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FÜR RESISTENZFORSCHUNG

MRSA at the Human-Animal Interface
Epidemiology and Antimicrobial Susceptibility of MRSA in Animals

Henrike Krüger-Haker and Stefan Schwarz
ISSSI 2024, 18 – 21 August 2024
Perth, Western Australia

Henrike Krüger-Haker, PhD | Institute of Microbiology and Epizootics, School of Veterinary Medicine, Freie Universität Berlin | Germany

Outline

(1) Short Introduction to MRSA

- Genetic basis of methicillin resistance
- Differentiation of MRSA lineages
- Who is at risk at the Human-Animal Interface?

(2) Global Epidemiology of MRSA

(3) Relevant Clonal Complexes

Outline

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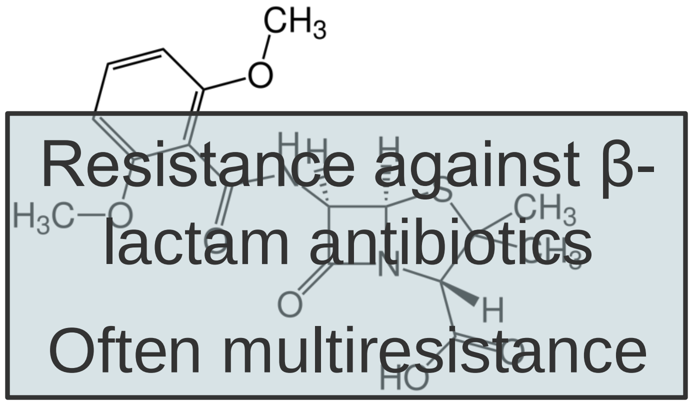
Methicillin-resistant *S. aureus* (MRSA)

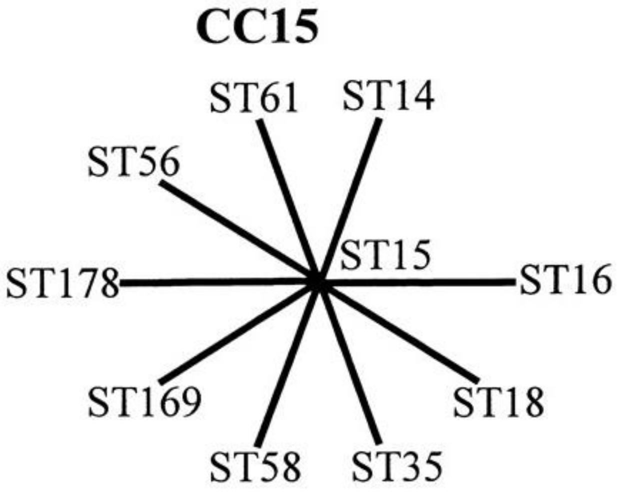
- **Methicillin** = first β-lactamase-stable penicillin (1959)
- Methicillin-resistance usually mediated by *mecA* and *mecC*
- located on mobile genetic element:
  Staphylococcal Cassette Chromosome *mec* (SCC*mec*)
- encode alternative penicillin-binding proteins with
  reduced affinity to β-lactams
- Sequence Type (**ST**): comparison of DNA sequences of internal fragments of seven house-keeping genes
  (multilocus sequence typing – MLST)
- Clonal Complex (**CC**): group of closely related STs

→ members have ≥ 5 of 7 loci in common with ≥ one other ST in the group



Resistance against β-lactam antibiotics

Often multiresistance



Feil et al., 2003, J Bacteriol, 185: 3307-16

MRSA

HA-MRSA = healthcare-associated MRSA

CA-MRSA = community-associated MRSA

LA-MRSA = livestock-associated MRSA

Pictures from pixabay.com

MRSA

	HA-MRSA	**CA-MRSA**	**LA-MRSA**
virulence	low	high	very low
antimicrobial resistance	high	low	variable

Panton-Valentine Leukocidin (PVL)
Toxic Shock Syndrome Toxin 1 (TSST-1)
various enterotoxins

almost no virulence genes
very rarely enterotoxin genes,
except: CC9/CC5 – *egc*

MRSA at the Human-Animal Interface

Who is at risk?

Animal owners in close contact to their animal(s)

→ change of the status of pet animals over the years

→ “family members” that enjoy particular privileges and veterinary care

Pictures from pixabay.com

MRSA at the Human-Animal Interface

Who is at risk?


Birgit Walther

108 dog owners in Germany

- sharing of house (88.9%), sofa (68.5%), and bed (39.8%)
- dogs are allowed to lick hands (93.5%) and face (52.8%), are washed in the same bathtub (32.4%)


PLoS one

Sharing More than Friendship — Nasal Colonization with Coagulase-Positive Staphylococci (CPS) and Co-Habitation Aspects of Dogs and Their Owners

Birgit Walther[1]*, Julia Hermes[2], Christiane Cuny[3], Lothar H. Wieler[1], Szilvia Vincze[1], Yassmin Abou Elnaga[1], Ivonne Stamm[4], Peter A. Kopp[4], Barbara Kohn[5], Wolfgang Witte[3], Andreas Jansen[2], Franz J. Conraths[6], Torsten Semmler[1], Tim Eckmanns[2], Antina Lübke-Becker[1]

1 Institute of Microbiology and Epizootics, Veterinary Faculty, Freie Universität Berlin, Germany, **2** Department for Infectious Disease Epidemiology, Robert Koch Institute, Berlin, Germany, **3** National Reference Centre for Staphylococci, Robert Koch Institute, Wernigerode Branch, Germany, **4** Vet Med Labor GmbH, Division of IDEXX Laboratories, Ludwigsburg, Germany, **5** Clinic of Small Animals, Veterinary Faculty, Freie Universität Berlin, Berlin, Germany, **6** Institute of Epidemiology, Friedrich-Loeffler-Institut, Federal Research Institute for Animal Health, Wusterhausen, Germany


Pictures from pixabay.com

MRSA at the Human-Animal Interface

Who is at risk?

People with **occupational** contact to animals

→ animal caretakers, veterinarians, vet med students, farmers, abattoir workers, …

→ in part, work environment in which commonly diseased animals are present and antimicrobial agents are used

Pictures from pixabay.com and Malisa Wille

MRSA at the Human-Animal Interface

Who is at risk?

Christiane Cuny

Nasal Colonization of Humans with Methicillin-Resistant *Staphylococcus aureus* (MRSA) CC398 with and without Exposure to Pigs

Christiane Cuny[1], Rolf Nathaus[3], Franziska Layer[1], Birgit Strommenger[1], Doris Altmann[2], Wolfgang Witte[1]*

1 Robert Koch Institute, Wernigerode Branc, Wernigerode, Germany, 2 Robert Koch Institute, Division of Epidemiology, Berlin, Germany, 3 Rolf Nathaus, Veterinary Practice, Reken, Germany

Source: https://www.lachschon.de/item/25314-hehe/

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(3) **Relevant Clonal Complexes**


OPEN ACCESS Freely available online

PLoS one

A Field Guide to Pandemic, Epidemic and Sporadic Clones of Methicillin-Resistant *Staphylococcus aureus*

Stefan Monecke[1,13]*, Geoffrey Coombs[2], Anna C. Shore[3], David C. Coleman[3], Patrick Akpaka[4], Michael Borg[5], Henry Chow[6], Margaret Ip[6], Lutz Jatzwauk[7], Daniel Jonas[8], Kristina Kadlec[9], Angela Kearns[10], Frederic Laurent[11], Frances G. O'Brien[12], Julie Pearson[2], Antje Ruppelt[1], Stefan Schwarz[9], Elizabeth Scicluna[5], Peter Slickers[13], Hui-Leen Tan[2], Stefan Weber[14], Ralf Ehricht[13]

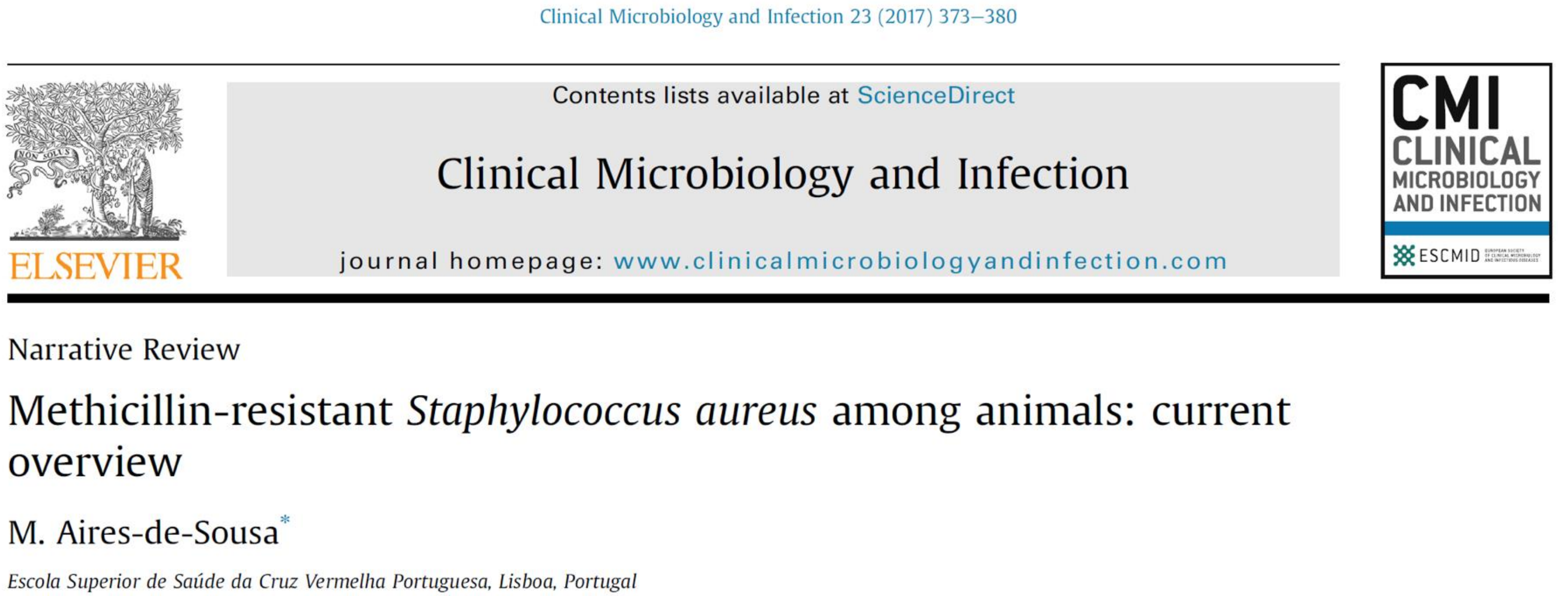
1 Institute for Medical Microbiology and Hygiene, Technical University of Dresden, Dresden, Germany, **2** Department of Microbiology and Infectious Diseases, PathWest Laboratory Medicine - WA, Royal Perth Hospital, Perth, Western Australia, Australia, **3** Microbiology Research Unit, Dublin Dental University Hospital, University of Dublin, Trinity College, Dublin, Ireland, **4** Department of Para-Clinical Sciences, The University of the West Indies, St. Augustine, Trinidad and Tobago, **5** Infection Control Unit, Mater Dei Hospital, Msida, Malta, **6** Department of Microbiology, Faculty of Medicine, The Chinese University of Hong Kong, Shatin, Hong Kong, China, **7** Infection Control Unit, Dresden University Hospital, Dresden, Germany, **8** Department of Environmental Health Sciences, Freiburg University Medical Centre, Freiburg, Germany, **9** Institute of Farm Animal Genetics, Friedrich-Loeffler-Institut (FLI), Neustadt-Mariensee, Germany, **10** Staphylococcus Reference Unit, Centre for Infections, Health Protection Agency, London, United Kingdom, **11** Université Lyon, Centre National de Référence des Staphylocoques, Lyon, France, **12** School of Biomedical Sciences, Curtin University, Perth, Western Australia, Australia, **13** Alere Technologies GmbH, Jena, Germany, **14** Sheikh Khalifa Medical City, Abu Dhabi, United Arab Emirates


