International Journal of Infectious Diseases 51 (2016) 31–35

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Diversity of methicillin-resistant *Staphylococcus aureus* CC22-MRSA-IV from Saudi Arabia and the Gulf region

Abiola Senok [a], Ali Somily [b], Adeola Raji [a], Darius Gawlik [c,d], Fatimah Al-Shahrani [e], Shehla Baqi [e], Samar Boswihi [f], Leila Skakni [g], Edet E. Udo [f], Stefan Weber [h], Ralf Ehricht [i,j], Stefan Monecke [c,i,j,*]

[a] *Department of Microbiology and Immunology, College of Medicine, Alfaisal University, Riyadh, Kingdom of Saudi Arabia*
[b] *Department of Pathology and Laboratory Medicine, College of Medicine, King Khalid University Hospital and King Saud University, Riyadh, Kingdom of Saudi Arabia*
[c] *Institute for Medical Microbiology and Hygiene (IMMH), Technische Universität Dresden, Dresden, Germany*
[d] *Hamm-Lippstedt University, Hamm, Germany*
[e] *Department of Medicine, Division of Infectious Diseases, King Khalid University Hospital, Riyadh, Kingdom of Saudi Arabia*
[f] *Department of Microbiology, Faculty of Medicine, Kuwait University, Safat, Kuwait*
[g] *Molecular Pathology Laboratory, King Fahad Medical City, Riyadh, Kingdom of Saudi Arabia*
[h] *Sheikh Khalifa Medical City, Abu Dhabi, United Arab Emirates*
[i] *Alere Technologies GmbH, Jena, Germany*
[j] *InfectoGnostics Research Campus, Jena, Germany*

ARTICLE INFO

Article history:
Received 13 July 2016
Received in revised form 19 August 2016
Accepted 23 August 2016

Corresponding Editor: Eskild Petersen, Aarhus, Denmark.

Keywords:
Staphylococcus aureus
MRSA
SCCmec
Molecular typing

SUMMARY

Objectives: CC22-MRSA-IV, UK-EMRSA-15/Barnim EMRSA, is a common and pandemic strain of methicillin-resistant *Staphylococcus aureus* (MRSA) that has been found mainly in Western Europe, but also in other parts of the world including some Gulf countries. One suspected case of an infection with this strain in a patient who was admitted to the surgical unit in Riyadh, Kingdom of Saudi Arabia (KSA) was investigated in order to check whether this strain has reached KSA.
Methods: Besides the index isolate, 46 additional isolates of CC22-MRSA-IV from patients from KSA, Abu Dhabi, Kuwait, and Germany (patients with a history of travel in the Middle East), were characterized by microarray hybridization.
Results: The study revealed a regional presence of as many as six distinct 'strains' of CC22-MRSA-IV that could be distinguished based on carriage of SCC*mec* IV subtypes and virulence factors. No true UK-EMRSA-15/Barnim EMRSA was identified in Riyadh; all suspected isolates from Riyadh were assigned to other, albeit related strains. However, this strain was identified in Abu Dhabi and Kuwait.
Conclusions: CC22-MRSA-IV from KSA could be linked to other epidemic strains from the Middle East and possibly India, rather than to the Western European UK-EMRSA-15/Barnim EMRSA. High-resolution typing methods, including SCC*mec* subtyping, might help to differentiate related epidemic strains and to monitor routes of transmission.

1. Introduction

Epidemic methicillin-resistant *Staphylococcus aureus* (EMRSA)-15 (CC22-MRSA-IV) was first identified in the UK in the early 1990s and has become the most prevalent hospital-acquired strain of methicillin-resistant *Staphylococcus aureus* (MRSA) in the UK.[1,2] This pandemic MRSA strain has also been reported from many other regions of the world, including Ireland, Germany (where it is called 'Barnim EMRSA' after the county in which it was first found), Denmark, Belgium, Spain, Portugal, Malta, Sweden, Singapore, Australia, New Zealand, Qatar, and Kuwait.[1,3–21] CC22-MRSA-IV that differ in harbouring *tst1* (encoding toxic shock toxin) have been reported from the Gaza Strip, Jordan, the United Arab Emirates (UAE), the Kingdom of Saudi Arabia (KSA), Kuwait, the USA, and Italy.[11,20,22–26] Furthermore, CC22-MRSA-IV harbouring the genes encoding the Panton–Valentine leukocidin (PVL) have

* Corresponding author.
E-mail address: monecke@rocketmail.com (S. Monecke).

http://dx.doi.org/10.1016/j.ijid.2016.08.016

frequently been observed in the Middle East,[5,11,27] Iran,[28] and India,[29–31] and also in sporadic cases[32] and localized outbreaks[33] in other regions, such as Western Europe.

