



## Symposium 3.2

### VISA/hVISA and VRSA, mechanism and clinical significance

**Keiichi Hiramatsu**

Department of Bacteriology  
Juntendo University, Japan

Vancomycin has still been the major therapeutic agent for MRSA infection widely used in the world. However, limited tissue penetration and insufficient cytotoxic activity of the agent have frequently lead to unsatisfactory clinical outcome. Therapeutic failure of vancomycin occurs even if the vancomycin MIC of the causative MRSA strain is within "susceptible range" (2 mg/L or below). If the MIC is 4 mg/L or above, vancomycin therapy is considered unreliable. The strains with MICs 4 or 8 mg/L are designated VISA. If the MIC is 16 or greater, it is defined as VRSA.

VRSA is supposed to be the most dreadful of all in terms of its resistance level and presumed transmissibility of resistance trait among VRE and MRSA clinical strains. However, only a few VRSA have been isolated in USA against our fear for the dreadful scenario of VRSA pandemic.

On the other hand, what annoys us mostly in the daily clinical setting is VISA/hVISA. It is an insidious occurrence in nature, having no simple resistance gene, nor any easy sign to recognize them before vancomycin therapy turns unsuccessful. VISA/hVISA has unique resistance mechanisms. Unlike most of the resistance bacteria in the past having had acquired resistance via transmissible genetic elements such as plasmid, transposon, and genomic islands represented by SCCmec. Instead, VISA/hVISA have had accumulated multiple mutations to achieve the level of vancomycin resistance which is a minimal one just covering the limited vancomycin concentration in the body of patients. Significant feature of the resistance mechanism is a thickening of cell wall and change of cell physiology. Important regulator genes that govern cell physiology are frequently involved in the resistance. However, genetic basis for each clinical VISA/hVISA is diverse. This diversity should reflect the extraordinary polymorphism of the genetic backgrounds of MRSA strains habitant in the world. Evidently, VISA/hVISA is ubiquitous across the countries of the world. The fact that MRSA is still prevalent in many countries implies that MRSA, as a super-successful subspecies of *S. aureus*, has already conquered the genocidal threat of vancomycin.