Stefan Monecke


Ralf Ehricht


Geoffrey Coombs

Marta Aires-de-Sousa



Clinical Microbiology and Infection 23 (2017) 373–380

Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Narrative Review

Methicillin-resistant *Staphylococcus aureus* among animals: current overview

M. Aires-de-Sousa*

Escola Superior de Saúde da Cruz Vermelha Portuguesa, Lisboa, Portugal

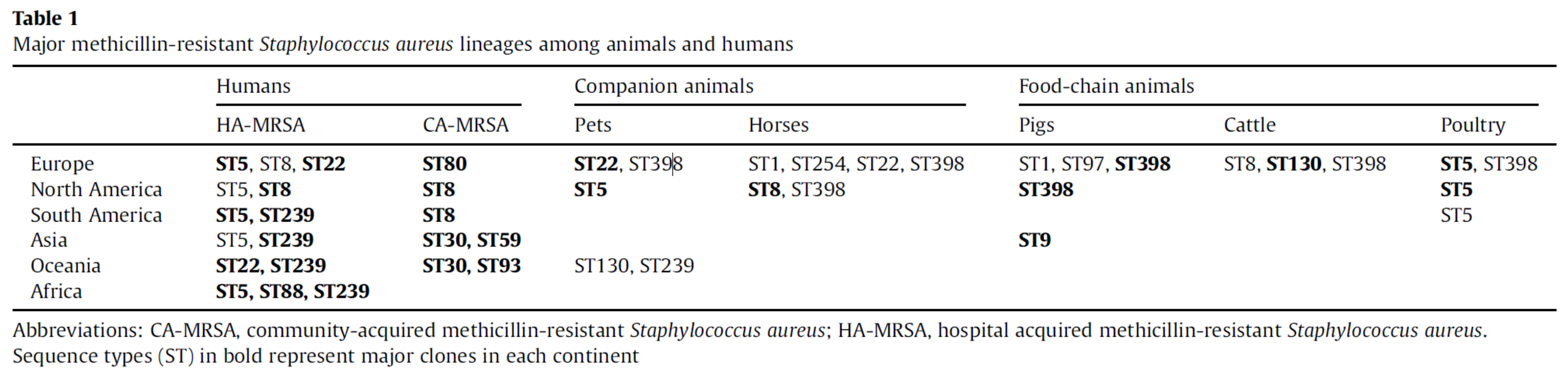
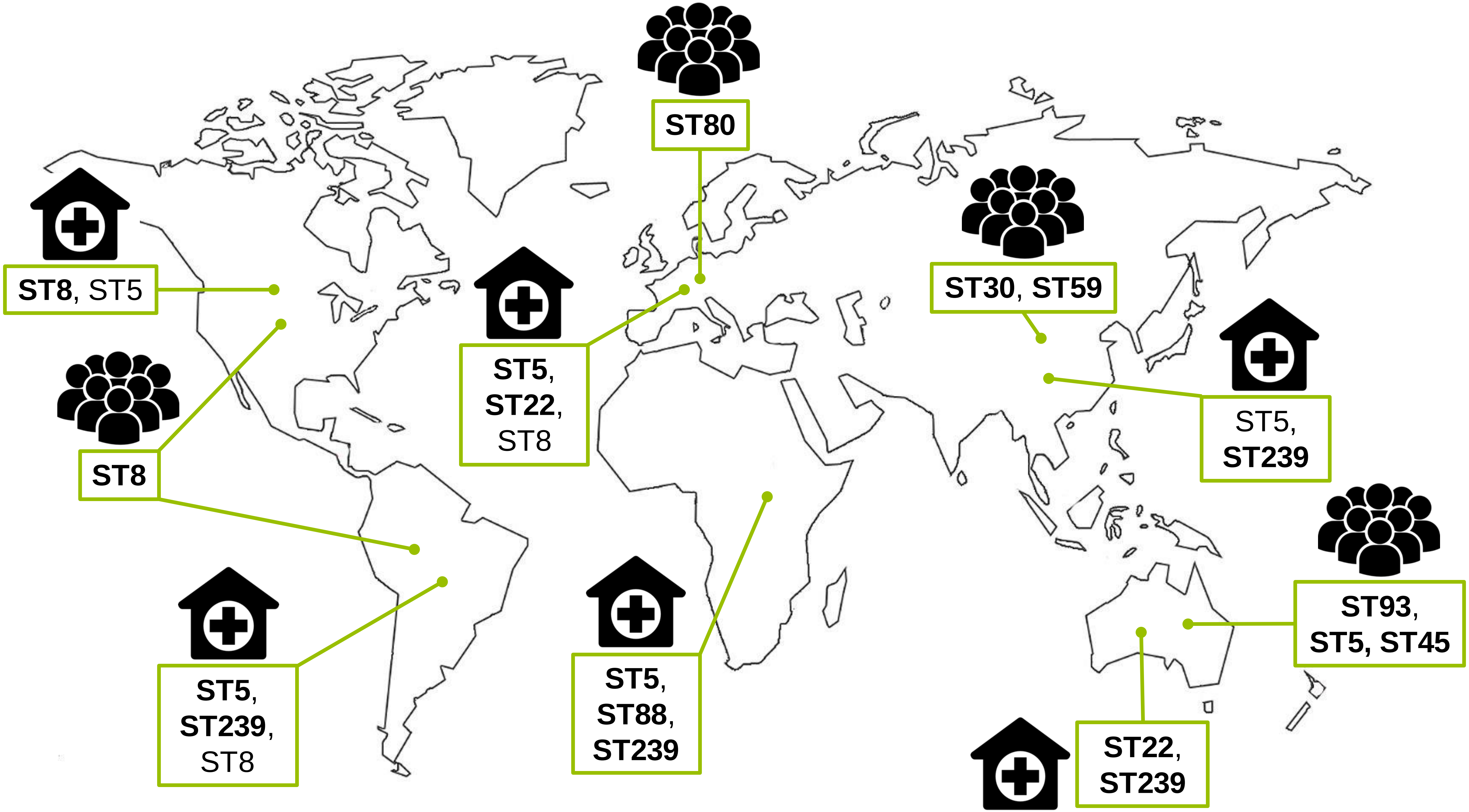


Table 1

Major methicillin-resistant *Staphylococcus aureus* lineages among animals and humans

	Humans		Companion animals		Food-chain animals		
	HA-MRSA	CA-MRSA	Pets	Horses	Pigs	Cattle	Poultry
Europe	**ST5**, ST8, **ST22**	**ST80**	**ST22**, ST398	ST1, ST254, ST22, ST398	ST1, ST97, **ST398**	ST8, **ST130**, ST398	**ST5**, ST398
North America	ST5, **ST8**	**ST8**	**ST5**	**ST8**, ST398	**ST398**		**ST5**
South America	**ST5, ST239**	**ST8**					ST5
Asia	ST5, **ST239**	**ST30, ST59**			**ST9**		
Oceania	**ST22, ST239**	**ST30, ST93**	ST130, ST239				
Africa	**ST5, ST88, ST239**						

Abbreviations: CA-MRSA, community-acquired methicillin-resistant *Staphylococcus aureus*; HA-MRSA, hospital acquired methicillin-resistant *Staphylococcus aureus*. Sequence types (ST) in bold represent major clones in each continent



ST80

ST8, ST5

ST5, ST22, ST8

ST30, **ST59**

ST5, **ST239**

ST8

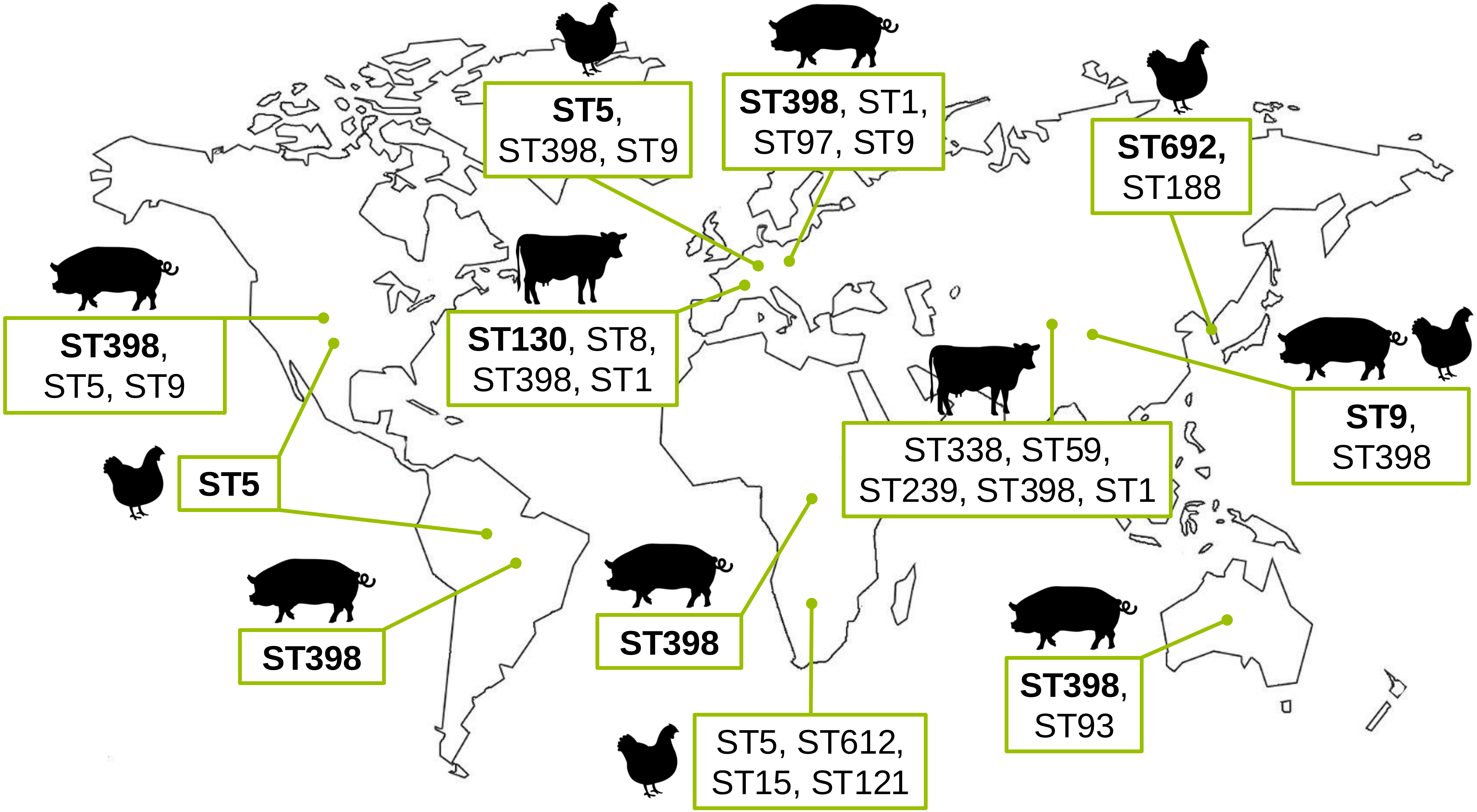
ST93, ST5, ST45

ST5, ST239, ST8

ST5, ST88, ST239

ST22, ST239

Icons from flaticon.com



ST5,
ST398, ST9

ST398, ST1,
ST97, ST9

ST692,
ST188

ST398,
ST5, ST9

ST130, ST8,
ST398, ST1

ST9,
ST398

ST338, ST59,
ST239, ST398, ST1

ST5

ST398

ST398

ST398,
ST93

ST5, ST612,
ST15, ST121

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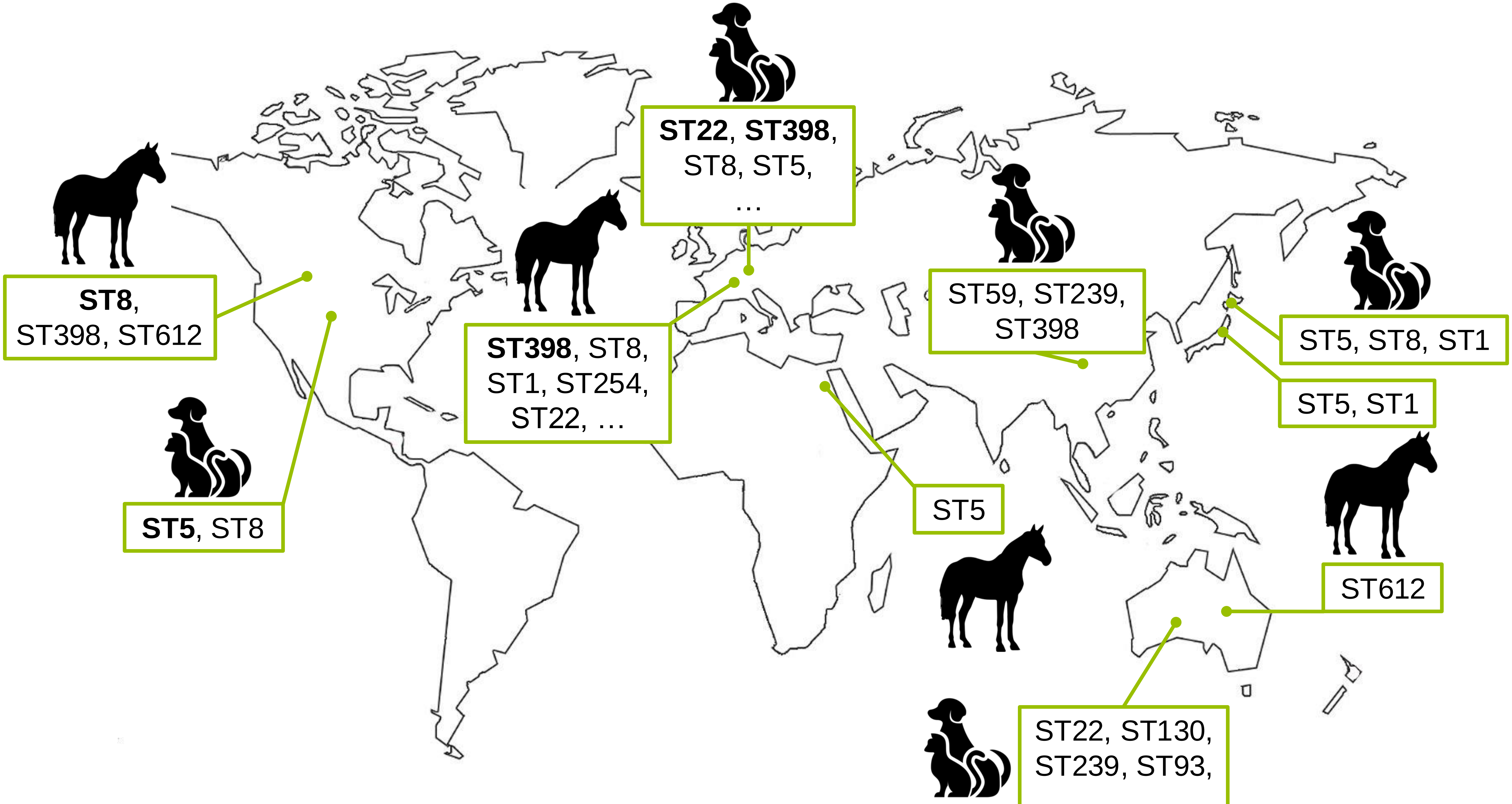

ST8,
ST398, ST612

ST5, ST8

ST398, ST8,
ST1, ST254,
ST22, …

ST22, **ST398**,
ST8, ST5,
…

ST5

ST59, ST239,
ST398

ST5, ST8, ST1

ST5, ST1

ST612

ST22, ST130,
ST239, ST93,
…

Icons from flaticon.com

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MRSA CC398

MRSA CC398 – Of swine and men

Netherlands 2004

young mother suffering from mastitis and high fever

- mother, baby, husband (pig farmer) MRSA-positive
- screening of contact persons and pigs:
  3 farm workers and 8/10 pigs MRSA-positive