In this report, the characteristics of CC22-MRSA-IV causing an infection in a patient who presented to the surgical unit of King Khalid University Hospital (KKUH) in Riyadh, KSA, are presented. Furthermore, the molecular typing of CC22-MRSA-IV isolated in the Arabian Gulf region and from patients from Germany with a history of previous travel to the Middle East is discussed.

2. Materials and methods

2.1. Case history

A middle-aged male patient presented to the surgical unit of KKUH with a history of intermittent fever and peri-umbilical pain, with an associated peri-umbilical discharge of 2-week duration. The patient gave a history of travel to Egypt (including healthcare exposure) and of two previous surgical interventions at different hospitals during the last few years. The first one was a gastric bypass procedure; the second one an abdominal herniorrhaphy with mesh implant. He received antibiotics, but neither details of the antibiotic therapy nor information on the laboratory investigations were available. There was no history of any chronic illness apart from the presenting complaints. No family members were documented to have recurrent skin or soft tissue infections.

On admission, the patient had stable vital signs. Physical examination revealed an anterior abdominal wall scar running from the xiphoid process to the umbilicus and a discharging wound in the umbilical area. There was associated tenderness in the paraumbilical and left hypogastric areas. Investigations carried out at presentation included an abdominal computed tomography scan, which was significant for thickening of the anterior abdominal wall with minimal subcutaneous collection. A culture of the wound swab collected at presentation yielded a mixed growth of *Klebsiella pneumoniae*, which was sensitive to all tested antibiotics, and MRSA, which was resistant to penicillin, ampicillin, and imipenem but susceptible to gentamicin, ciprofloxacin, erythromycin, rifampicin, trimethoprim/sulfamethoxazole, tetracycline, and vancomycin. The patient underwent wound debridement with partial mesh removal and drainage a day after presentation, and the postoperative period was uneventful. He was discharged 3 days after presentation on a combination of clindamycin (450 mg, 8-hourly) and ciprofloxacin (750 mg, 12-hourly). At the 2-week follow-up visit, the patient's wound had healed completely.

2.2. Additional isolates

Additional isolates were included for comparison. All had previously been identified as CC22-MRSA-IV using the StaphyType DNA microarray (see below). These included isolates with hybridization profiles consistent with UK-EMRSA-15/Barnim EMRSA, as well as some randomly selected PVL- or *tst1*-positive CC22-MRSA-IV strains. These isolates originated from Riyadh (KSA; five isolates sampled in 2014 and 13 sampled in 2010/11), Abu Dhabi (UAE; $n = 16$ sampled in 2009/10), and Kuwait ($n = 6$; 2013), as well as from Germany. The German isolates included some local UK-EMRSA-15/Barnim EMRSA isolates ($n = 4$; 2015/16) and some PVL- or *tst1*-positive CC22-MRSA-IV from patients with a history of recent travel in the Middle East ($n = 3$; 2014–2016).

2.3. Array procedures

Molecular characterization of the MRSA isolate from the index case was performed as part of a wider study in which archived MRSA isolates from KKUH were characterized using the StaphyType DNA microarray (Alere Technologies GmbH, Jena, Germany). Probes, primers, and procedures have been described previously in detail,[11,34] and protocols are provided by the manufacturer.

