Staphylococcus aureus

Olivier Denis
Université Libre De Bruxelles
Staphylococcus aureus

- Major opportunistic pathogen responsible for infections both in hospitals and in the community

- Clinical manifestations
  - Pyogenic infections: Skin and soft tissue infections to endocarditis
  - Toxin mediated diseases: SSSS, SFP, TSS

- Master of creating/picking up resistance determinants

![Diagram showing the timeline of resistance determinants acquisition]

- 1942 Pen R
- 1961 Oxa R
- 1969 Genta R
- 1997 Vanco I
- 2002 Vanco R
Penicillin resistance

• **Production of penicillinase**
  – Encoding by *blaZ*
  – Inhibited by clavulanic acid
  – Tested by cefinase test or by disk diffusion method
  – Difficult to detect in coagulase negative staphylococci

![Susceptible](image1.png) ![Resistant](image2.png)

Examples of inhibition zones for *Staphylococcus aureus* with benzylpenicillin.

- a) Fuzzy zone edge and zone diameter ≥ 26 mm. Report susceptible.
- b) Sharp zone edge and zone diameter ≥ 26 mm. Report resistant.
Methicillin-resistant *S. aureus* (MRSA)

- **Acquisition of** *mec* **gene encoding** PBP2a
  - PBP2a shows low affinity to β-lactams
  - **Cross-resistance** to all β-lactams, except for the novel anti-MRSA cephalosporins
  - Three different types described: *meca*, *(mecB)*, *mecC*

- **The** *mec* **gene is integrated into mobile genetic element**
  - Staphylococcal cassette chromosome *mec* (SCC*mec*)
  - Chromosomal insertion at the attB_{SCC} at the end of orfX
  - Often contain plasmids or transposons carrying resistance genes

  ![Methicillin-resistant S. aureus (MRSA) Diagram](image)

Ito t. et al. Antimicrob Agents Chemother 2012;4997
Staphylococcal Cassette Chromosome mec

Classification according to
- **Types**: combination of mec and ccr
- **Variants**: difference into junkyard regions.

<table>
<thead>
<tr>
<th>SCCmec</th>
<th>Type ccr</th>
<th>Type mec</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (1B)</td>
<td>1</td>
<td>A1B1</td>
</tr>
<tr>
<td>II (2A)</td>
<td>2</td>
<td>A2B2</td>
</tr>
<tr>
<td>III (3A)</td>
<td>3</td>
<td>A3B3</td>
</tr>
</tbody>
</table>

Novel Type XII Staphylococcal Cassette Chromosome mec Harboring a New Cassette Chromosome Recombinase, CcrC2

Zhaowei Wu, a Fan Li, a Dongliang Liu, a Huping Xue, a Xin Zhao a,b
College of Animal Science and Technology, Northwest A&F University, Yangling, Shaanxi, People’s Republic of China; Department of Animal Science, McGill University, Ste. Anne de Bellevue, Quebec, Canada

Which penicillins to test for detection of methicillin resistance?

*S. aureus* with oxacillin MIC > 2 mg/l are mostly MRSA due to the presence of *mecA* gene

**Staphylococcus** spp.

<table>
<thead>
<tr>
<th>Penicillins</th>
<th>MIC breakpoint (mg/L)</th>
<th>Disk content (μg)</th>
<th>Zone diameter breakpoint (mm)</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benzylpenicillin, <em>S. aureus</em></td>
<td>0.125&lt;sup&gt;1&lt;/sup&gt;, 0.125&lt;sup&gt;1&lt;/sup&gt;</td>
<td>1 unit</td>
<td>S &lt;br&gt; R &gt;</td>
<td>Numbered notes relate to general comments and/or MIC breakpoints. Lettered notes relate to the disk diffusion method.</td>
</tr>
<tr>
<td>Benzylpenicillin, <em>S. lugdunensis</em></td>
<td>0.125&lt;sup&gt;1&lt;/sup&gt;, 0.125&lt;sup&gt;1&lt;/sup&gt;</td>
<td>1 unit</td>
<td>S &gt; &lt;br&gt; R &lt;</td>
<td></td>
</tr>
<tr>
<td>Benzylpenicillin, <em>Coagulase-negative staphylococci</em></td>
<td>Note&lt;sup&gt;2&lt;/sup&gt;</td>
<td>2 &lt;br&gt; Isovaleric acid &lt;br&gt; Phenoxymethylpenicillin</td>
<td>Note&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Ampicillin, <em>S. caprophilus</em></td>
<td>Note&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Amoxicillin-sulbactam</td>
<td>Note&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
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<tr>
<td>Amoxicillin</td>
<td>Note&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Amoxicillin-clavulanic acid</td>
<td>Note&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
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<tr>
<td>Piperacillin</td>
<td>Note&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Piperacillin-tazobactam</td>
<td>Note&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;3&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Ticarcillin</td>
<td>Note&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Ticarcillin-clavulanic acid</td>
<td>Note&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Phenoxymethylpenicillin</td>
<td>Note&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Oxacillin&lt;sup&gt;4&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Cloxacillin</td>
<td>Note&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Dicloxacillin</td>
<td>Note&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;2&lt;/sup&gt;</td>
<td></td>
</tr>
<tr>
<td>Flucloxacillin</td>
<td>Note&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;1&lt;/sup&gt;</td>
<td>Note&lt;sup&gt;2&lt;/sup&gt;</td>
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**Macrolins (uncomplicated UTI only)**