Annals of Clinical Microbiology and Antimicrobials

Research

Community-acquired MRSA and pig-farming

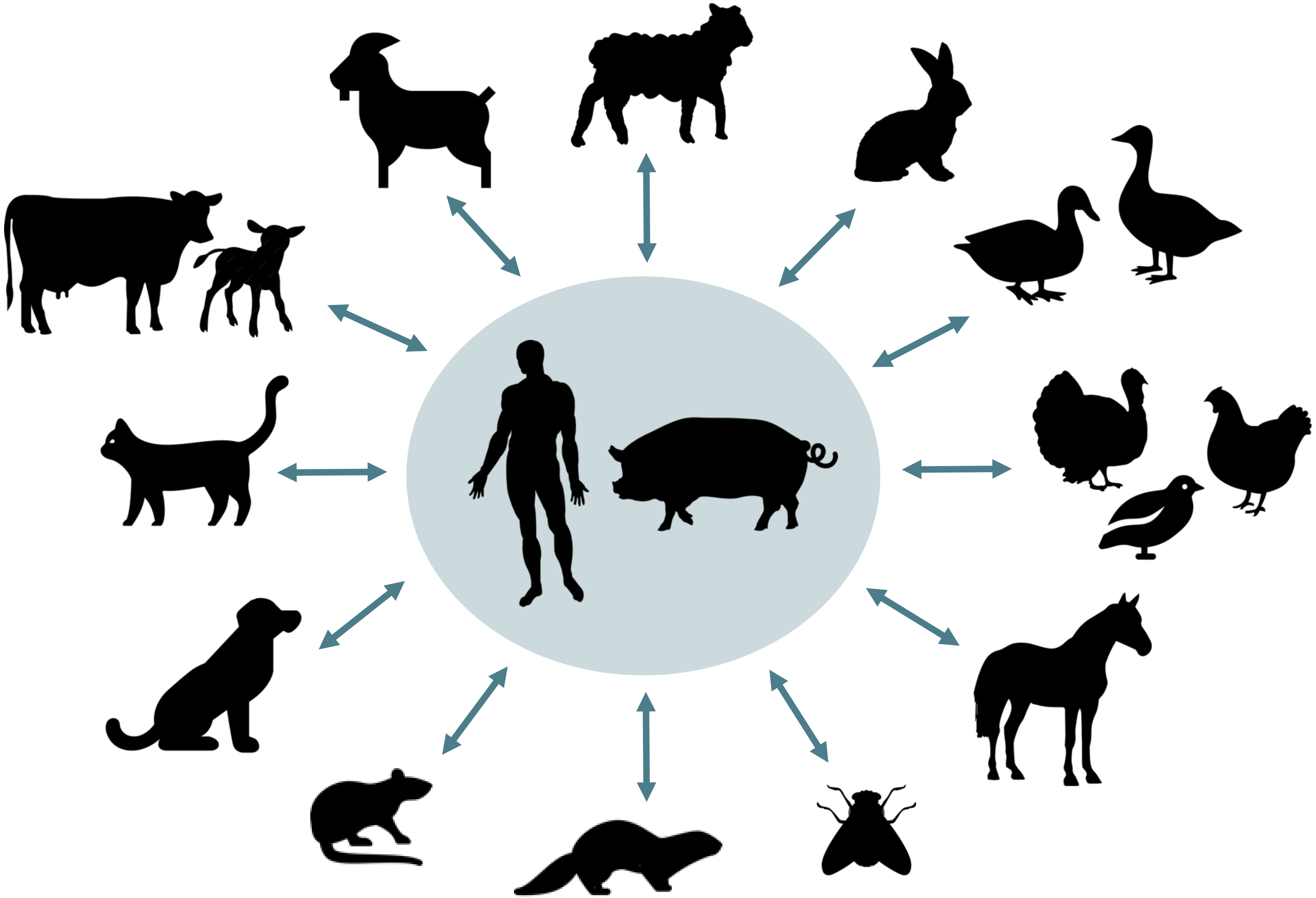
Xander W Huijsdens*[1], Beatrix J van Dijke[2], Emile Spalburg[1], Marga G van Santen-Verheuvel[1], Max EOC Heck[1], Gerlinde N Pluister[1], Andreas Voss[3,4], Wim JB Wannet[1] and Albert J de Neeling[1]

Further screening studies

- pig farms (pigs, farm workers)
- other people with occupational exposure to pigs (veterinarians, veterinary students, abattoir workers)
- other animals

Icons from flaticon.com and picture from Ulrike Amler

MRSA CC398 – Of swine and men



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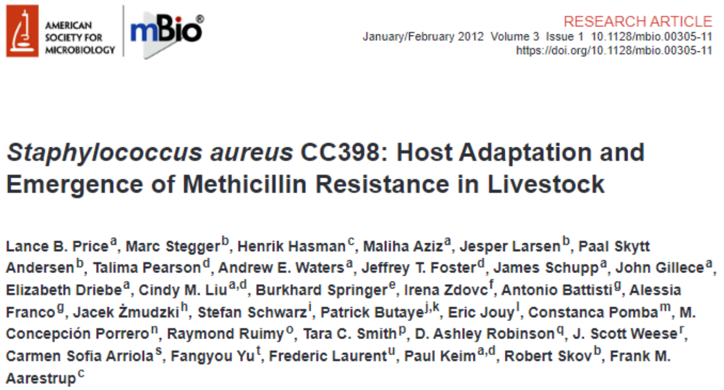
MRSA CC398 – Of swine and men

Whole genome analysis of 89 CC398 isolates (MRSA and MSSA) obtained from humans and animals in 19 countries and 4 continents


AMERICAN SOCIETY FOR MICROBIOLOGY | mBio®

RESEARCH ARTICLE
January/February 2012 Volume 3 Issue 1 10.1128/mbio.00305-11
https://doi.org/10.1128/mbio.00305-11

Staphylococcus aureus CC398: Host Adaptation and Emergence of Methicillin Resistance in Livestock

Lance B. Price[a], Marc Stegger[b], Henrik Hasman[c], Maliha Aziz[a], Jesper Larsen[b], Paal Skytt Andersen[b], Talima Pearson[d], Andrew E. Waters[a], Jeffrey T. Foster[d], James Schupp[a], John Gillece[a], Elizabeth Driebe[a], Cindy M. Liu[a,d], Burkhard Springer[e], Irena Zdovc[f], Antonio Battisti[g], Alessia Franco[g], Jacek Żmudzki[h], Stefan Schwarz[i], Patrick Butaye[j,k], Eric Jouy[l], Constanca Pomba[m], M. Concepción Porrero[n], Raymond Ruimy[o], Tara C. Smith[p], D. Ashley Robinson[q], J. Scott Weese[r], Carmen Sofia Arriola[s], Fangyou Yu[t], Frederic Laurent[u], Paul Keim[a,d], Robert Skov[b], Frank M. Aarestrup[c]

\- ΦSa3/IEC
\+ tetracycline resistance
\+ methicillin resistance


MSSA

Host jump

MRSA

Zoonotic transmission

\+ ΦSa3/IEC ?

MSSA CC398

MSSA → MRSA CC398

MRSA CC398

Icons from flaticon.com

MRSA CC398 – Of swine and men

AMERICAN SOCIETY FOR MICROBIOLOGY | Microbiology Spectrum

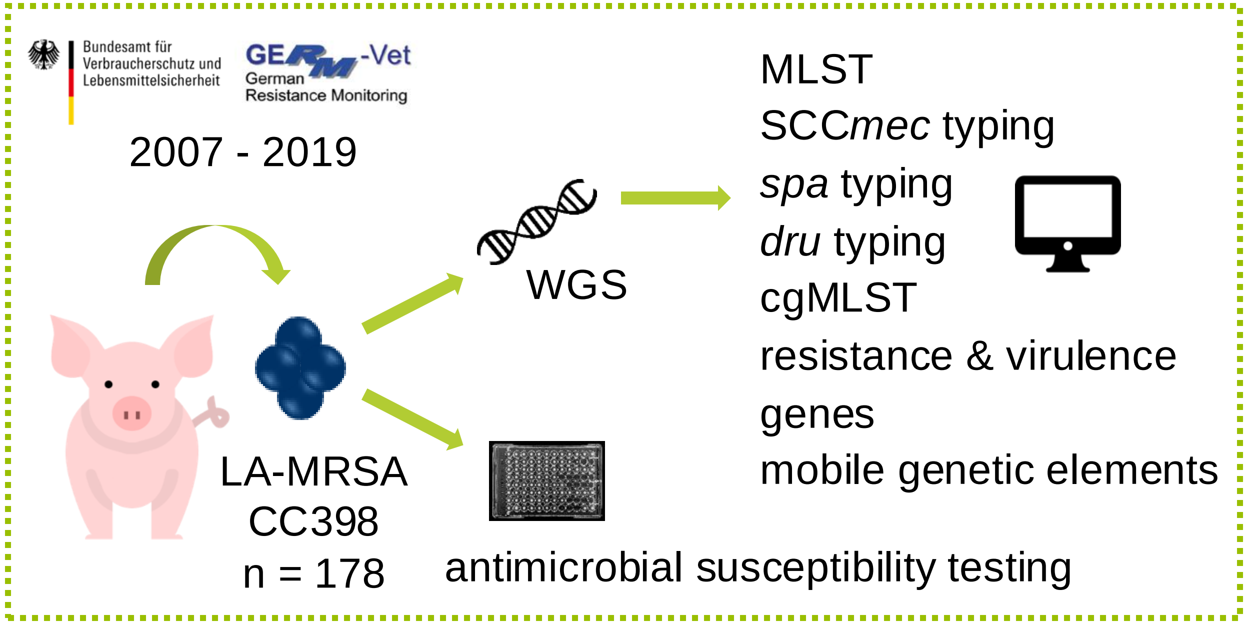
RESEARCH ARTICLE

Check for updates

Genomic Diversity of Methicillin-Resistant *Staphylococcus aureus* CC398 Isolates Collected from Diseased Swine in the German National Resistance Monitoring Program GE*RM*-Vet from 2007 to 2019

Henrike Krüger-Haker,[a,b] Xing Ji,[c] Dennis Hanke,[a,b] Stefan Fiedler,[d] Andrea T. Feßler,[a,b] Nansong Jiang,[e] Heike Kaspar,[d] Yang Wang,[e] Congming Wu,[e] Stefan Schwarz[a,b,e]

[a]Institute of Microbiology and Epizootics, Centre for Infection Medicine, School of Veterinary Medicine, Freie Universität Berlin, Berlin, Germany
[b]Veterinary Centre for Resistance Research (TZR), School of Veterinary Medicine, Freie Universität Berlin, Berlin, Germany
[c]Jiangsu Key Laboratory for Food Quality and Safety, State Key Laboratory, Cultivation Base of Ministry of Science and Technology, Institute of Food Safety and Nutrition, Jiangsu Academy of Agricultural Sciences, Nanjing, China
[d]Federal Office of Consumer Protection and Food Safety (BVL), Berlin, Germany
[e]Key Laboratory of Animal Antimicrobial Resistance Surveillance, MARA, College of Veterinary Medicine, China Agricultural University, Beijing, China



Bundesamt für Verbraucherschutz und Lebensmittelsicherheit

GE*RM*-Vet German Resistance Monitoring

2007 - 2019

LA-MRSA
CC398
n = 178

WGS

MLST
SCC*mec* typing
spa typing
dru typing
cgMLST
resistance & virulence genes
mobile genetic elements

antimicrobial susceptibility testing

Porcine MRSA CC398 from Germany harbored numerous antimicrobial resistance properties, including resistance to oxazolidinones in one case

- ~ 89% (158/178) of the isolates were multiresistant
- many of the resistance genes were part of mobile genetic elements such as transposons and plasmids → horizontal gene transfer

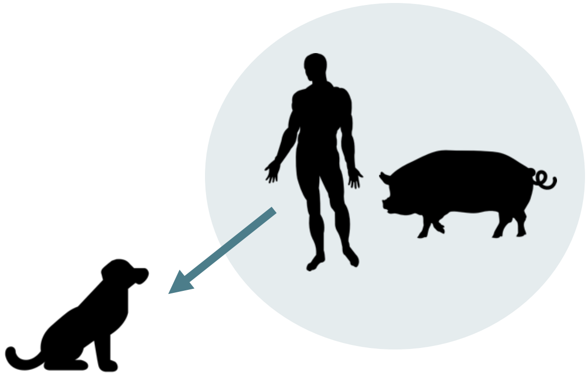
MRSA CC398 – Of swine and men

Journal of Antimicrobial Chemotherapy
doi:10.1093/jac/dkp243
Advance Access publication 16 July 2009

Ulrike Nienhoff

Transmission of methicillin-resistant *Staphylococcus aureus* strains between humans and dogs: two case reports

Ulrike Nienhoff[1], Kristina Kadlec[2], Iris F. Chaberny[3], Jutta Verspohl[4], Gerald-F. Gerlach[4], Stefan Schwarz[2]*, Daniela Simon[1] and Ingo Nolte[1]



Case 1:

LA-MRSA (ST398-t034) was transferred from a colonized specialist veterinarian for swine diseases to his dog