Additional probes and primers were used in order to discern SCC*mec* subtypes and CC22 strains (Table 1). Amplification and hybridization protocols were identical to those described previously.[11,34]

3. Results

The recovered isolate harboured the accessory gene regulator (*agrI*) and capsular genes type 5 (*cap*5), as well as genes for collagen adhesin (*cna*), *Staphylococcus aureus* surface protein G (*sasG*), and the *egc* cluster. This was in accordance with previously characterized CC22 isolates and strains.[11,34] Furthermore, it harboured *mecA* as part of an SCC*mec* IV element. It lacked the genes encoding fibronectin-binding protein B (*fnbB*), exfoliative toxin (*etA*, *etB*, and *etD*), toxic shock toxin (*tst*), and PVL, as well as the arginine catabolic mobile element (ACME). Based on this profile, the isolate was preliminarily regarded as CC22-MRSA-IV, UK-EMRSA-15/Barnim EMRSA. Staphylokinase (*sak*), chemotaxis-inhibiting protein (*chp*), and Staphylococcus complement inhibitor (*scn*) genes were present, and enterotoxin C and L genes (*sec* and *sel*) were absent.

SCC*mec* subtyping using new probes revealed that this isolate differed in SCC*mec* subtype from Western European UK-EMRSA-15/Barnim EMRSA isolates (that harbour SCC*mec* IV h/j) in the carriage of an SCC*mec* element of subtype IVa. The hybridization pattern of the actual isolate (Table 2) matched the computed/predicted pattern for the sequence of strain CMFT503, GenBank HF569113.1, yielding signals for *mecA*, *ugpQ*, delta *mecR1*, *mvaS*, *cstB*-SCC2, Q93IB7, *ccrA/B-2*, and 'SCCterm 1' (an intergenic region between *orfX* and the first codons of the SCC element that is alternative to *dcs*).

Based on this observation, a convenience sample of 46 additional isolates was selected and subtyped for comparison (see Materials and methods). When focusing on SCC*mec* IV subtypes as well as on the carriage of PVL and *tst1* genes, these 46 isolates could be categorized into six distinct variants, or strains. Details are shown in Table 2. All Saudi isolates differed from the Western European UK-EMRSA-15/Barnim EMRSA CC22-MRSA-IV h/j. However, this strain was identified in Abu Dhabi (UAE) and Kuwait.

4. Discussion

The changing epidemiology of MRSA necessitates the continuous surveillance of patients. Well-documented hospital and community strains of MRSA in Saudi Arabia include ST239-MRSA-III, ST80-MRSA-IVc, and ST30-MRSA-IV.[27]

In this report, the characteristics of a CC22-MRSA-IV (CC22-IV) isolate from a patient in Saudi Arabia are presented; this isolate was similar but not identical to the widely distributed UK-EMRSA-15/Barnim EMRSA. On investigating this case and other similar isolates from KSA and other regions, several different strains (or very distinct variants) of CC22-IV could be distinguished based on SCC*mec* IV subtypes and the carriage of clinically important toxin genes.

These included UK-EMRSA-15/Barnim EMRSA as described from Western Europe (see Introduction). These isolates have SCC*mec* IV h/j elements and do not carry *tst1* or PVL genes, but frequently harbour enterotoxin C and L genes (*sec* and *sel*). Usually they are phenotypically resistant to ciprofloxacin, often also to erythromycin and clindamycin (mediated by *erm*(C)). Other resistance properties, however, are rather rare. This strain is also susceptible to weak lysis by phage 75.[1]

