Live Attenuated Vaccine Against Group A Streptococcus Infection

Tech ID: 31831 / UC Case 2020-158-0

BACKGROUND

Streptococcus pyogenes (group A Streptococcus [GAS]) is a leading health and economic burden worldwide, with an estimated 700 million infections occurring annually. Among these are 18.1 million severe cases that result in over 500,000 deaths. Despite active research, a protective vaccine remains elusive, leaving antimicrobial agents as the sole pharmacological intervention against GAS. To date, penicillin remains a primary drug of choice for combating GAS infections. However, despite no apparent emergence of resistant isolates, the rate of treatment failures with penicillin has increased to nearly 40% in certain regions of the world. Due to the high prevalence of GAS infection and the decreasing efficacy of the available repertoire of countermeasures, it is critical to investigate alternative approaches against GAS infection. An emerging strategy for combating pathogenic bacteria involves targeting virulence. To avoid immune clearance, GAS expresses a wide variety of secreted and cell-associated virulence factors to facilitate survival during infection. Despite decades of inquiry into the role and regulation of GAS virulence factors, the function and potential importance of many proteins involved in pathogenicity remain unknown.

TECHNOLOGY DESCRIPTION

Researchers at UC San Diego have new methodology to facilitate the exploration of virulence factors by recently developing Biomimetic Virulomics, a tool that uses nanotechnology-enabled affinity enrichment coupled with multiplexed quantitative proteomics. This tool successfully enriched red blood cell (RBC)-specific effector proteins secreted by GAS. Among the identified proteins were known blood toxins, such as Streptolysin O and CAMP factor, as well as several proteins of unknown function. One of these unknown proteins (S protein) was characterized using an in-frame deletion mutant (Δess-GAS) and tested on the impact of S protein on GAS physiology. In vivo, the absence of S protein results in a striking attenuation of virulence in mice. In addition, the researchers showed that the Δess-GAS mutant protected mice later infected with wild-type GAS while those mice which did not receive Δess- mutant GAS before the challenge with wild-type GAS resulted in a 90% mortality rate. Preliminary data suggests that infection with the Δess-mutant GAS stimulated an IFN-mediated immune response that resulted in the development of adaptive immunity.

APPLICATIONS

The innovation of this work is twofold: 1) S protein shows promise for the development of a vaccine against GAS as it can potentially prevent not only strep throat and impetigo but also more serious invasive disease and postinfectious complications like rheumatic fever, 2) S protein is an ideal target for anti-virulence therapeutics as inactivation of S protein function would make GAS vulnerable to host immunity.

ADVANTAGES

The absence of S protein attenuates virulence to a greater extent than other key and long-studied GAS virulence factors at equal inoculum (e.g. Streptolysins and M protein), with mice demonstrating 100% survival when challenged with an S protein-null strain of GAS. Therefore, S protein as a target for therapeutic development against GAS is of high significance. Moreover, the identified immune pathways associated with immune memory are strongly associated with positive outcomes against GAS infection. These host factors could be a starting point for future investigation into host-centered GAS therapies.

STATE OF DEVELOPMENT

The inventors have shown that S protein can protect mice against successive systemic infection with a wild type strain. They have also experimented with dosage amounts for the protection. Functional experiments further show that deletion of S protein significantly alters the GAS “surfome” (display of surface exposed proteins), including M protein, the best studied and most abundant GAS virulence factor.

INTELLECTUAL PROPERTY INFO

The invention is patent-pending and is available for licensing and collaborations.

RELATED MATERIALS

▶ Wierzbicki IH, Campeau A, Dehaini D, Holay M, Wei X, Greene T, Ying M, Sands JS, Lamsa A, Zuniga E, Pogliano K, Fang RH, LaRock CN, Zhang L, Gonzalez DJ. Group A Streptococcal S Protein Utilizes Red Blood Cells as Immune Camouflage and Is a Critical Determinant for Immune Evasion. Cell Rep. 2019 Dec 3;29(10):2979-2989.e15. doi: 10.1016/j.celrep.2019.11.001. - 12/03/2019

PATENT STATUS

Patent Pending

CONTACT

University of California, San Diego
Office of Innovation and Commercialization
innovation@ucsd.edu
tel: 858.534.5815.

OTHER INFORMATION

KEYWORDS

Streptococcus pyogenes, vaccine, group A Streptococcus, GAS, anti-virulence therapeutics

CATEGORIZED AS

▶ **Medical**
▶ Disease: Infectious Diseases
▶ Disease: Respiratory and Pulmonary System
▶ Vaccines

RELATED CASES

2020-158-0

University of California, San Diego
Office of Innovation and Commercialization
9500 Gilman Drive, MC 0910, ,
La Jolla,CA 92093-0910

Tel: 858.534.5815
innovation@ucsd.edu
https://innovation.ucsd.edu
Fax: 858.534.7345