Whole Genome Sequencing of a Clinical Methicillin-Resistant *Staphylococcus aureus* from Terengganu Led to the Discovery of a Novel 58.4 kb Conjugative Plasmid

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Abstract

Methicillin-resistant *Staphylococcus aureus* (MRSA) has been listed by the World Health Organization as a priority antibiotic-resistant nosocomial pathogen in urgent need of new antimicrobials [1]. Plasmids are a key factor in the pathology and epidemiology of MRSA isolates and play important roles in their evolution. In our on-going efforts to better understand the genetic background and molecular epidemiology of MRSA isolates from Terengganu, Malaysia, whole genome sequencing using Illumina HiSeq platform (HiSeq-PE150) was performed on a 31 selection of clinical isolates obtained from the main tertiary hospital, Hospital Sultanah Nur Zahirah (HSNZ). One of these isolates, designated *S. aureus* SauR23, was isolated from pus in 2016 and was resistant to seven classes of antimicrobials and thus categorized as multidrug resistant (MDR). Analysis of the genome sequence of SauR23 showed it belonged to the ST22 clone with a SCCmec class IV(2B) and harbored the *blaZ*, *mecA*, *norA*, *lmrS*, *mepR* and *ermC* resistance genes, which corresponded to its MDR phenotype. Besides the *norA*-encoded efflux pump, fluoroquinolone resistance in SauR23 could also be due to the S84L point mutation in its *gyrA*-encoded DNA gyrase. SauR23 was found to carry three plasmids, designated pSauR23-1 (58,422 bp), pSauR23-2 (3,011 bp), and pSauR23-3 (2,473 bp). The smallest plasmid, pSauR23-3 was a RepL-family plasmid that encoded the *ermC* gene and was likely responsible for the inducible macrolide-lincosamide-streptogrammin B (iMLSb) phenotype exhibited by the host strain. Plasmid pSauR23-2 was a Rep_1 family small cryptic plasmid. On the other hand, pSauR23-1 is a novel, potentially conjugative plasmid that contains a replicase of the RepA_N domain (repUS20) that shared low sequence identity (34%) to the RepA_N replicase of pWBG749, a known staphylococcal conjugative plasmid. The putative conjugative region of pSauR23-1 differed from the conjugative transfer system of pWBG749 as well as other known conjugative systems in the database. Nevertheless, genes which contained conserved motifs for the MobL relaxase, the TraG/TraD-like conjugative transfer protein, and a type VI secretion system ATPase were detected within this region of the plasmid.
Table 1: characteristic of SauR23 plasmids

<table>
<thead>
<tr>
<th>Plasmid code</th>
<th>Size (in kb)</th>
<th>Replicon-type</th>
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<tbody>
<tr>
<td>pSauR23-1</td>
<td>58</td>
<td>RepA_N</td>
</tr>
<tr>
<td>pSauR23-2</td>
<td>3</td>
<td>Rep_1</td>
</tr>
<tr>
<td>pSauR23-3</td>
<td>2.4</td>
<td>Rep_L</td>
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</tbody>
</table>

Keywords
Conjugative plasmid, Multidrug resistance, MRSA

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References