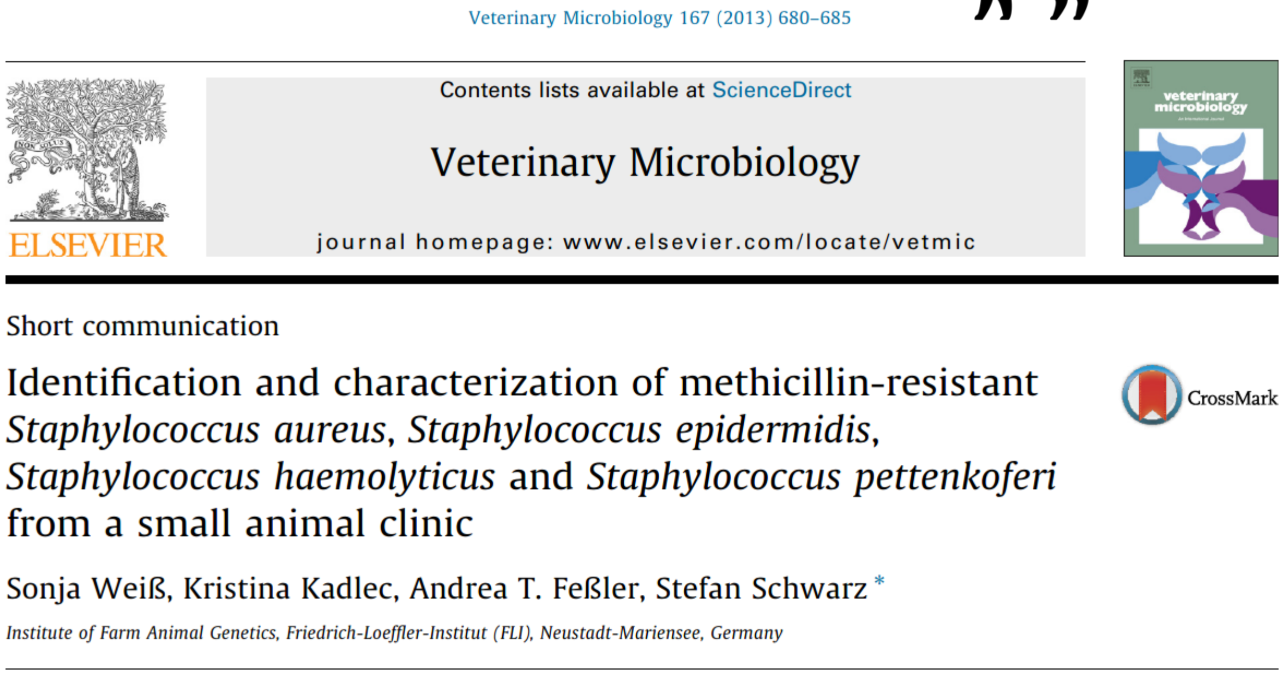
Man → dog transfer of MRSA

First description of MRSA ST398 from a **dog**

Icons from flaticon.com

MRSA CC398

Sonja Weiß



Veterinary Microbiology 167 (2013) 680–685

Contents lists available at ScienceDirect

Veterinary Microbiology

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

ELSEVIER

Short communication

Identification and characterization of methicillin-resistant *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus haemolyticus* and *Staphylococcus pettenkoferi* from a small animal clinic

Sonja Weiß, Kristina Kadlec, Andrea T. Feßler, Stefan Schwarz *

Institute of Farm Animal Genetics, Friedrich-Loeffler-Institut (FLI), Neustadt-Mariensee, Germany

First description of MRSA ST398 from a cat

One stray cat that lived in/around livestock stables

→ Cat – cattle interactions at farm level?

?

Icon from flaticon.com and pictures via reddit and tumblr

MRSA CC398

Andrea T. Feßler

Veterinary Microbiology 160 (2012) 77–84

Contents lists available at SciVerse ScienceDirect

Veterinary Microbiology

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

ELSEVIER

Characterization of methicillin-resistant *Staphylococcus aureus* CC398 obtained from humans and animals on dairy farms

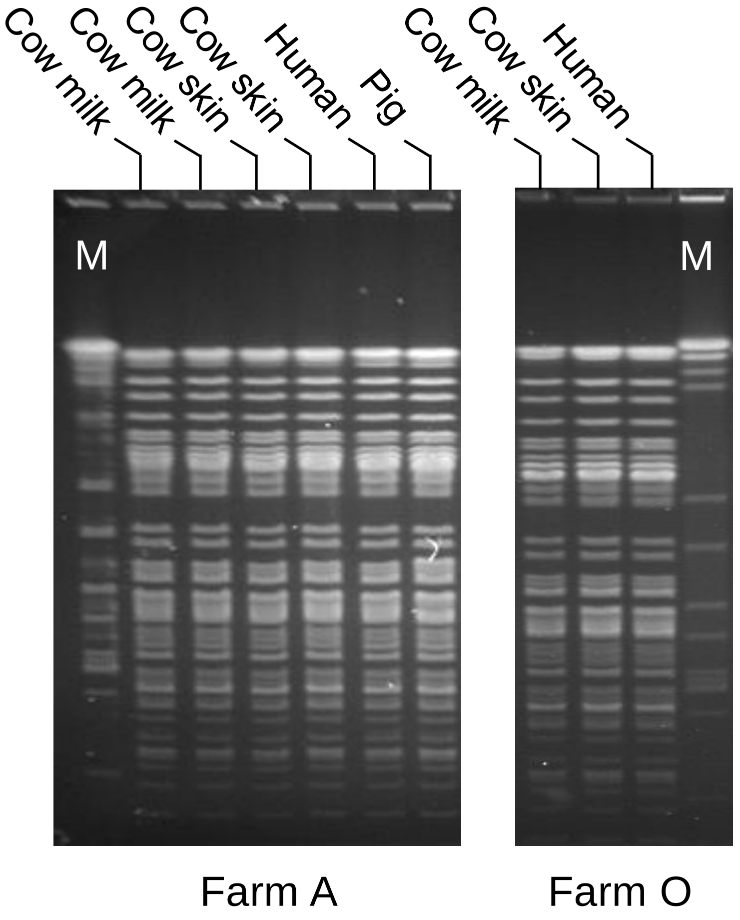
Andrea T. Feßler[a], Richard G.M. Olde Riekerink[b,1], Anja Rothkamp[b,2], Kristina Kadlec[a], Otlis C. Sampimon[b,3], Theo J.G.M. Lam[b,c], Stefan Schwarz[a,*]

[a] *Institute of Farm Animal Genetics, Friedrich-Loeffler-Institut (FLI), Neustadt-Mariensee, Germany*
[b] *GD Animal Health Service Deventer, Deventer, The Netherlands*
[c] *Utrecht University, Faculty of Veterinary Medicine, Department of Farm Animal Health, Utrecht, The Netherlands*

26 dairy farms

LA-MRSA ST398 was detected among dairy cattle, milkers, and occasionally also among other animals of the same farm (pigs, sheep, goats, dogs)

Occasionally more than one subtype per farm



Animal ↔ human exchange of LA-MRSA ST398 on dairy farms

Icons from flaticon.com

MRSA CC9

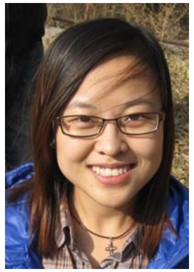
MRSA CC9

MRSA ST9 have among other countries mainly been recovered from pigs or pig farm workers in mainland China, Hong Kong, and Malaysia.

The lineage is also described as an emerging clone in some areas with intensive industrial livestock production in the United States.

Icons from flaticon.com and pictures via Reuters and reddit

MRSA CC9



Jun Li

Veterinary Microbiology 201 (2017) 183–187

Contents lists available at ScienceDirect

Veterinary Microbiology

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

Short communication

Characterization of pig-associated methicillin-resistant *Staphylococcus aureus*

Jun Li[a,b], Nansong Jiang[a], Yuebin Ke[c], Andrea T. Feßler[b], Yang Wang[a], Stefan Schwarz[a,b,d,*], Congming Wu[a,**]

[a] *Beijing Advanced Innovation Center for Food Nutrition and Human Health, College of Veterinary Medicine, China Agricultural University, Beijing 100193, PR China*
[b] *Institute of Farm Animal Genetics, Friedrich-Loeffler-Institut (FLI), Neustadt-Mariensee, Germany*
[c] *Key Laboratory of Genetics & Molecular Medicine of Shenzhen, Shenzhen Center for Disease Control and Prevention, Shenzhen 518055, PR China*
[d] *Institute of Microbiology and Epizootics, Department of Veterinary Medicine, Freie Universität Berlin, Robert-von-Ostertag-Straße 7-13, 14163 Berlin, Germany*

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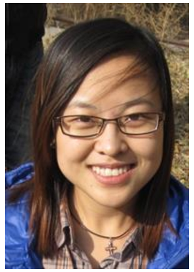
MRSA CC9



Jun Li

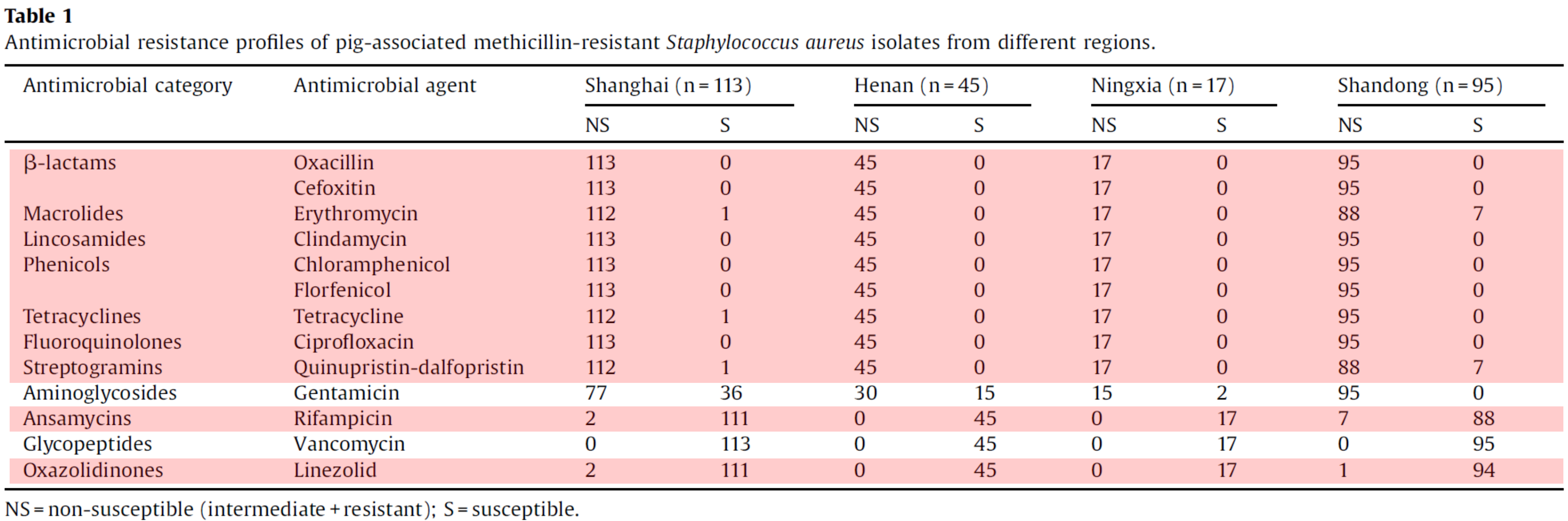


Table 1
Antimicrobial resistance profiles of pig-associated methicillin-resistant *Staphylococcus aureus* isolates from different regions.

Antimicrobial category	Antimicrobial agent	Shanghai (n = 113)		Henan (n = 45)		Ningxia (n = 17)		Shandong (n = 95)	
		NS	S	NS	S	NS	S	NS	S
β-lactams	Oxacillin	113	0	45	0	17	0	95	0
	Cefoxitin	113	0	45	0	17	0	95	0
Macrolides	Erythromycin	112	1	45	0	17	0	88	7
Lincosamides	Clindamycin	113	0	45	0	17	0	95	0
Phenicols	Chloramphenicol	113	0	45	0	17	0	95	0
	Florfenicol	113	0	45	0	17	0	95	0
Tetracyclines	Tetracycline	112	1	45	0	17	0	95	0
Fluoroquinolones	Ciprofloxacin	113	0	45	0	17	0	95	0
Streptogramins	Quinupristin-dalfopristin	112	1	45	0	17	0	88	7
Aminoglycosides	Gentamicin	77	36	30	15	15	2	95	0
Ansamycins	Rifampicin	2	111	0	45	0	17	7	88
Glycopeptides	Vancomycin	0	113	0	45	0	17	0	95
Oxazolidinones	Linezolid	2	111	0	45	0	17	1	94

NS = non-susceptible (intermediate + resistant); S = susceptible.

