CHAPTER I

INTRODUCTION

The focus of this thesis is on group C *Streptococcus* (GCS) and group G *Streptococcus* (GGS). The clinical significant of these organisms are similar to group A *Streptococcus* (GAS) which is a major pathogen in human. The streptococci are usually found as parasites of humans and other animals and some strains are normal flora of the alimentary, respiratory and genital tracts by colonizing the skin and mucous membrane. These organisms can cause a wide range of infection varying from clinically mild infections such as respiratory tract, skin and soft tissue infection to severe infection such as streptococcal toxic shock syndrome (STSS). Some strains can also cause serious complication following an immunological response to an acute GAS infection. The most serious complications are acute rheumatic fever and acute glomerulonephritis. GAS can be typed in different way, e.g., M typing, T typing, R typing, and OF typing. However, M protein is a major virulence factor that was correlated to clinical significance. For example, post-streptococcal infections, acute rheumatic fever are associated with rheumatogenic strains which have M type 1, 6 and 12 and acute glomerulonephritis are associated with nephritogenic strain which have M type 1, 5, 6 and 19. Therefore, M typing is the most important typing system. M typing that detected the variation in the M protein molecule between different strains is the basis of the Lancefield M serotyping scheme for *S. pyogenes*. M protein has also been found in some group C and G strains.

M proteins are very important and the function of M protein is a major virulence factor that has highly resistant to phagocytosis. N-terminal of M protein has hypervariable part that is highly heterogeneous for M serotyping or Lancefield M serotyping. Serological M typing has identified more than 100 M types. M serotyping is very useful in epidemiological study, and can be used to identify source of outbreaks. M typing can also be used to monitor streptococcal carriage within region of endemicity and is useful to monitor and follow up of diseases when rheumatogenic and

nephritogenic strains were identified. In addition, antibody to hypervariable part of M protein is protective. It was proposed that effective vaccine should compose of M protein from multiple types. Therefore, M typing is important in vaccine development of these organisms. However, M serotyping has several limitations. First, producing of type specific M typing antisera is difficult and specialized. There are problems from cross reactivity of antibody and the lack of expression of M protein after in vitro subculture. In addition, production of M type precipitating antisera is very expensive. The potential usefulness of a nonserologic typing system for sequencing the 5' end of the M protein (*emm*) gene toward a molecular based typing system was examined. *Emm* gene is a virulent gene that encoded the M protein. *Emm* gene is located between *mga* and *spcA* gene, this cluster, called *vir* regulon. The structure of *emm* gene, at 5' end or amino terminus, which is highly heterogeneous, was used to identify the strain of the *Streptococcus*. This system is called *emm* typing. The *emm* typing system has the potential to classify isolates that cannot be typed by serological methods. It is unnecessary for producing of antibody and there is high level of sensitivity and specificity. Therefore, *emm* typing is the useful and reliable epidemiological tool for subdividing GAS, GCS and GGS.

In this study, we are interested in *emm* typing in GCS and GGS. There are higher incidences of GCS and GGS infection in human and other animals that associated with severe infection and complication, which is similarity to GAS infections. In addition, there are evidences demonstrating horizontal gene transfer of *emm* gene between 3 group of *Streptococcus* (A, C, and G). However, the study of *emm* typing in GCS and GGS are much less than in GAS infections. Therefore, we studied the variation of *emm* gene in GCS and GGS from Thai patients and also compared the sequences of *emm* gene between non invasive and invasive isolates. *Emm* typing by direct sequencing were used relies upon the use of the two highly conserved primers to amplify a large portion of the *emm* gene and the hypervariable sequence encoding M serospecificity lies adjacent to one of the amplifying primer sequences, allowing for sequencing. The samples were grouped into invasive and non invasive isolates from each GCS and GGS in order to compare the different sequence types of *emm* gene.

These data will provide information of the pattern of *emm* gene from GCS and GGS in Thai patients and the differences in invasive and non-invasive groups, which might also be useful in vaccine development to *Streptococcus* in Thailand.