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**EUCAST Clinical Breakpoint Tables v. 6.0, valid from 2016-01-01**

**Disk diffusion (EUCAST standardised disk diffusion method)**
- **Medium**: Mueller-Hinton agar
- **Inoculum**: McFarland 0.5
- **Incubation**: Aerobic, 35±1°C, 18±2h
- **Reading**: Read zone edges as the point showing no growth viewed from the back of the plate against a dark background illuminated with reflected light (except for benzylpenicillin and lincomycin, see below).
- **Quality control**: *Staphylococcus aureus* ATCC 29213

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<sup>1</sup> Most staphylococci are penicillinase producers, which are resistant to benzylpenicillin, phenoxymethylpenicillin, ampicillin, amoxicillin, piperacillin and ticarcillin. Isolates negative for penicillinase and susceptible to methicillin can be reported susceptible to these agents. Isolates positive for penicillinase and methicillin susceptible are susceptible to beta-lactamase inhibitor combinations and isoxazolylpenicillins (oxacillin, cloxacillin, dicloxacillin and fluclaxacillin).

<sup>2</sup> Methicillin-resistant isolates are, with few exceptions, resistant to all beta-laactam agents.

<sup>3</sup> No currently available method can reliably detect penicillinase production in coagulase-negative staphylococci.

<sup>4</sup> All isolates resistant to amoxicillin and amoxicillin-sulbactam are likely to be resistant to other beta-lactam agents.

<sup>5</sup> All isolates resistant to amoxicillin-clavulanic acid are likely to be resistant to other beta-lactam agents.

<sup>6</sup> All isolates resistant to piperacillin-tazobactam are likely to be resistant to other beta-lactam agents.

<sup>7</sup> All isolates resistant to ticarcillin or ticarcillin-clavulanic acid are likely to be resistant to other beta-lactam agents.

<sup>8</sup> The corresponding oxacillin MIC for coagulase-negative staphylococci other than *S. saprophyticus* and *S. lugdunensis* is ≤0.25 mg/L.
Which cephalosporins to test?

**Cefoxitin**
- Interpretation for all penicillins, cephalosporins and carbapenems with the exception of anti-MRSA cephalosporins (ceftaroline, ceftobiprole)
- Disk diffusion
- Interpretative criteria according to species

<table>
<thead>
<tr>
<th>Cefoxitin (screen), S. aureus, S. lugdunensis and S. saprophyticus</th>
<th>Disk content</th>
<th>S≥</th>
<th>R&lt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Note³</td>
<td>30</td>
<td>22⁰</td>
<td>22⁰</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cefoxitin (screen), Coagulase-negative staphylococci other than S. lugdunensis and S. saprophyticus</th>
<th>Disk content</th>
<th>S≥</th>
<th>R&lt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Note⁴</td>
<td>30</td>
<td>25⁰</td>
<td>25⁰</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cefoxitin (screen), S. pseudintermedius</th>
<th>Disk content</th>
<th>S≥</th>
<th>R&lt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Note⁴</td>
<td>30</td>
<td>35⁰</td>
<td>35⁰</td>
</tr>
</tbody>
</table>

- MIC values > 4 mg/l can be considered as methicillin-resistant
- Confirmation
  - PCR for mecA and mecC genes
  - PBP2a detection by immunochromatographic or latex assay
Methicillin-resistant *S. aureus*?

