclass. Protection is dependent on IFN-g, and IFN-g-deficient mice show a specific reduction in IgG2c levels. Our findings suggest that inclusion of the 2W T cell epitope in the M protein confers essential qualitative alterations in the adaptive immune response against GAS, and that sparsity in IFN-g-promoting Th cell epitopes in the M protein may constitute an immune evasion mechanism, evolved to allow the pathogen to avoid attack by complement-fixing antibodies.
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