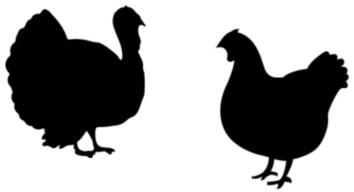
Li et al., 2017, Vet Microbiol, 201: 183-7

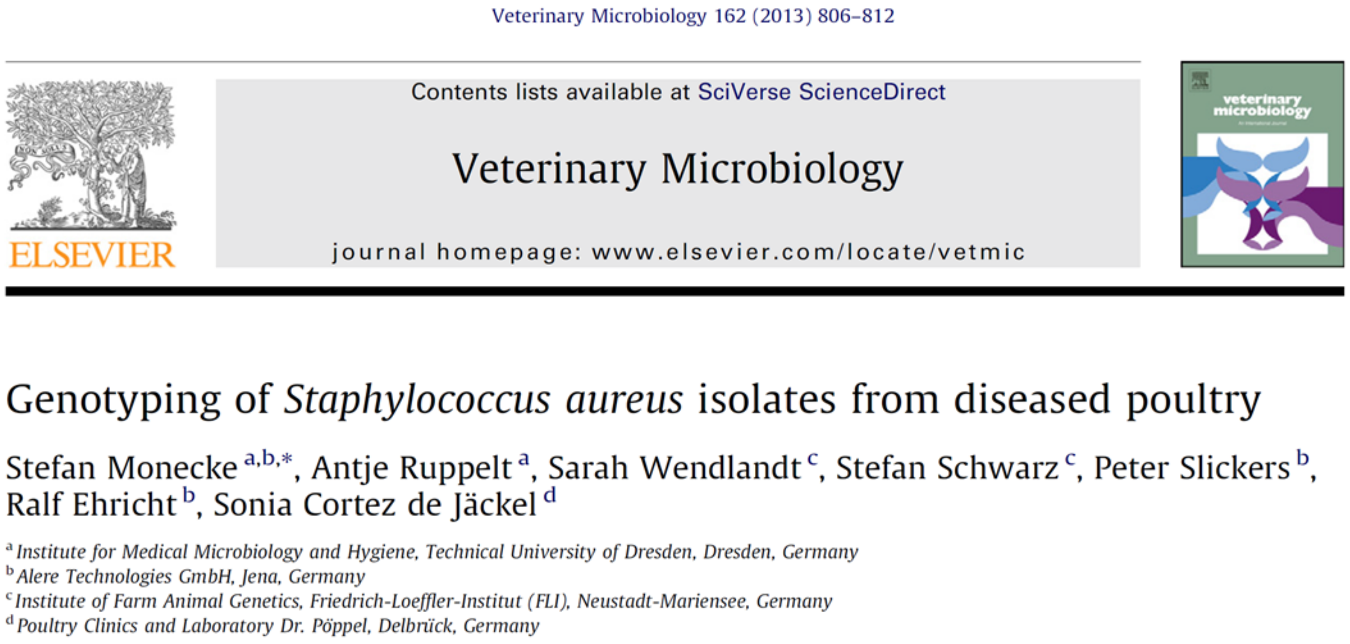
- Overall very high resistance rates, which also include fluoroquinolones and streptogramins
- Resistance to oxazolidinones and rifampicin in rare cases

Icon from flaticon.com

MRSA CC9

MRSA ST9 have also been identified in turkeys, chicken and poultry meat





Veterinary Microbiology 162 (2013) 806–812

Contents lists available at SciVerse ScienceDirect

Veterinary Microbiology

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

ELSEVIER

Genotyping of *Staphylococcus aureus* isolates from diseased poultry

Stefan Monecke[a,b,*], Antje Ruppelt[a], Sarah Wendlandt[c], Stefan Schwarz[c], Peter Slickers[b], Ralf Ehricht[b], Sonia Cortez de Jäckel[d]

[a] *Institute for Medical Microbiology and Hygiene, Technical University of Dresden, Dresden, Germany*
[b] *Alere Technologies GmbH, Jena, Germany*
[c] *Institute of Farm Animal Genetics, Friedrich-Loeffler-Institut (FLI), Neustadt-Mariensee, Germany*
[d] *Poultry Clinics and Laboratory Dr. Pöppel, Delbrück, Germany*

Applied and Environmental Microbiology, Oct. 2011, p. 7151–7157 Vol. 77, No. 20
0099-2240/11/$12.00 doi:10.1128/AEM.00561-11
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Characterization of Methicillin-Resistant *Staphylococcus aureus* Isolates from Food and Food Products of Poultry Origin in Germany$^{\nabla}$

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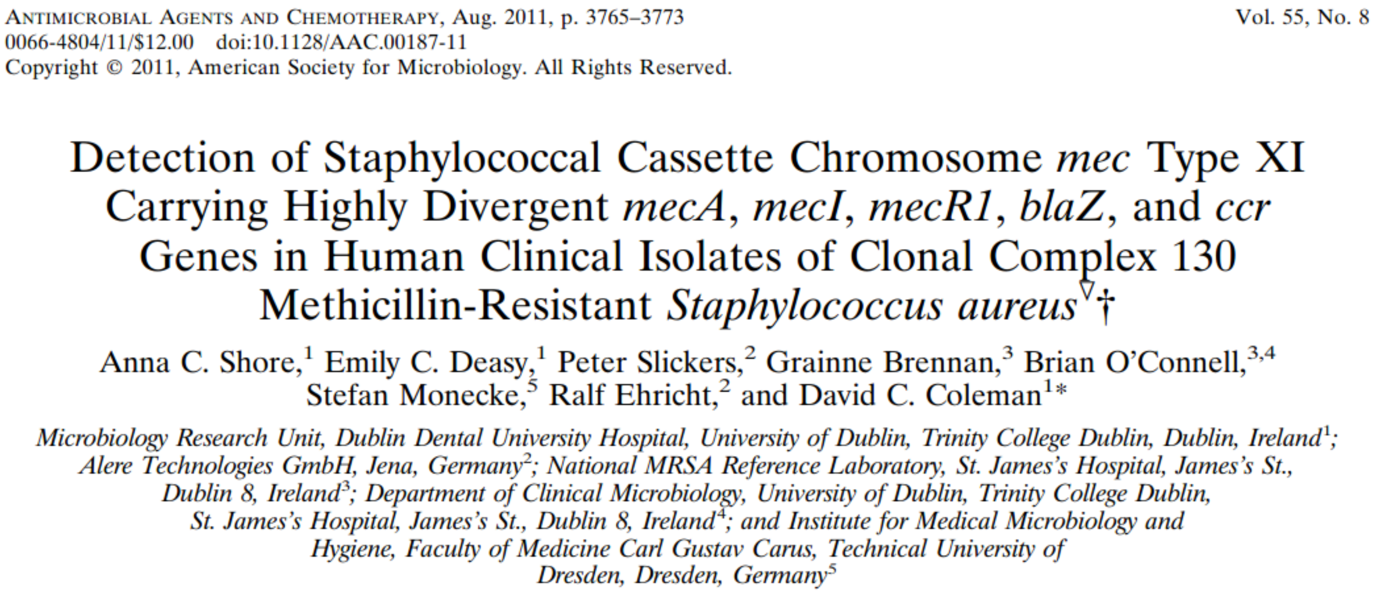
Received 11 March 2011/Accepted 14 June 2011

Icons from flaticon.com

MRSA CC130

MRSA CC130


Anna C. Shore


ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, Aug. 2011, p. 3765–3773 Vol. 55, No. 8
0066-4804/11/$12.00 doi:10.1128/AAC.00187-11

Detection of Staphylococcal Cassette Chromosome *mec* Type XI Carrying Highly Divergent *mecA*, *mecI*, *mecR1*, *blaZ*, and *ccr* Genes in Human Clinical Isolates of Clonal Complex 130 Methicillin-Resistant *Staphylococcus aureus*▽†

Anna C. Shore,[1] Emily C. Deasy,[1] Peter Slickers,[2] Grainne Brennan,[3] Brian O'Connell,[3,4]
Stefan Monecke,[5] Ralf Ehricht,[2] and David C. Coleman[1]*

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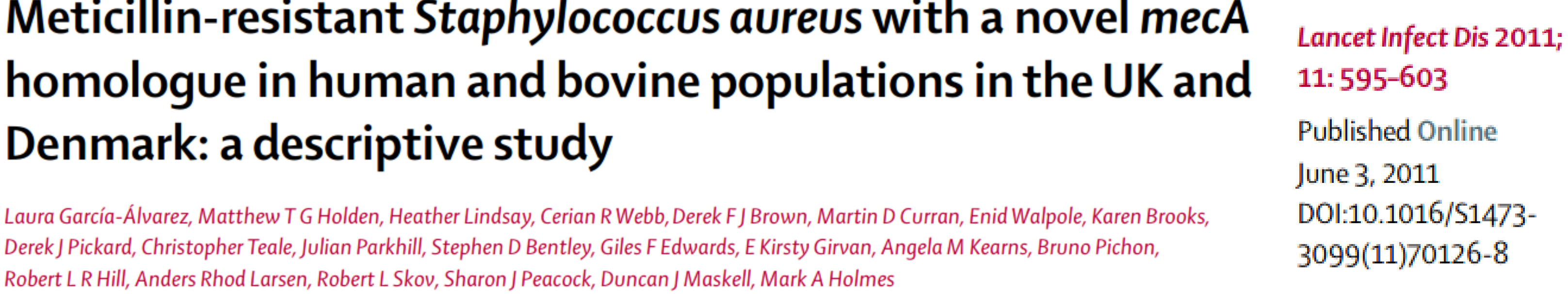
Laura García-Álvarez



Meticillin-resistant *Staphylococcus aureus* with a novel *mecA* homologue in human and bovine populations in the UK and Denmark: a descriptive study

Laura García-Álvarez, Matthew T G Holden, Heather Lindsay, Cerian R Webb, Derek F J Brown, Martin D Curran, Enid Walpole, Karen Brooks, Derek J Pickard, Christopher Teale, Julian Parkhill, Stephen D Bentley, Giles F Edwards, E Kirsty Girvan, Angela M Kearns, Bruno Pichon, Robert L R Hill, Anders Rhod Larsen, Robert L Skov, Sharon J Peacock, Duncan J Maskell, Mark A Holmes

Lancet Infect Dis 2011; 11: 595–603

DOI:10.1016/S1473-3099(11)70126-8

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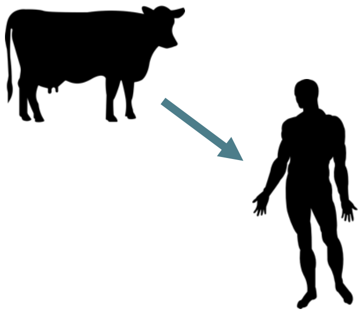
*mec*C-mediated methicillin resistance

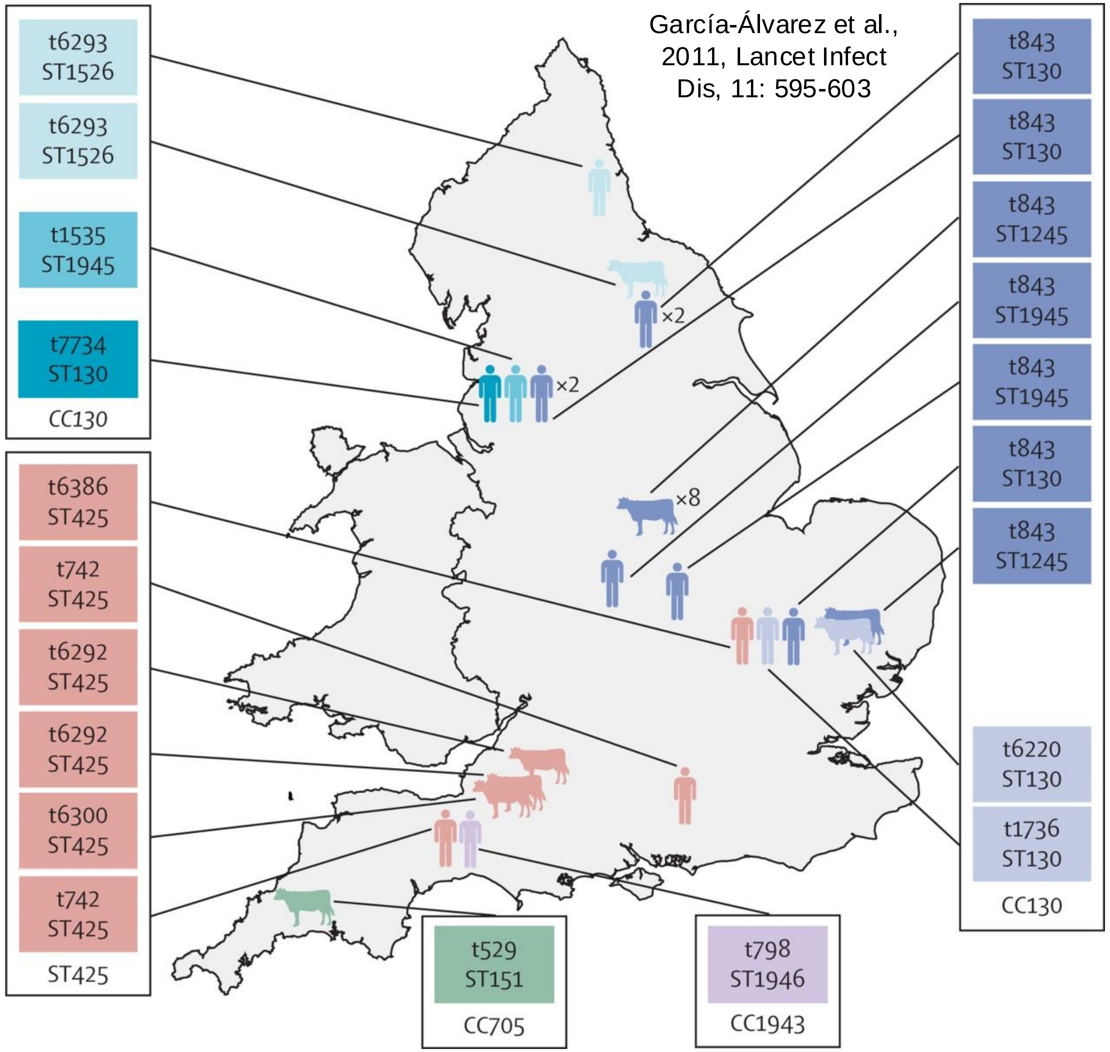
Laura García-Álvarez

- found in MRSA of various sequence types
  - **ST130 / t843**
  - ST425
  - **ST1526 / t6293**
  - ST1945
  - ST1946
  - ST151
  - ST1245



- found in strains from humans and cattle that had the same MLST and *spa* types

→ exchange



García-Álvarez et al., 2011, Lancet Infect Dis, 11: 595-603

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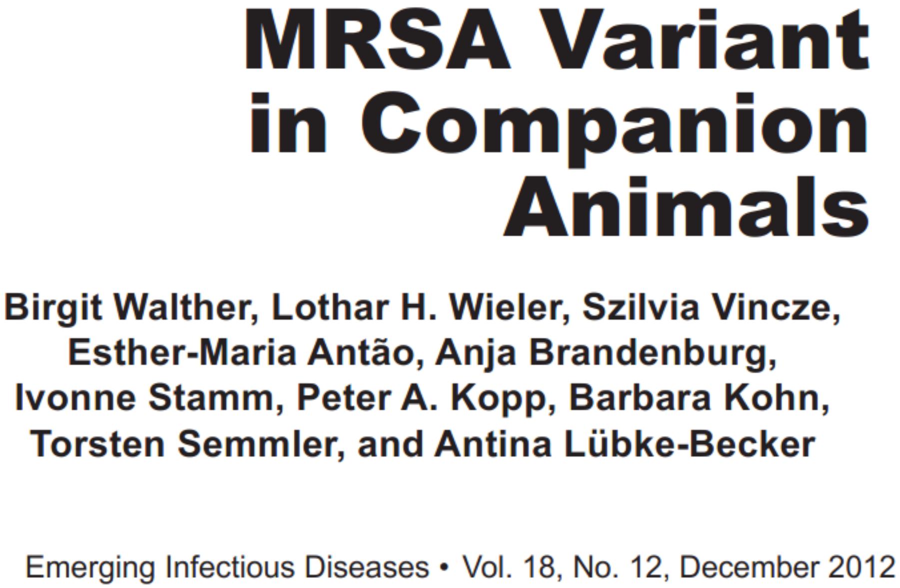
MRSA CC130