Table 1
Markers used for subtyping of CC22-MRSA-IV

Gene	Gene product/function	Probe(s)	Primer(s)
agr groups I–IV, capsule type 5 and 8	*agr*- and capsule-specific probes (*agr* I and capsule type 8 alleles present in CC22)	[11,34]	[11,34]
mecA	Modified penicillin binding protein (PBP2a) causing oxacillin/methicillin resistance and thus defining MRSA	[11,34]	[11,34]
ccrA/B-2	Cassette chromosome recombinase A allele found in SCC*mec* II and IV elements	[11,34]	[11,34]
mvaS-SCC	Truncated 3-hydroxy-3-methylglutaryl CoA synthase, variably present in SCC*mec* I, II, IV, V	BA000033.2 [37280:37304] and BA000033.2 [37432:37460]	BA000033.2 [37307:37326:r] and BA000033.2 [37488:37510:r]
cstB-scc2 (IVa)	CsoR-like sulfur transferase-regulated genes B/ metallo-beta-lactamase superfamily protein (truncated); present in SCC*mec* X, variably present in SCC*mec* I and IV; marker for IVa	CP000046.1 [54284:54313:r] and CP000046.1 [53882:53910:r]	CP000029.1 [2492569:2492590:r] and CP000046.1 [53836:53854]
B2Y834	Abortive phage resistance protein used for identification of SCC*mec* IV A, G, c and SCC*mec* MRSAZH47	AE015929.1 [51095:51119]	AE015929.1 [51124:51144:r]
B6VQU0	Putative protein used for identification of SCC*mec* IVh/j	AB425824.1 [20412:20443]	AB425824.1 [20498:20525:r]
Q93IB71	LytTR domain DNA-binding regulator present in some SCC*mec* III elements and in IVa from CMFT503 GenBank HF569113.1	FN433596.1 [434532:434550]	FN433596.1 [68041:68058]
Q9XB68-dcs	Located at the terminus of SCC*mec* directly next to *orfX*, comprises the downstream constant segment (*dcs*) that includes a copy of the SCC direct repeat DR_SCC (AGAAGCTTATCATAAGTAA)	[11,34]	[11,34]
SCCmec Terminus 1	SCC integration site alternate to *dcs*	GU235983.1 [568:594]	FN433596.1 [67354:67380:r]
SCCmec Terminus 5	SCC integration site alternate to *dcs*	AB425427.1 [754:779]	AB425427.1 [800:824:r]
erm(C)	rRNA adenine N-6-methyltransferase macrolide–lincosamide–streptogramin B resistance protein	[11,34]	[11,34]
aacA-aphD	Bifunctional enzyme Aac/Aph, 6′-aminoglycoside N-acetyltransferase/2′′-aminoglycoside phosphotransferase; gentamicin and tobramycin resistance	[11,34]	[11,34]
aadD	Aminoglycoside adenyltransferase, tobramycin resistance	[11,34]	[11,34]
dfrA	Dihydrofolate reductase, mediates trimethoprim resistance	[11,34]	[11,34]
lukF/S-PV	Panton–Valentine leukocidin	[11,34]	[11,34]
tst1	Toxic shock syndrome toxin	[11,34]	[11,34]
sec+sel	Enterotoxins C and L	[11,34]	[11,34]
egc cluster	Enterotoxin gene cluster (comprising *seg*, *sei sem*, *sen*, *seo*, *seu*)	[11,34]	[11,34]
sak, *chp*, *scn*	Staphylokinase, chemotaxis-inhibiting protein, staphyl. complement inhibitor	[11,34]	[11,34]
eta, *etb*, *etd*	Exfoliative toxins	[11,34]	[11,34]
ACME	Arginine catabolic mobile element	[11,34]	[11,34]
fnbB	Fibronectin binding protein B, variably detected in CC22 because it is in some strains fused with *fnbA*	[11,34]	[11,34]
cna, *sasG*	Collagen adhesin; *Staphylococcus aureus* surface protein G (present in CC22)	[11,34]	[11,34]

Although some were superficially similar, not a single one of the 18 KSA isolates characterized herein could be assigned to UK-EMRSA-15/Barnim EMRSA, mainly because of the carriage of other SCC*mec* IV subtypes. Some isolates from Kuwait and Abu Dhabi matched this strain. Furthermore, two additional isolates from Abu Dhabi had an SCC*mec* IV variant element that has apparently not yet been described or sequenced.

Another related epidemic strain – ST22-MRSA-IVa – is usually reported to carry *tst1* as well as SCC*mec* IVa. It is probably widely distributed in the Middle East and the Mediterranean, and is sometimes dubbed the 'Gaza epidemic strain'.[11,20,22–25,27] Study isolates that could be assigned to this strain originated from KSA, Abu Dhabi, and Kuwait, or were isolated in Germany from patients with a history of travel to the Middle East.

There were also *tst1*-negative isolates with SCC*mec* IVa elements. Previously observed UK-EMRSA-15/Barnim EMRSA-like isolates from KSA have belonged to this category,[27] as well as the isolate from the case described herein. It can be assumed that they might rather be *tst1* deletion mutants of the Middle Eastern 'Gaza epidemic strain' than derived from imported European UK-EMRSA-15/Barnim EMRSA.

