ABSTRACT

We attempt to genetically modify oral non-pathogenic streptococci (Streptococcus gordonii) to express a virulence factor of the periodontal pathogen Tannerella forsythia. We will test in a mouse model to see if streptococci expressing surface antigen BspA provides protection against T. forsythia infection. My objectives during the past research period were to generate the recombinant DNA constructs for BspA-expression S. gordonii. The bspA gene was amplified by PCR from the T. forsythia genomic DNA and cloned into a plasmid vector for chromosomal integration into S. gordonii by genetic transformation. Our preliminary data showed that immunization with the recombinant BspA protein in mice elicits BspA-specific serum IgG response, and protects mice against T. forsythia infection. As a proof of principal concept of recombinant vaccine for periodontitis and other infections, genetically modified S. gordonii expressing BspA (Sg-BspA) will be tested against T. forsythia infection in a mouse model of periodontitis. We predict that oral immunization with Sg-BspA vaccine would reduce T. forsythia infection and the associated alveolar (jaw) bone loss in mice.

OBJECTIVES

• To genetically modify non-pathogenic oral streptococci, Streptococcus gordonii, to heterologously express the BspA protein of the periodontal pathogen Tannerella forsythia.
• BspA is a potential target antigen of T. forsythia, the immunization by which protect mice against T. forsythia infection.
• We will test in a mouse model of periodontitis if oral colonization with such modified streptococci provides protection against T. forsythia.

RESULTS

Figure 7: A genetic fragment of BspA gene can be successfully cloned (2200 bp).

MATERIALS & METHODS

4(a) Source: Oramd.com

The Problem: Periodontal Disease

Healthy Gums
Gingivitis
Periodontitis
Advanced Periodontitis

Figure 1: Progression of Periodontitis (Source: Oramd.com)

The Problem: Periodontal Disease

• Expensive and painful dental procedures and surgeries
• Sore teeth and swollen, bleeding, sensitive gums
• Embarrassing bad breath
• Increased risk of heart attack and stroke
• Digestive disorders and bone loss

The Cause: Tannerella forsythia – Major Culprit of Periodontitis

• Periodontitis is a progressive inflammation of the periodontium, which often leads to tooth loss.
• Periodontitis is a polymicrobial disease in which the red-complex bacteria Tannerella forsythia, Porphyromonas gingivalis, and Treponema denticola are strongly implicated.
• In this study, we delve into T. forsythia since it is one of the major bacteria known to enhance the deterioration of tooth attachment in periodontitis.

The Solution: Streptococcus gordonii for Vaccine Delivery

• Streptococcus gordonii is a non-pathogenic commensal organism of the human oral cavity.
• It can be genetically engineered to surface-express or secrete heterologous vaccine antigens or therapeutic proteins.
• Genetically modified live bacteria can colonize mucosal surfaces and deliver vaccines or therapeutic molecules; these vectors can also provide ‘herd immunity.’
• It does not require special storage/handling which makes it easy to use.

PRELIMINARY DATA

Figure 6: BspA is an important virulence factor that can act as a protective antigen in potential periodontal vaccination.

REFERENCES