Birgit Walther



MRSA Variant in Companion Animals

Birgit Walther, Lothar H. Wieler, Szilvia Vincze, Esther-Maria Antão, Anja Brandenburg, Ivonne Stamm, Peter A. Kopp, Barbara Kohn, Torsten Semmler, and Antina Lübke-Becker

Emerging Infectious Diseases • Vol. 18, No. 12, December 2012

- *mecC* found in strains of MLST types ST130, ST599 and ST1945 from dogs, cats and a guinea pig
- ST130/t843 strains were detected in a cat and the guinea pig

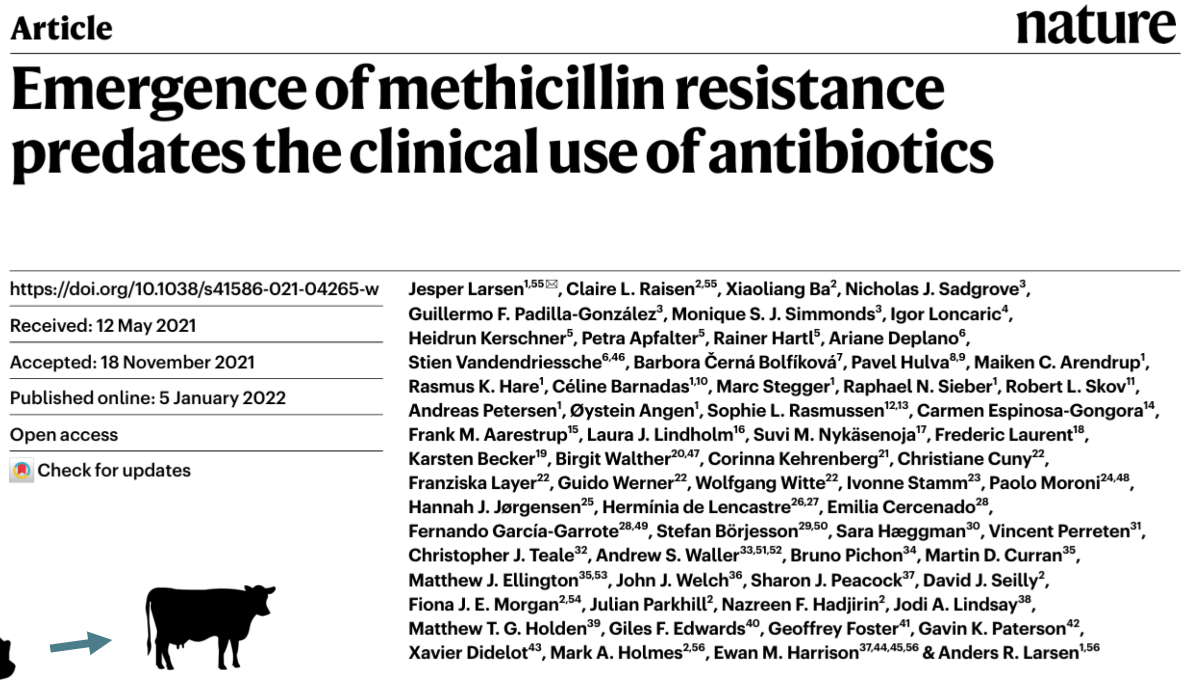
→ even wider dissemination and *mecC* not exclusively associated with CC130

→ no phenotypic resistance toward non-β-lactams

Pictures from pixabay.com

MRSA CC130

- 75% of 222 *mecC*-MRSA from European hedgehogs belonged to CC130
- European hedgehogs are a **natural reservoir** of zoonotic *mecC*-MRSA lineages, which predate the antibiotic era
- hedgehogs are the most likely primary host in some countries, but dairy cows and other domesticated animals probably act as intermediate hosts and vectors in **zoonotic transmission** from hedgehogs to humans



Article

nature

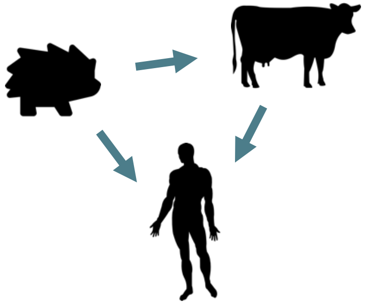
Emergence of methicillin resistance predates the clinical use of antibiotics

https://doi.org/10.1038/s41586-021-04265-w

Received: 12 May 2021

Accepted: 18 November 2021

Jesper Larsen[1,55]✉, Claire L. Raisen[2,55], Xiaoliang Ba[2], Nicholas J. Sadgrove[3], Guillermo F. Padilla-González[3], Monique S. J. Simmonds[3], Igor Loncaric[4], Heidrun Kerschner[5], Petra Apfalter[5], Rainer Hartl[5], Ariane Deplano[6], Stien Vandendriessche[6,46], Barbora Černá Bolfíková[7], Pavel Hulva[8,9], Maiken C. Arendrup[1], Rasmus K. Hare[1], Céline Barnadas[1,10], Marc Stegger[1], Raphael N. Sieber[1], Robert L. Skov[11], Andreas Petersen[1], Øystein Angen[1], Sophie L. Rasmussen[12,13], Carmen Espinosa-Gongora[14], Frank M. Aarestrup[15], Laura J. Lindholm[16], Suvi M. Nykäsenoja[17], Frederic Laurent[18], Karsten Becker[19], Birgit Walther[20,47], Corinna Kehrenberg[21], Christiane Cuny[22], Franziska Layer[22], Guido Werner[22], Wolfgang Witte[22], Ivonne Stamm[23], Paolo Moroni[24,48], Hannah J. Jørgensen[25], Hermínia de Lencastre[26,27], Emilia Cercenado[28], Fernando García-Garrote[28,49], Stefan Börjesson[29,50], Sara Hæggman[30], Vincent Perreten[31], Christopher J. Teale[32], Andrew S. Waller[33,51,52], Bruno Pichon[34], Martin D. Curran[35], Matthew J. Ellington[35,53], John J. Welch[36], Sharon J. Peacock[37], David J. Seilly[2], Fiona J. E. Morgan[2,54], Julian Parkhill[2], Nazreen F. Hadjirin[2], Jodi A. Lindsay[38], Matthew T. G. Holden[39], Giles F. Edwards[40], Geoffrey Foster[41], Gavin K. Paterson[42], Xavier Didelot[43], Mark A. Holmes[2,56], Ewan M. Harrison[37,44,45,56] & Anders R. Larsen[1,56]



Nature. 2022, 602:135-141. doi: 10.1038/s41586-021-04265-w.

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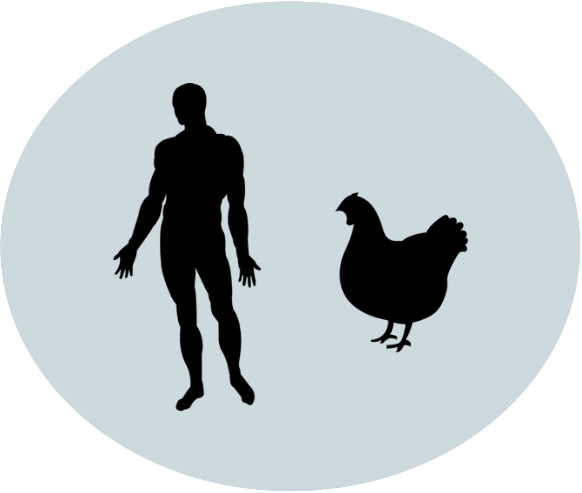
MRSA CC5

MRSA CC5



- common and widespread CC
- comprises a large number of different MRSA strains
  - HA- and CA-MRSA
  - some have spread pandemically
  - also detected in poultry
- carries the enterotoxin gene cluster
- several human strains harbor important virulence genes, e.g. the genes for the Panton-Valentine leukocidin (PVL) or the toxic shock syndrome toxin 1 (TSST-1)
- many additional resistance-associated genes, isolates from poultry in Germany showed also resistance to tetracyclines, macrolides-lincosamides-streptogramin B antibiotics, spectinomycin, and enrofloxacin

Icons from flaticon.com

MRSA CC5

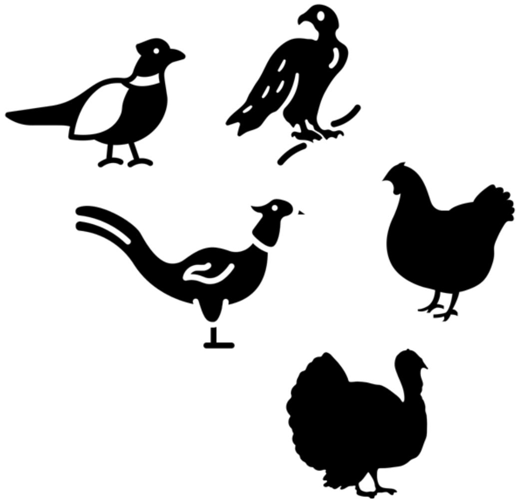
PNAS

Recent human-to-poultry host jump, adaptation, and pandemic spread of *Staphylococcus aureus*

Bethan V. Lowder[a], Caitriona M. Guinane[a], Nouri L. Ben Zakour[a], Lucy A. Weinert[b], Andrew Conway-Morris[c], Robyn A. Cartwright[a], A. John Simpson[c], Andrew Rambaut[b], Ulrich Nübel[d], and J. Ross Fitzgerald[a,1]

[a]The Roslin Institute and Centre for Infectious Diseases, Royal (Dick) School of Veterinary Studies, [b]Institute of Evolutionary Biology, and [c]Centre for Inflammation Research, Queens Medical Research Institute, University of Edinburgh, Edinburgh EH8 9YL, Scotland, United Kingdom; and [d]Robert Koch Institut, 38855 Wernigerode, Germany

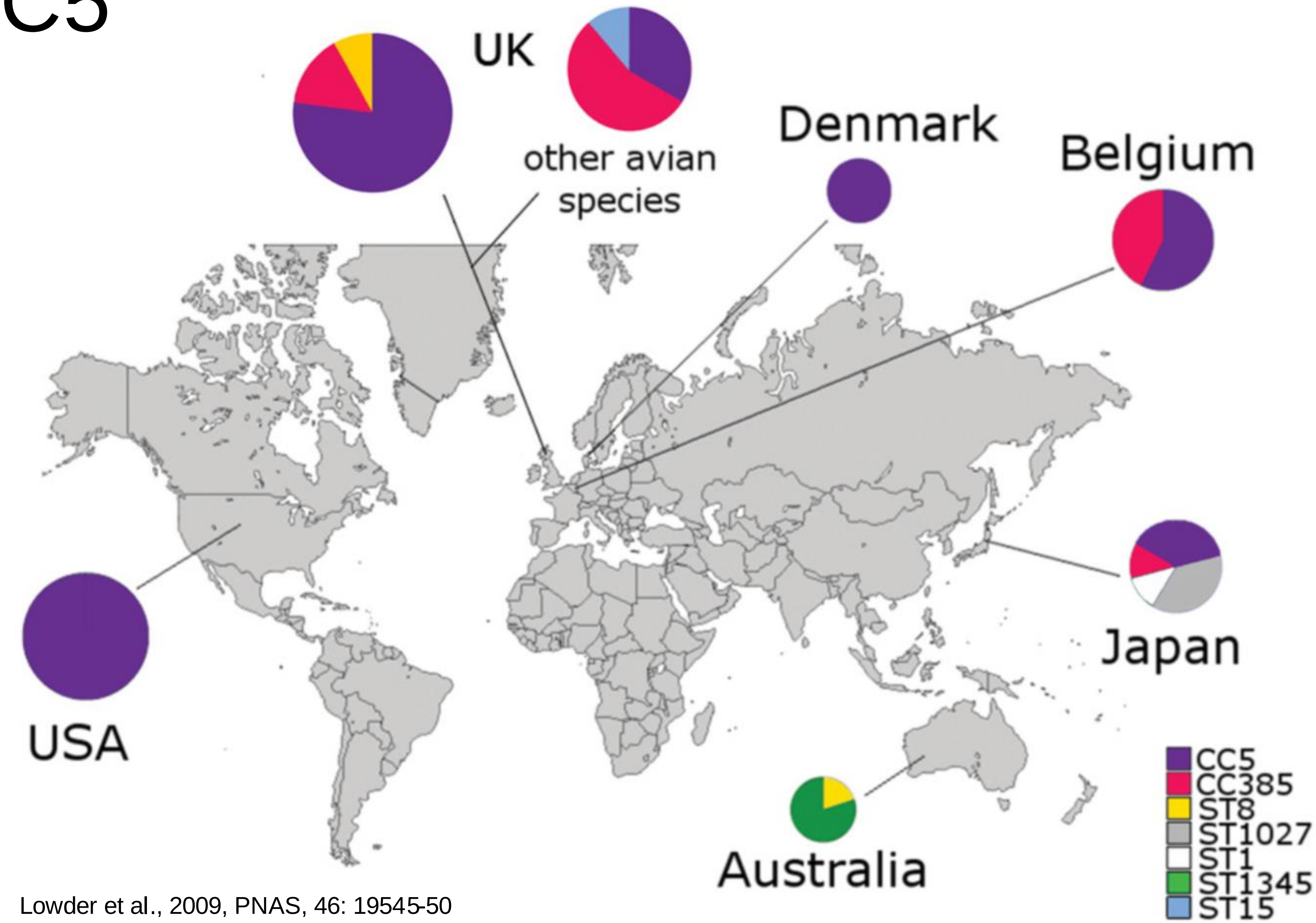
Edited by Richard P. Novick, New York University School of Medicine, New York, NY, and approved September 18, 2009 (received for review August 14, 2009)