Furthermore, three *tst1*-negative isolates (one each from KSA, Abu Dhabi, and Kuwait) were found to carry SCC*mec* IV b/d/i elements.

Finally, there were a number of PVL-positive CC22-IV. All characterized isolates of PVL-positive CC22-MRSA-IV had SCC*mec* IVc elements, ruling out the possibility that they directly evolved from UK-EMRSA-15/Barnim EMRSA by acquisition of a PVL phage. This strain also appears to be present in India (with two recent genome sequences being virtually identical to the isolates tested herein: http://www.ncbi.nlm.nih.gov/bioproject/PRJDB1743 and http://www.ncbi.nlm.nih.gov/bioproject/PRJDB2070). This suggests an epidemiological link to the Arabian Gulf, as previously also assumed for other MRSA.[35]

Table 2
CC22-MRSA-IV strains and isolates

Isolates	CC22-MRSA-IV with SCC*mec* IVa	UK-EMRSA-15/Barnim EMRSA with SCC*mec* IV h/j	CC22-MRSA-IV with unknown SCC*mec* IV h/j variant	*tst1*-positive 'Gaza epidemic strain' with SCC*mec* IVa	CC22-MRSA-IV with SCC*mec* IV b/d/i	PVL-positive CC22-MRSA-IV with SCC*mec* IVc
	Index case from the case report and 3 others from Riyadh (2010/11)	7 isolates from Abu Dhabi (2009/10), 2 from Kuwait (2013), and, for comparison, 4 from Dresden (locals; 2015/16)	2 from Abu Dhabi (2009/10)	2 isolates from Abu Dhabi (2009/10), 2 from Kuwait (2013), 2 from Riyadh (2014), 4 from Riyadh (2010/11), 2 from Dresden (with travel history; 2016)	1 from Riyadh (2014), 1 from Abu Dhabi (2009/10), 1 from Kuwait (2013)	4 from Abu Dhabi (2009/10), 1 from Kuwait (2013), 1 from Riyadh (2014), 6 from Riyadh (2010/11), 1 from Dresden (with travel history; 2014)
mecA	**Positive**	**Positive**	**Positive**	**Positive**	**Positive**	**Positive**
ccrA/B-2	**Positive**	**Positive**	**Positive**	**Positive**	**Positive**	**Positive**
mvaS-SCC	**Positive**	**Positive**	**Positive**	**Positive**	**Positive**	Negative
cstB-scc2 (IVa)	**Positive**	Negative	**Positive**	**Positive**	Negative	Negative
B2Y834 (IVc)	Negative	Negative	Negative	Negative	Negative	**Positive**
B6VQU0 (IV h/j)	Negative	**Positive**	**Positive**	Negative	Negative	Negative
Q93IB71	**Positive**	Negative	Negative	**Positive**	Negative	Negative
Q9XB68-dcs	Negative	**Positive**	Negative	Negative	**Positive**	**Positive**
SCC*mec* Terminus 1	**Positive**	Negative	Negative	**Positive**	Negative	Negative
SCC*mec* Terminus 5	Negative	Negative	**Positive**	Negative	Negative	Negative
erm(C)	Negative	*Variable*	Negative	*Variable*	*Variable*	*Variable*
aacA-aphD	Negative	Negative	Negative	Negative	Negative	**Positive**
aadD	Negative	Negative	Negative	Negative	Negative	*Variable*
dfrA	Negative	Negative	Negative	Negative	Negative	*Variable*
lukF/S-PV	Negative	Negative	Negative	Negative	Negative	**Positive**
tst1	Negative	Negative	Negative	**Positive**	Negative	Negative
sec+sel	Negative	*Variable*	Negative	Negative	**Positive**	Negative
egc cluster	**Positive**	**Positive**	**Positive**	**Positive**	**Positive**	**Positive**
fnbB	Negative	Negative	Negative	Negative	*Variable*	*Variable*

In conclusion, 'true' UK-EMRSA-15/Barnim EMRSA was not identified from KSA, with all tested CC22-MRSA-IV differing either in toxin carriage and/or in SCC*mec* subtype. UK-EMRSA-15/Barnim-like strains from KSA might have evolved independently from other Middle Eastern CC22-MRSA-IV (by loss of *tst1*) or directly from methicillin-sensitive *S. aureus*, by acquisition of SCC*mec* IV b/d/i.