- CMI oxacillin: 6 mg/l
- CMI cefoxitin: 24 mg/l
- Negative PCR *mecA*
- Positive PCR *mecC*

Less than 1% of MRSA sent to reference lab.
Epidemiology and host range

*mecC* MRSA found in multiple host species across Europe
Anti-MRSA cephalosporins

Ceftaroline

- New anti-MRSA cephalosporin
- Increased affinity to PBP2a
- Low emergence of ceftaroline resistant *S. aureus*
  - From mutations in native pbp genes (PBP2 and PBP3) or *mecA*
  - Overexpression of pbp4 gene

Identification of non-PBP2a resistance mechanisms in *Staphylococcus aureus* after serial passage with ceftaroline: involvement of other PBPs

Sushmita D. Lahiri† and Richard A. Alm‡†

Argudin M et al. JAC 2016
Lahiri SD JAC 2016
**MLS resistance in staphylococci**

<table>
<thead>
<tr>
<th>Genes</th>
<th>Mode of action</th>
<th>Resistance phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Ery</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Clinda</td>
</tr>
<tr>
<td><strong>ermA, ermC</strong></td>
<td>Target modification</td>
<td>MLSb&lt;sub&gt;iouc&lt;/sub&gt;</td>
</tr>
<tr>
<td>(other ermB,</td>
<td></td>
<td>R</td>
</tr>
<tr>
<td>ermT)</td>
<td></td>
<td>R/s *</td>
</tr>
<tr>
<td><strong>msrA/B</strong></td>
<td>Efflux</td>
<td>M</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S</td>
</tr>
<tr>
<td><strong>lnu (rare)</strong></td>
<td>Acetylation</td>
<td>L</td>
</tr>
<tr>
<td></td>
<td></td>
<td>S</td>
</tr>
<tr>
<td></td>
<td></td>
<td>R</td>
</tr>
</tbody>
</table>

* According to the phenotype inducible or constitutive
Resistance phenotype to ML

If presence of antagonism between clindamycin and erythromycin, clindamycin should be reported as resistant
**Aminoglycoside modifying enzymes**

<table>
<thead>
<tr>
<th>Genes</th>
<th>Resistance phenotype</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>aph(3’)</td>
<td>Kana, amika*, isepa*</td>
</tr>
<tr>
<td>ant(4’)</td>
<td>Kana, Tobra, amika*, isepa*</td>
</tr>
<tr>
<td>aac(6’)-aph(2’’)</td>
<td>Kana, Tobra, Genta, amika*, isepa*, netil*</td>
</tr>
</tbody>
</table>

**Resistance to amikacin** is determined by using **kanamycin** (MIC > 8 mg/l)
Breakpoints are different between S. aureus and coagulase-negative staphylococci.
Aminoglycosides resistance

Phenotype KTG

*aac6’-aph2 ’’*

Phenotype K

*aph3’*

Phenotype KT

*ant4’*

Resistance to amikacin can be deducted by kanamycin resistance (MIC > 8 mg/L)
Vancomycin resistance in *Staphylococcus aureus*

**Susceptible population**

**Hetero low-level resistance (hVISA)**
Heterogenous population
10^{-6} to 10^{-9} resistant bacteria

**Low-level resistance (VISA)**
Homogenous population

**High resistance (VRSA)**
Homogenous population

*Methicillin-resistant Staphylococcus aureus clinical strain with reduced vancomycin susceptibility*


K. Hiramatsu*, H. Hanaki*, T. Ino⁶, K. Yabuta⁶, T. Oguri⁷ and F. C. Tenover⁷
# Glycopeptide Breakpoints for *Staphylococci*, 2016

<table>
<thead>
<tr>
<th></th>
<th>MIC (mg/L) for</th>
<th></th>
<th></th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Vancomycin</td>
<td></td>
<td>Teicoplanin</td>
</tr>
<tr>
<td></td>
<td>S</td>
<td>I</td>
<td>R</td>
</tr>
<tr>
<td>EUCAST for <em>S. aureus</em></td>
<td>≤2</td>
<td>&gt;2</td>
<td>≤2</td>
</tr>
<tr>
<td>EUCAST for CoNS</td>
<td>≤4</td>
<td>&gt;4</td>
<td>≤4</td>
</tr>
<tr>
<td>CLSI for <em>S. aureus</em></td>
<td>≤2</td>
<td>4-8</td>
<td>≥16</td>
</tr>
<tr>
<td>CLSI for CoNS</td>
<td>≤4</td>
<td>8-16</td>
<td>≥32</td>
</tr>
</tbody>
</table>