- 57 avian *S. aureus* isolates, including 48 from healthy or diseased broiler chicken, collected in 8 countries on 4 continents during 54 years
- 32 / 48 (67%) isolates from broiler chickens belonged to ST5 or its single locus variants ST1342, ST1346 and ST1350

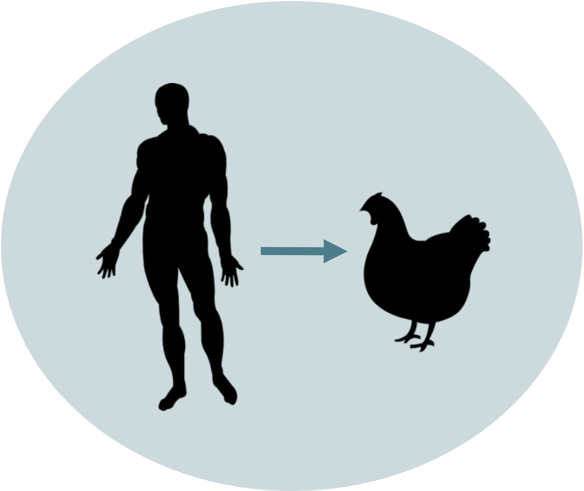
Icons from flaticon.com

MRSA CC5



Lowder et al., 2009, PNAS, 46: 19545-50

MRSA CC5



According to the phylogenetic analysis

- all poultry isolates closely related to each other
- no separate clades for diseased and asymptomatic birds

The poultry ST5 clade belongs to a ST5 sub-lineage

- includes human strains that were circulating in Poland in the 1990s

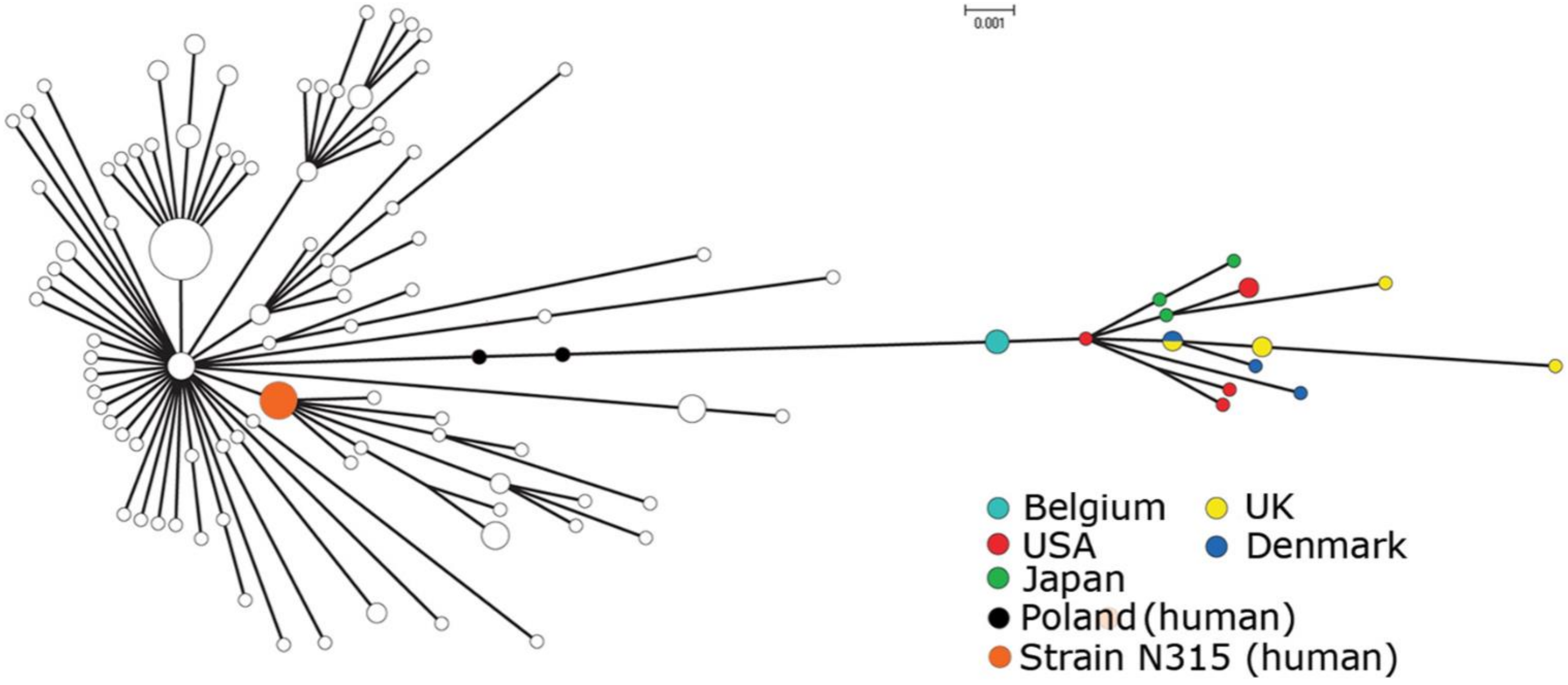
→ distribution of SNPs indicates that these isolates are basal to all isolates in the clade

→ host switch from humans to poultry occurred approximately in the early 1970s
(95% CI 30 to 63 years)

Icons from flaticon.com

MRSA CC5

The poultry ST5 clade has undergone rapid intercontinental dissemination

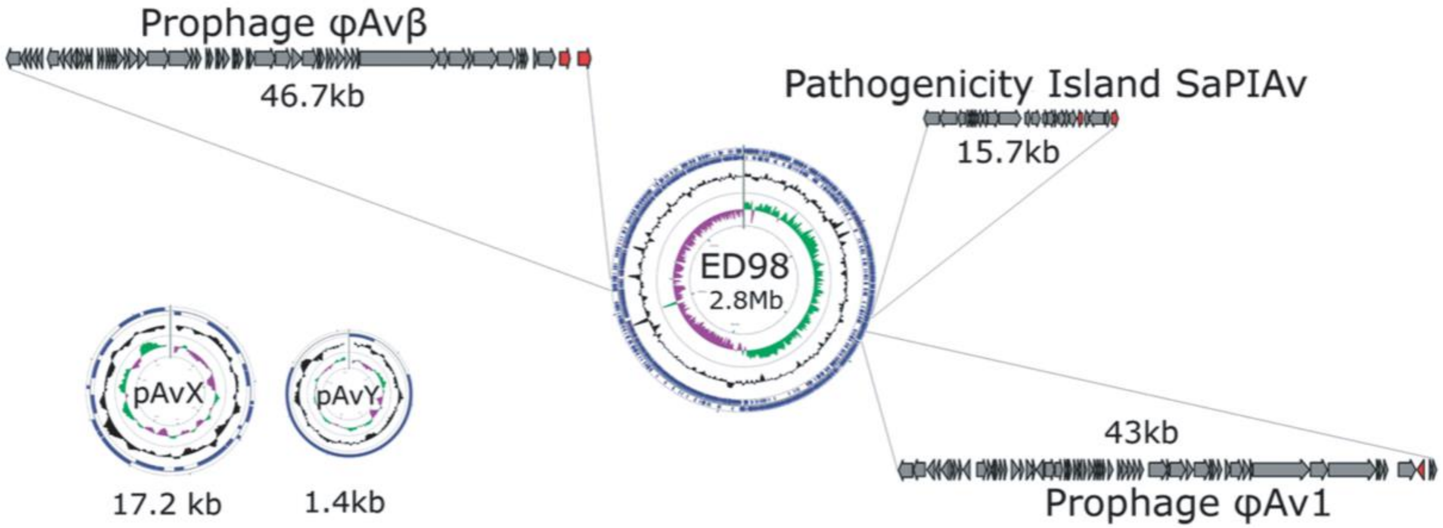


Lowder et al., 2009, PNAS, 46: 19545-50

MRSA CC5

With the host jump, the poultry ST5 isolates gained

- two prophages
- one pathogenicity island
- two plasmids



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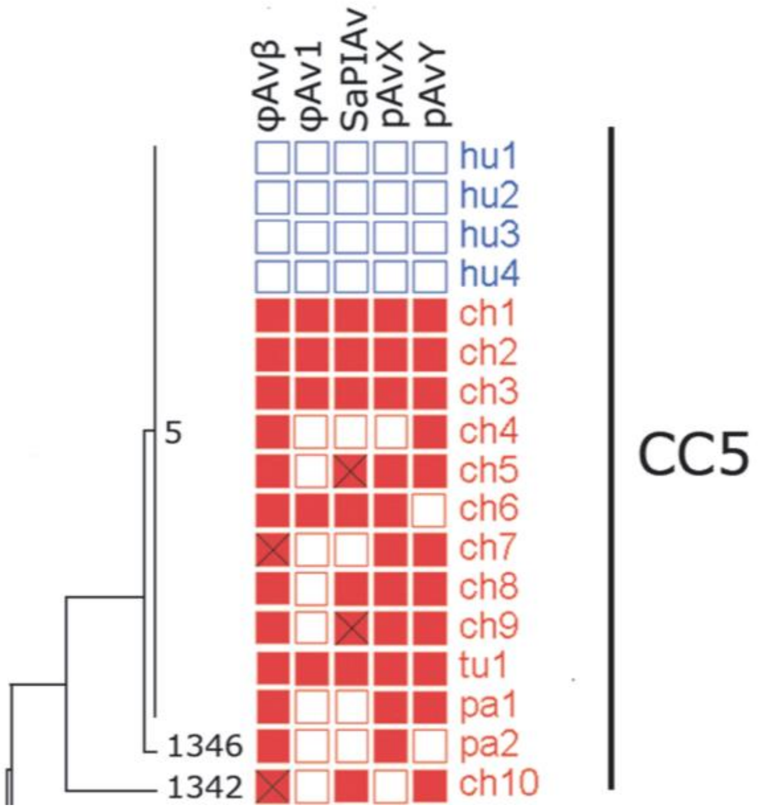
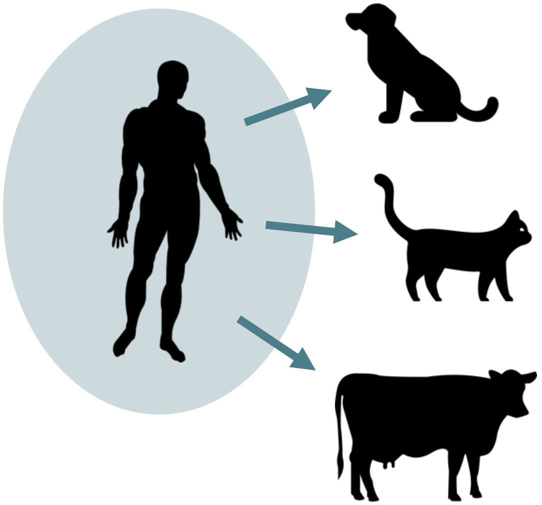


	φAvβ	φAv1	SaPIAv	pAvX	pAvY
hu1	☐	☐	☐	☐	☐
hu2	☐	☐	☐	☐	☐
hu3	☐	☐	☐	☐	☐
hu4	☐	☐	☐	☐	☐
ch1	🟥	🟥	🟥	🟥	🟥
ch2	🟥	🟥	🟥	🟥	🟥
ch3	🟥	🟥	🟥	🟥	🟥
ch4	🟥	☐	☐	☐	🟥
ch5	🟥	☐	☒	🟥	🟥
ch6	🟥	🟥	🟥	🟥	☐
ch7	☒	☐	☐	🟥	🟥
ch8	🟥	☐	🟥	🟥	🟥
ch9	🟥	☐	☒	🟥	🟥
tu1	🟥	🟥	🟥	🟥	🟥
pa1	🟥	☐	☐	🟥	🟥
pa2	🟥	☐	☐	🟥	☐
ch10	☒	☐	🟥	☐	🟥

MRSA CC22

MRSA CC22



- common and widespread CC
- emergence of different MRSA strains
- commonly occurs in humans as pandemic strains, e.g. UK-EMRSA-15

→ UK-EMRSA-15 detected also in dogs, cats and dairy cows

→ suggests human source for isolates infecting companion and livestock animals

Icons from flaticon.com

MRSA CC22

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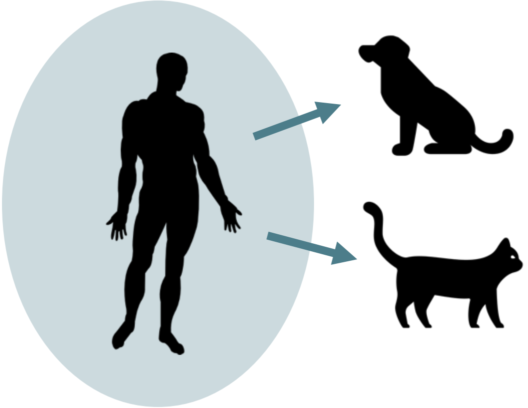
RESEARCH ARTICLE

A Shared Population of Epidemic Methicillin-Resistant *Staphylococcus aureus* 15 Circulates in Humans and Companion Animals

Ewan M. Harrison,[a] Lucy A. Weinert,[a] Matthew T. G. Holden,[b] John J. Welch,[c] Katherine Wilson,[a] Fiona J. E. Morgan,[a] Simon R. Harris,[b] Anette Loeffler,[d] Amanda K. Boag,[d] Sharon J. Peacock,[b,e] Gavin K. Paterson,[f] Andrew S. Waller,[g] Julian Parkhill,[b] Mark A. Holmes[a]