Due to the small number of isolates characterized herein, it is not possible to state that UK-EMRSA-15/Barnim EMRSA does not exist in KSA at all, or whether it is just less common than the other CC22-MRSA-IV strains.

UK-EMRSA-15/Barnim EMRSA was found in other countries in the region. The higher prevalence of this strain in Kuwait and the UAE than in KSA could possibly be attributed to the higher number of European expatriates and tourists in Kuwait and the UAE.

One might also wonder what makes CC22-MRSA-IV so successful an entity that at least six different CC22-MRSA-IV strains co-exist in the Arabian Gulf region.

The isolation and characterization of these isolates underscores the diversity of CC22 MRSA strains based on SCC*mec* subtyping, as well as the potential of SCC*mec* subtyping for molecular epidemiology. It also calls for continued surveillance and screening, including the application of highly sensitive molecular methods for the characterization of isolates.

Acknowledgements

The authors thank the clinical and laboratory staff of the institutions involved in caring for the patients, culturing *S. aureus*, and performing conventional identification and susceptibility tests. We acknowledge E. Müller, A. Reissig, B. Stieber (Jena), and A. Ruppelt-Lorz (Dresden) for their technical support with the array experiments, as well as P. Slickers (Jena) for bioinformatics work.

Funding: There was no external funding for this work. Each of the participating institutions covered the costs of experiments performed in the respective institutions, as well as granted the time needed to perform this study.

Ethical approval: MRSA typing (research project E-15-1406) at King Khalid University Hospital, Riyadh, Kingdom of Saudi Arabia, was reviewed and approved by the Institutional Review Board. Any identifying information on the index case has been omitted. The patient gave consent for the publication of this anonymized report. The other parts of this study deal with molecular typing/epidemiological surveillance based on archived isolates without accompanying patient-related information, for which no ethical approval was required.

Conflict of interest: Ralf Ehricht and Stefan Monecke are employees of Alere Technologies, the company that manufactures the microarrays used in this study. The arrays used herein are (or will be developed to be) a marketed product.

References

1. O'Neill GL, Murchan S, Gil-Setas A, Aucken HM. Identification and characterization of phage variants of a strain of epidemic methicillin-resistant *Staphylococcus aureus* (EMRSA-15). *J Clin Microbiol* 2001;**39**:1540–8.
2. Richardson JF, Reith S. Characterization of a strain of methicillin-resistant *Staphylococcus aureus* (EMRSA-15) by conventional and molecular methods. *J Hosp Infect* 1993;**25**:45–52.
3. Aires de Sousa M, Correia B, de Lencastre H. Changing patterns in frequency of recovery of five methicillin-resistant *Staphylococcus aureus* clones in Portuguese hospitals: surveillance over a 16-year period. *J Clin Microbiol* 2008;**46**:2912–7.
4. Albrecht N, Jatzwauk L, Slickers P, Ehricht R, Monecke S. Clonal replacement of epidemic methicillin-resistant *Staphylococcus aureus* strains in a German university hospital over a period of eleven years. *PLoS One* 2011;**6**:e28189.
5. El-Mahdy TS, El-Ahmady M, Goering RV. Molecular characterization of methicillin-resistant *Staphylococcus aureus* isolated over a 2-year period in a Qatari hospital from multinational patients. *Clin Microbiol Infect* 2014;**20**:169–73.

