CHAPTER 1

INTRODUCTION

1. 1 Rational

Staphylococcus aureus is one of the most common causes of community-acquired and nosocomial infections in human. Penicillin was the first antibiotic that was produced to treat these infections. However, with an increased use of this drug, the treatment was encountered by the ability of the bacteria that can resist to the drug. Methicillin then was developed to resolve the problem. Unfortunately, methicillin resistant *S. aureus* (MRSA) was discovered soon after the drug was introduced. Vancomycin has been considered as a drug of choice for treating infections caused by MRSA. However, the first *S. aureus* strain with reduced susceptibility to vancomycin, designated vancomycin-intermediate *S. aureus* (VISA), was reported from Japan in 1997 (Hiramatsu *et al*., 1997). Since then, VISA strains have been increasingly reported all over the world (Bierbaum *et al*., 1999; Cui *et al*., 2003; Bozdogan *et al*., 2004; Song *et al*., 2004; Rybak *et al*., 2008). It is speculated that the emergence and spread of resistant strains have arisen from using vancomycin therapy in various countries and causes concern about possibility of losing the potential treatment option for the resistant strains (Koehl *et al*., 2004; Cui *et al*., 2005). In 2001, heterogeneous VISA (hVISA) which displays lower level of vancomycin resistance than VISA and possesses a small subpopulation with higher level of resistance was reported from Thailand (Trakulsomboon *et al*., 2001). Similarly, Song *et al.* (2004) and Lulitanond *et al.* (2006) reported the finding of hVISA from patients in Thailand. The presence of hVISA may represent a warning for the possible emergence of vancomycin resistant strains in the future.

Vancomycin resistant strains of *S. aureus* have features that differ from those of vancomycin susceptible *S. aureus* strains such that thickened cell wall and reduced autolytic activity (Pfeltz *et al*., 2000; Cui *et al*., 2003; Utaida *et al*., 2006). However, mechanisms of occurrence are still unclear.

In this study, we subjected clinical isolates of MRSA to increasing concentrations of vancomycin to increase vancomycin resistant level in these isolates. Then, we characterized the laboratory-derived VISA strains achieved comparing to those of their vancomycin susceptible parental strains. It is expected that this will give us more insights into the development of vancomycin resistance in *S. aureus*.

1.2 Objectives

To characterize laboratory-derived vancomycin-intermediate *S. aureus* strains.

1.3 Research Methodology

1. Induction of vancomycin-intermediate *S. aureus* strains in the laboratory.
2. Characterization of laboratory-derived vancomycin-intermediate *S. aureus* strains.