Qac resistant genes

Biocides based on QACs are widely used for disinfection and preventing the infection and the transmission of bacteria in a hospital, veterinary or industrial environment. Extensive and inadequate use of these disinfectants for disinfection could lead to a selective pressure for survival of bacterial strains with *qac* resistance genes, thus creating a potentially serious problem of infection control in hospitals and clinical settings.

Consequently, the emergence of *qac* resistance genes that code for resistance to disinfectants among various subtypes of staphylococci, including *S. aureus* and coagulase-negative staphylococci (CNS), have been reported in human clinical isolates and general environment and several *qac* genes have been identified52, 66, 68, 93, 96.. (1) In general, QAC resistant genes are plasmid-born and code for the expression of multidrug efflux pumps, which are membrane-bound transport proteins. These proteins are PMF-dependent cation export proteins for expelling toxic substrates including QACs, some other cationic biocides, and intercalating dyes, such as ethidium bromide (EBR) (21). Presence of these genes may allow microorganisms to survive in a hostile environment containing disinfectants and antimicrobial agents. According to their different structures, the gene determinants belong to one of two membrane transportation families, the major facilitator family (MFS) and the small multidrug resistant family (SMR)52. Information about location and resistance patterns to biocides of these *qac* genes can be seen in *Table* 2.

QacA/B and smr, ranked the first two, are the most frequently reported *qac* genes. The increased resistance to biocides is closely associated with the presence of both *qacA* and *smr.* (23).

In 1999, Noguchi performed a study to investigate the distribution of the *S. aureus* isolates carrying *qacA/B* or *qacC* gene in clinical isolates in Japan. According to his results, the prevalence of *qacA/B* was 10/71 (14%) and *qacC* was 20/71 (28%) MRSA isolates. Later studies also performed by Noguchi revealed that the prevalence of MRSA with *qacA/B* had reached 41. 6% (372/894) across the Asian area, and MRSA with *qacC* gene in India was up to 31. 6%. Similar studies conducted in Hong Kong reported different results95, with 41. 2% (21/51) *S. aureus* isolated from nurses found to carry the *qacA/B* gene, and frequency of *qacC* gene was only 11. 8% (6/51), which was quite low compared to Noguchi's study82.[1]

In addition, MRSA isolates resistant to disinfectants and antiseptics have been reported (7). In the isolates of MRSA, the carriage of *qacA* was more common than *smr* (9).

Recently, several novel plasmid-borne genes, qacG, qacH, *qacJ* , *qacE* and *qacE* Δ *1,* were detected in staphylococci and some gram negative bacteria associated with infection diseases(1). However, the prevalence of these genes are commonly quite lower than that of qacA/B.

qac A/B gene

QacA and *qacB* resistance genes are harboured on plasmids which belong to the MFS family. Lyon et al. demonstrated that the *qacA* gene was present on plasmid pSK57 together with resistance genes for β-lactamase and heavy metals (21, 23). It is suggested that *qacA* is homological with another antibiotic resistant gene *tet* , and encodes the QacA protein which has 514 amino acids and belongs to the major facilitator superfamily (MFS) 92.

Sequence analysis suggests that the *qacA* pump, which has a 14 TMS configuration, confers resistance via the export of the compound by the proton motive force (PMF) to a wide range of structurally diverse hydrophobic drugs including QACs (such as cetrimide), ethidium bromide, and other organic cations.

The *qacB* gene is located on plasmid pSK23 again together with β-lactam and heavy metal resistance genes which shows high similarity with *qacA* 73 (23-24). *QacA* and *qacB* are considered to be virtually the same as it is not possible to distinguish between them by simple PCR, there being differences in only seven nucleotide substitutions. The molecular structure difference between *qacA* and *qacB* is just 7 nucleotide substitutions, these two transporters have similar binding affinities and identical binding sites for monovalent cations. However, qacA mediates resistance to both monovalent and divalent cations while qacB confers less or no resistance to divalent cations and can only expel QACs and intercalating dyes from the cell.

Smr gene

QacC , which has also been known as *qacD* or *ebr* , has been renamed *smr.* It is plasmid borne, often on small plasmids of less than 3kb and belongs to the SMR family.

Smr is the smallest of the multidrug resistance transporters. Its small size makes it unique as a secondary transporter. The product encoded by *qacC* gene contains 107 amino acids and has four large hydrophobic segments, all which have the potential to traverse the cell membrane. Studies101 have

shown that QacC protein not only mediates multidrug export but functions as a multidrug exporter.

Smr can transport several different compounds such as QACs, ethidium bromide and other compounds, but it is more limited than *qacA* (9, 26).[2] The schematic representation of the QacC polypeptide can be seen in Fig. 3.

This gene was mostly detected in clinical isolates of *S. aureus* and other staphylococci species(15). The *smr* gene has been shown to be located on a large (> 20kb) conjugative plasmid with multiple resistance determinants such as pSK41 and on small (<3kb) nonconjugative plasmids such as pSK89 (17, 20, 23). A recent study83 has revealed that the *qacC* gene in *S. epidermidis* confers resistance to a number of *beta* -lactam antibiotics and to ethidium bromide, and this is the first report of a small multidrug resistance pump involved in resistance to *beta* -lactam antibiotics.

qacG gene

qacG gene was first isolated from staphylococcal plasmid pST94 with 2. 3kb in 199952. The 107 amino acid protein *QacG* encoded by *qacG* gene, belonging to the SMR family, shows 69. 2% and 45% similarity with small multidrug resistant protein Smr and QacE, respectively. The *qacG* – and *smr* -harbouring isolates showed small differences in MIC values to BC (8–10 mg/l) and Eb (20–40 mg/l).

QacG protein confers resistance to Eb and QACs via proton dependent efflux. There is little differences between *qacG* isolates and *smr* isolates in MIC values of BC and Eb, and it is suggested that the *QacG* protein uses the

same resistance mechanism as the Smr protein52. The location of the hydrophobic amino acid in *QacG* and Smr is similar, however, *QacG* differed from Smr in 33 of 107 amino acid proteins dispersed throughout the protein52.

qacH gene

In 1998, Heir93 isolated *a* new staphylococcal gene, *qacH,* from a strain of *Staphylococcus saprophyticus* . The *qacH* gene is harbored on the 2. 4kb plasmid (p2H6), and mediates resistance to QACs. *QacH* protein encoded by the *qacH* gene contains 107 amino acids and shows strong homology with the small multidrug resistance protein family. Further study suggests that similarity of *QacH* with Smr and *QacG* is 78% and 70%, respectively93. However, *QacH* conferred high-level resistance to ethidium bromide and low-level resistance to proflavine, which differs from Smr and *QacG* . 93

qacJ gene

QacJ gene locates on a 2650bp plasmid pNVH01 in equine *S. aureus* , *S. intermedius* and *S. simulans* , and was first identified in Norway, 200367. The plasmid pNVH01 belongs to the plasmid pC194 family of rolling circle replication and contains two open reading frame, designated repNVH01 and *qacJ 67* . *qacJ* encodes a putative protein *QacJ* with 107 amino acid. Homology analysis shows that *QacJ* is a new group of the Smr protein family, and the similarity with other smr protein members is shown to be: Smr (72. 5%), *QacG* (82. 6%), and *QacH* (73. 4%). Compared with Smr, QacG and QacH, *QacJ* confers an increased resistance level to BC, but mediates the same resistant level against CTAB with Smr67.