6. Enright M, Robinson D, Randle G, Feil E, Grundmann H, Spratt B. The evolutionary history of methicillin-resistant *Staphylococcus aureus* (MRSA). *Proc Natl Acad Sci U S A* 2002;**99**:7687–92.
7. Faria NA, Oliveira DC, Westh H, Monnet DL, Larsen AR, Skov R, et al. Epidemiology of emerging methicillin-resistant *Staphylococcus aureus* (MRSA) in Denmark: a nationwide study in a country with low prevalence of MRSA infection. *J Clin Microbiol* 2005;**43**:1836–42.
8. Gosbell IB, Barbagiannakos T, Neville SA, Mercer JL, Vickery AM, O'Brien FG, et al. Non-multiresistant methicillin-resistant *Staphylococcus aureus* bacteraemia in Sydney, Australia: emergence of EMRSA-15, Oceania, Queensland and Western Australian MRSA strains. *Pathology* 2006;**38**:239–44.
9. Hsu LY, Loomba-Chlebicka N, Koh YL, Tan TY, Krishnan P, Lin RT, et al. Evolving EMRSA-15 epidemic in Singapore hospitals. *J Med Microbiol* 2007;**56**:376–9.
10. Kinnevey PM, Shore AC, Brennan GI, Sullivan DJ, Ehricht R, Monecke S, et al. Extensive genetic diversity identified among sporadic methicillin-resistant Staphylococcus aureus isolates recovered in Irish hospitals between 2000 and 2012. *Antimicrob Agents Chemother* 2014;**58**:1907–17.
11. Monecke S, Coombs G, Shore AC, Coleman DC, Akpaka P, Borg M, et al. A field guide to pandemic, epidemic and sporadic clones of methicillin-resistant *Staphylococcus aureus*. *PLoS One* 2011;**6**:e17936.
12. Moore PC, Lindsay JA. Molecular characterisation of the dominant UK methicillin-resistant *Staphylococcus aureus* strains, EMRSA-15 and EMRSA-16. *J Med Microbiol* 2002;**51**:516–21.
13. Murchan S, Kaufmann ME, Deplano A, de Ryck R, Struelens M, Zinn CE, et al. Harmonization of pulsed-field gel electrophoresis protocols for epidemiological typing of strains of methicillin-resistant *Staphylococcus aureus*: a single approach developed by consensus in 10 European laboratories and its application for tracing the spread of related strains. *J Clin Microbiol* 2003;**41**:1574–85.
14. Nimmo GR, Coombs GW, Pearson JC, O'Brien FG, Christiansen KJ, Turnidge JD, et al. Methicillin-resistant *Staphylococcus aureus* in the Australian community: an evolving epidemic. *Med J Aust* 2006;**184**:384–8.
15. O'Brien FG, Lim TT, Chong FN, Coombs GW, Enright MC, Robinson DA, et al. Diversity among community isolates of methicillin-resistant *Staphylococcus aureus* in Australia. *J Clin Microbiol* 2004;**42**:3185–90.
16. Pérez-Roth E, Lorenzo-Díaz F, Batista N, Moreno A, Méndez-Álvarez S. Tracking methicillin-resistant *Staphylococcus aureus* clones during a 5-year period (1998 to 2002) in a Spanish hospital. *J Clin Microbiol* 2004;**42**:4649–56.
17. Scicluna E, Shore A, Thuermer A, Ehricht R, Slickers P, Borg M, et al. Characterisation of MRSA from Malta and the description of a Maltese epidemic MRSA strain. *Eur J Clin Microbiol Infect Dis* 2010;**29**:163–70.
18. Smith JM, Cook GM. A decade of community MRSA in New Zealand. *Epidemiol Infect* 2005;**133**:899–904.
19. Tavares A, Miragaia M, Rolo J, Coelho C, de Lencastre H. High prevalence of hospital-associated methicillin-resistant *Staphylococcus aureus* in the community in Portugal: evidence for the blurring of community–hospital boundaries. *Eur J Clin Microbiol Infect Dis* 2013;**32**:1269–83.
20. Udo EE, Al-Sweih N, Noronha B. Characterisation of non-multiresistant methicillin-resistant *Staphylococcus aureus* (including EMRSA-15) in Kuwait Hospitals. *Clin Microbiol Infect* 2006;**12**:262–9.