Department of Veterinary Medicine, University of Cambridge, Cambridge, United Kingdom[a]; Wellcome Trust Sanger Institute, Hinxton, United Kingdom[b]; Department of Genetics, University of Cambridge, Cambridge, United Kingdom[c]; Royal Veterinary College, University of London, North Mymms, Hertfordshire, England[d]; Department of Clinical Medicine, University of Cambridge, Cambridge, United Kingdom[e]; School of Biological, Biomedical and Environmental Sciences, University of Hull, Hull, United Kingdom[f]; Centre for Preventive Medicine, Animal Health Trust, Kentford, Newmarket, Suffolk, United Kingdom[g]

May/June 2014 Volume 5 Issue 3 e00985-13



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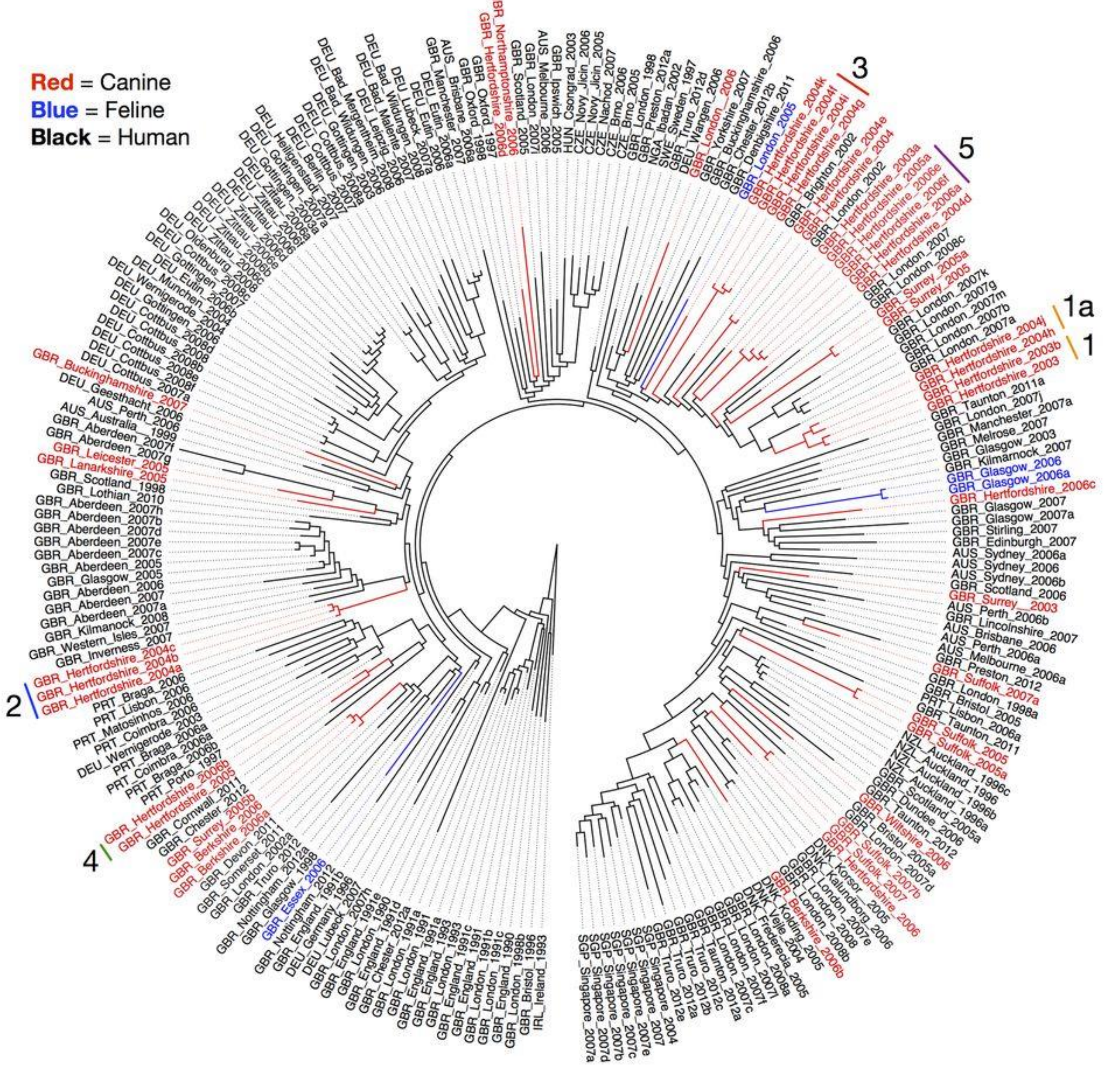
MRSA CC22

Harrison et al., 2014, mBio, 5: e00985-13

MRSA ST22 phylogeny

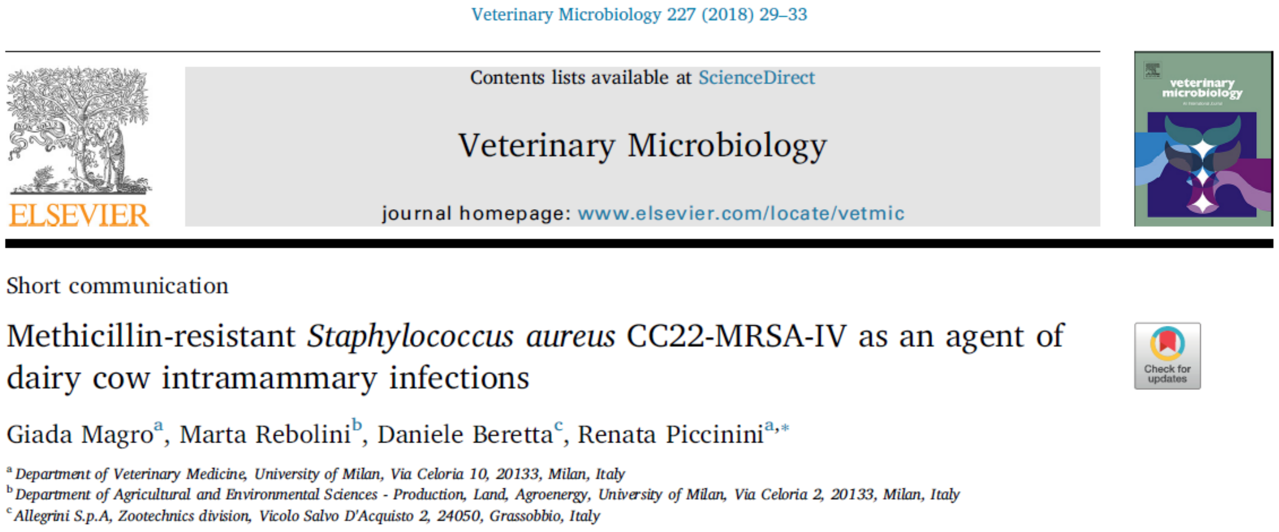
Isolates from companion animals

- fluoroquinolone resistance mutations in *grlA* (Ser80Phe) and *gyrA* (Ser84Leu)
- *erm*(C)-carrying plasmid less likely, but when present, *erm*(C) more likely to be constitutively expressed, thus mediating also clindamycin resistance



MRSA CC22

- UK-MRSA-15 was identified in four cows and one milker
- resistance to β-lactams, kanamycin and quinolones
- milker had been volunteering in a nursing home since months
- milker isolate differed mainly for absence of the untruncated β-haemolysin and presence of the immune evasion cluster



Veterinary Microbiology 227 (2018) 29–33

Contents lists available at ScienceDirect

Veterinary Microbiology

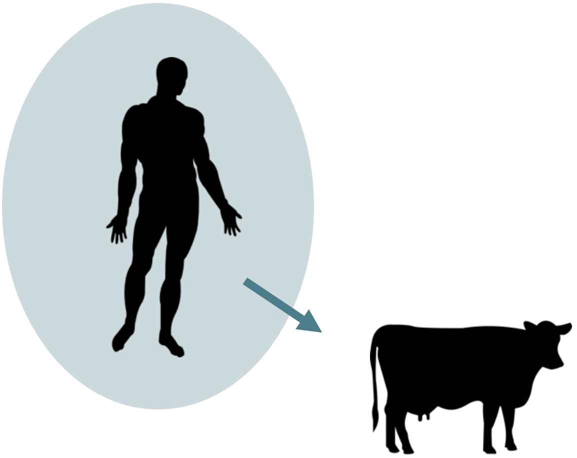
journal homepage: www.elsevier.com/locate/vetmic

Short communication

Methicillin-resistant *Staphylococcus aureus* CC22-MRSA-IV as an agent of dairy cow intramammary infections

Giada Magro[a], Marta Rebolini[b], Daniele Beretta[c], Renata Piccinini[a],*

[a] *Department of Veterinary Medicine, University of Milan, Via Celoria 10, 20133, Milan, Italy*
[b] *Department of Agricultural and Environmental Sciences - Production, Land, Agroenergy, University of Milan, Via Celoria 2, 20133, Milan, Italy*
[c] *Allegrini S.p.A, Zootechnics division, Vicolo Salvo D'Acquisto 2, 24050, Grassobbio, Italy*



Colonized milker played role of MRSA vector into the herd

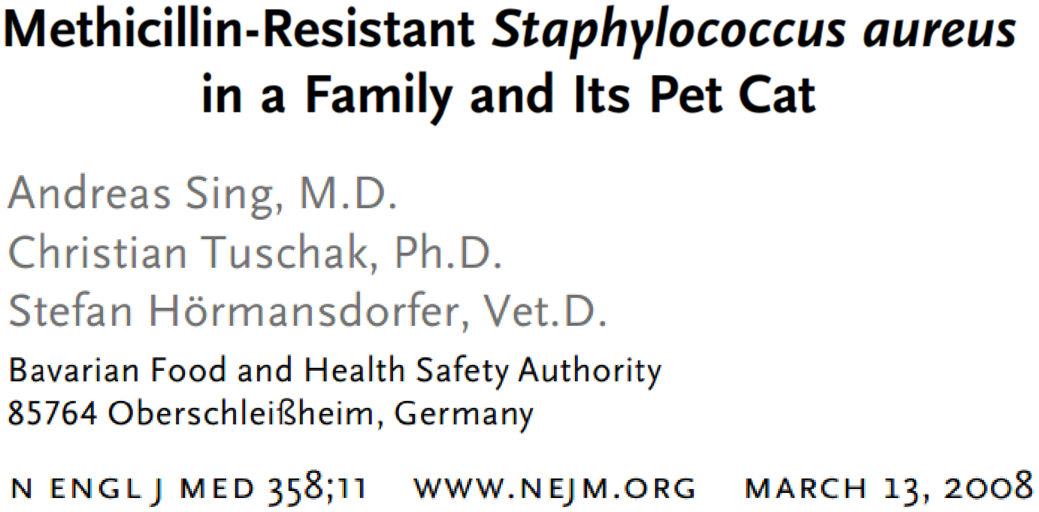
Adaptive capacity of MRSA to the bovine host

Icons from flaticon.com and picture from pixabay.com

MRSA CC80

MRSA CC80

- dominant clonal group among CA-MRSA of humans in Europe
- occasionally, CC80 strains occur also in pet animals



Methicillin-Resistant *Staphylococcus aureus* in a Family and Its Pet Cat

Andreas Sing, M.D.
Christian Tuschak, Ph.D.
Stefan Hörmansdorfer, Vet.D.
Bavarian Food and Health Safety Authority
85764 Oberschleißheim, Germany

N ENGL J MED 358;11 WWW.NEJM.ORG MARCH 13, 2008

MRSA (ST80-t131) was isolated from a woman who suffered from recurrent deep skin abscesses, her husband, her two kids, and a cat who lived in the same household.

Treatment success only after decolonization of all humans and the cat.

Transfer of MRSA between humans and a cat

MRSA-ST80 was PVL-positive and showed resistance to β-lactam and fusidic acid antibiotics

Picture by Jessica Rockowitz on Unsplash

Concluding Remarks

Icon from flaticon.com

Concluding Remarks

- There are dominant clonal complexes in the different animal species in different countries/continents.

Icons from flaticon.com

Concluding Remarks

- There are dominant clonal complexes in the different animal species in different countries/continents.
- MRSA from animals often harbor further resistance properties besides methicillin resistance, in part involving mobile genetic elements.

Icons from flaticon.com

Concluding Remarks

- There are dominant clonal complexes in the different animal species in different countries/continents.
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- MRSA can be exchanged between animals and humans in both directions.

Icons from flaticon.com

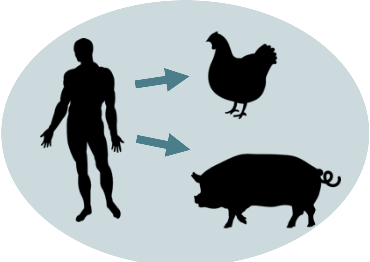
Concluding Remarks

- There are dominant clonal complexes in the different animal species in different countries/continents.
- MRSA from animals often harbor further resistance properties besides methicillin resistance, in part involving mobile genetic elements.
- MRSA can be exchanged between animals and humans in both directions.
- The close contact between humans and their pets favors the occurrence of „human“ clonal complexes in animals (CC22, CC80).

Icon from flaticon.com and Picture by Kevin Stark on Unsplash

Concluding Remarks

- There are dominant clonal complexes in the different animal species in different countries/continents.
- MRSA from animals often harbor further resistance properties besides methicillin resistance, in part involving mobile genetic elements.
- MRSA can be exchanged between animals and humans in both directions.
- The close contact between humans and their pets favors the occurrence of „human“ clonal complexes in animals (CC22, CC80).
- Host jumps have resulted in new clades within certain clonal complexes, the members of which are better adapted to the new host.



Icons from flaticon.com

Thanks a lot for your attention!

Picture by Andrea Schmidt, IMT