[http://www.eucast.org/clinical_breakpoints/](http://www.eucast.org/clinical_breakpoints/)
[CLSI 2014 M100-S24](http://www.eucast.org/clinical_breakpoints/)
Low level resistance

- **Genetic environment**
  - Multiple point mutations leading to modified peptidoglycans synthesis
  - No *van* genes and not linked to methicillin resistance

- **Thickness of cell wall**
  - ↑ synthesis of peptidoglycan, ↓ autolytic activity, ↑ residues D-Alanyl-D-Alanine

- **Absorption of GLYCOPEPTIDES** into bacterial cell wall before external membrane surface

⇒ **Low level resistance and reversible**
  - Teicoplanin > vancomycin
  - MIC to vancomycin 4 – 8 mg/L

Denis O. et al. JAC 2002;50:755
Mechanism of high level resistance

• Transfer of Tn1546 carrying vanA gene
  – *E. faecalis* ⇒ *S. aureus*

• Modification of peptidoglycan synthesis
  – Substitution of D-Ala-D-Ala by D-Ala-D-Lac
  – ↓↓ affinity to vancomycin $10^3$

• High level resistance
  – Vancomycin >> teicoplanin
  – MIC vancomycin > 16-256 mg/l

• Frequency
  – Only about 30 cases reported from USA, India, Iran, Brazil and Portugal

Gould IM Lancet Infect. Dis 2012
Challenge for detection of glycopeptide resistance in *Staphylococci*

- **Disk diffusion**
  - Cannot be used for (h-)GISA

- **Detection of (h-)GISA**
  - As proven difficult
  - Divided into screening and confirmation
  - Screening: macromethods, GRD, agar screen
  - Reversible phenotype
MIC determination for GISA and GRSA

• **Broth microdilution = gold standard**

• **May also be determined by**
  - Gradient strip methods (E-test), agar dilution and automated systems
  - E-tests show MICs with 0.5-1 two-fold dilution steps higher than broth microdilution
  - Isolates with MICs >2 mg/L should be confirmed

HIP5827
Screening method for GISA

• **Macromethod**
  – Should not be reported as MICs
  – Does not differentiate between hGISA and GISA
  – High inoculum (2,0 McF) on BHI agar for 48h

• **GISA detection by gradient test**
  – Double strip vancomycin and teicoplanin
  – 0.5 McF on MH agar for 24 and 48h
Laboratory performance of methods for detection hGISA

<table>
<thead>
<tr>
<th>Method</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vancomycin broth MIC&lt;sup&gt;b&lt;/sup&gt;</td>
<td>11%</td>
<td>100%</td>
<td>372</td>
</tr>
<tr>
<td>BHIA + vancomycin at 6 μg per ml, 10 μl of a 0.5-McFarland-standard suspension (BHIA6V)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>48 h, 4.5–12%</td>
<td>48 h, 68–100%</td>
<td>370, 389, 393</td>
</tr>
<tr>
<td>MHA + teicoplanin at 5 μg per ml, 10 μl of a 2-McFarland-standard suspension (MHA5T)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>48 h, 65–79%</td>
<td>48 h, 35–95%</td>
<td>82, 252, 370, 389, 393</td>
</tr>
<tr>
<td>MHA + teicoplanin at 5 μg per ml, 10 μl of a 2-McFarland-standard suspension&lt;sup&gt;e&lt;/sup&gt;</td>
<td>48 h, 98%</td>
<td>48 h, 53%</td>
<td>82</td>
</tr>
<tr>
<td>MHA + vancomycin at 5 μg per ml, 10 μl of a 0.5-McFarland-standard suspension</td>
<td>48 h, 1–20%</td>
<td>48 h, 59–99%</td>
<td>370, 372</td>
</tr>
<tr>
<td>Simplified PAP&lt;sup&gt;f&lt;/sup&gt;</td>
<td>48 h, 71%</td>
<td>48 h, 88%</td>
<td>372</td>
</tr>
<tr>
<td>Macromethod Etest (MET)</td>
<td>48 h, 69–98.5%</td>
<td>48 h, 89–94%</td>
<td>174, 289, 370, 372, 389</td>
</tr>
<tr>
<td>Etest GRD</td>
<td>24 h, 70–77%</td>
<td>24 h, 98–100%</td>
<td>174, 393</td>
</tr>
<tr>
<td></td>
<td>48 h, 93–94%</td>
<td>48 h, 82–95%</td>
<td></td>
</tr>
</tbody>
</table>