21. Witte W, Enright M, Schmitz FJ, Cuny C, Braulke C, Heuck D. Characteristics of a new epidemic MRSA in Germany ancestral to United Kingdom EMRSA 15. *Int J Med Microbiol* 2001;**290**:677–82.
22. Aqel AA, Alzoubi HM, Vickers A, Pichon B, Kearns AM. Molecular epidemiology of nasal isolates of methicillin-resistant *Staphylococcus aureus* from Jordan. *J Infect Public Health* 2015;**8**:90–7.
23. Biber A, Abuelaish I, Rahav G, Raz M, Cohen L, Valinsky L, et al. A typical hospital-acquired methicillin-resistant *Staphylococcus aureus* clone is widespread in the community in the Gaza Strip. *PLoS One* 2012;**7**:e42864.
24. Laham NA, Mediavilla JR, Chen L, Abdelateef N, Elamreen FA, Ginocchio CC, et al. MRSA clonal complex 22 strains harboring toxic shock syndrome toxin (TSST-1) are endemic in the primary hospital in Gaza. *Palestine PLoS One* 2015;**10**:e0120008.
25. Udo EE, Boswihi SS, Al-Sweih N. High prevalence of toxic shock syndrome toxin-producing epidemic methicillin-resistant *Staphylococcus aureus* 15 (EMRSA-15) strains in Kuwait hospitals. *New Microbes New Infect* 2016;**12**:24–30.
26. Wolter DJ, Chatterjee A, Varman M, Goering RV. Isolation and characterization of an epidemic methicillin-resistant *Staphylococcus aureus* 15 variant in the central United States. *J Clin Microbiol* 2008;**46**:3548–9.
27. Monecke S, Skakni L, Hasan R, Ruppelt A, Ghazal SS, Hakawi A, et al. Characterisation of MRSA strains isolated from patients in a hospital in Riyadh, Kingdom of Saudi Arabia. *BMC Microbiol* 2012;**12**:146.
28. Goudarzi M, Goudarzi H, Sá Figueiredo AM, Udo EE, Fazeli M, Asadzadeh M, et al. Molecular characterization of methicillin resistant *Staphylococcus aureus* strains isolated from intensive care units in Iran: ST22-SCC*mec* IV/t790 emerges as the major clone. *PLoS One* 2016;**11**:e0155529.
29. D'Souza N, Rodrigues C, Mehta A. Molecular characterization of methicillin resistant *Staphylococcus aureus* (MRSA) with emergence of epidemic clones ST 22 and ST 772, in Mumbai, India. *J Clin Microbiol* 2010;**48**:1806–11.
30. Nadig SD, Ramachandraraju SN, Arakere GN. Epidemic methicillin resistant *Staphylococcus aureus* (EMRSA-15) variants detected from healthy and diseased individuals in India. *J Med Microbiol* 2010;**59**:815–21.
31. Rajan V, Schoenfelder SM, Ziebuhr W, Gopal S. Genotyping of community-associated methicillin resistant *Staphylococcus aureus* (CA-MRSA) in a tertiary care centre in Mysore South India: ST2371-SCCmec IV emerges as the major clone. *Infect Genet Evol* 2015;**34**:230–5.
32. Rossney AS, Shore AC, Morgan PM, Fitzgibbon MM, O'Connell B, Coleman DC. The emergence and importation of diverse genotypes of methicillin-resistant *Staphylococcus aureus* (MRSA) harboring the Panton–Valentine leukocidin gene (*pvl*) reveal that *pvl* is a poor marker for community-acquired MRSA strains in Ireland. *J Clin Microbiol* 2007;**45**:2554–63.
33. Linde H, Wagenlehner F, Strommenger B, Drubel I, Tanzer J, Reischl U, et al. Healthcare-associated outbreaks and community-acquired infections due to MRSA carrying the Panton–Valentine leucocidin gene in southeastern Germany. *Eur J Clin Microbiol Infect Dis* 2005;**24**:419–22.
34. Monecke S, Slickers P, Ehricht R. Assignment of *Staphylococcus aureus* isolates to clonal complexes based on microarray analysis and pattern recognition. *FEMS Immunol Med Microbiol* 2008;**53**:237–51.
35. Monecke S, Baier V, Coombs GW, Slickers P, Ziegler A, Ehricht R. Genome sequencing and molecular characterisation of *Staphylococcus aureus* ST772-MRSA-V, ''Bengal Bay Clone''. *BMC Res Notes* 2013;**6**:1–7.