As low prevalence, low positive predictive value
Confirmation test

- Population analysis profile-area under curve (PAP-AUC)
  - Isolate screening positive for reduced susceptibility
  - Not identified as GRSA or GISA by MIC determination

- Method
  - Population analysis for vancomycin
  - Determine ratio of AUC of test organism vs Mu3 (ATCC 700698)
Linezolid resistance

- **Mechanisms of resistance**
  - Mutations in domain V of 23S rRNA (G2576T) or other genes encoding ribosomal proteins
  - **Transferable mechanisms on plasmids**
    - Methylation of nucleotide A2503 encoded by *cfr* gene located on plasmids resistance to PhLOPS<sub>A</sub>
    - ABC transporter encoded by *optrA* gene only in *S. sciuri* resistance to PhO
- **Described in** *S. aureus* and CoNS isolates from animals and humans including Belgium
- Resistance: rare (<1%) but outbreaks occurred

Vanderhaeghen W, et al. JAC 2012
Diaz L et al. AAC 2012
Morales G et al. CID 2012
Sánchez García M et al. JAMA 2010

Clinical Outbreak of Linezolid-Resistant *Staphylococcus aureus* in an Intensive Care Unit

Context: Linezolid resistance is extremely uncommon in *Staphylococcus aureus.*
cfr-Positive MRSA ST398

- LA-MRSA ST398
- Resistance to chloramphenicol and clindamycin
- Linezolid susceptible?
- Not detected by disk diffusion using CLSI guidelines
- MIC to linezolid = 12 mg/L
Emergence of cfr-positive \textit{S. aureus} in Belgium

- **Humans**
  - 1464 \textit{S. aureus} isolates from 2013 to 2015 sent by 167 laboratories
  - 30 resistant to chloramphenicol, clindamycin and/or linezolid
  - One cfr-positive MRSA belonging to CC398 collected from patient with SSI
  - Linezolid MIC = 12 mg/l

- **Animals**
  - Occasionally found in \textit{S. aureus} and non \textit{S. aureus}
  - Pigs, veals

\textbf{Characterization of methicillin-resistant non-\textit{Staphylococcus aureus} staphylococci carriage isolates from different bovine populations}

\textbf{Results}: The MRNAS (n=101) carriage rate was estimated as 30.29\% (95\% CI 6.14\%–74.28\%) in veal calves, 13.1\% (95\% CI 1.28\%–63.72\%) in dairy cows and 24.8\% (95\% CI 11.97\%–44.42\%) in beef cows. Carriage rates were not significantly different between the three populations (P > 0.05). meCA_{6393} was not detected. Most (n=80) MRNAS were identified as \textit{Staphylococcus sciuri}, \textit{Staphylococcus lentus} or \textit{Staphylococcus aureus}. Resistance to ampicillin, clindamycin, lincomycin, streptomycin, tetracycline, and \textit{ciprofloxacin} was frequently detected. Two linezolid-resistant MRNAS from veal calves carried the multidrug-resistance gene cfr. SCCmec cassettes of type III predominated (n=46); another 40 SCCmec cassettes harbored a class B mec complex. In all isolates, the meca gene was present.\textit{Staphylococcus} and \textit{Staphylococcus aureus} MRNAS were detected in low frequencies, especially in methicillin-resistant \textit{Staphylococcus epidermidis}.

\textbf{Conclusions}: The SCCmec types predominating in bovine MRNAS differ from those mostly detected in livestock-associated methicillin-resistant \textit{S. aureus} strains. Yet, the detection of cfr and the high level of other antimicrobial resistances suggest a potentially important role of bovine MRNAS as a reservoir for resistance determinants other than SCCmec.
Mupirocin resistance

MRSA + mupA

High-level of mupirocin resistance conferred by mupA > 256 mg/l
MRSA + \textit{mupA} négatif

Low-level resistance to mupirocin (2-256 mg/l)
Few examples
MRSA
MRSA

Phenotype GTK

$\text{aac}(6')-\text{aph}(2'')$

$\implies$ resistance to amikacin
MRSA

constitutive MLS\textsubscript{b} + erm\textsubscript{A}
MSSA

inducible MLS_b

ermC
MRSA
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