

MRSA epidemic clones from inside and outside the hospital

Hermínia de Lencastre, PhD

Laboratory of Molecular Genetics
Instituto de Tecnologia Química e Biológica (ITQB)

Laboratory of Microbiology, The Rockefeller University

8th ECCMID Summer School
Porto, Portugal, 11-17 July 2009

Ecological sites for MRSA evolution

Hospital

Community

HA-MRSA

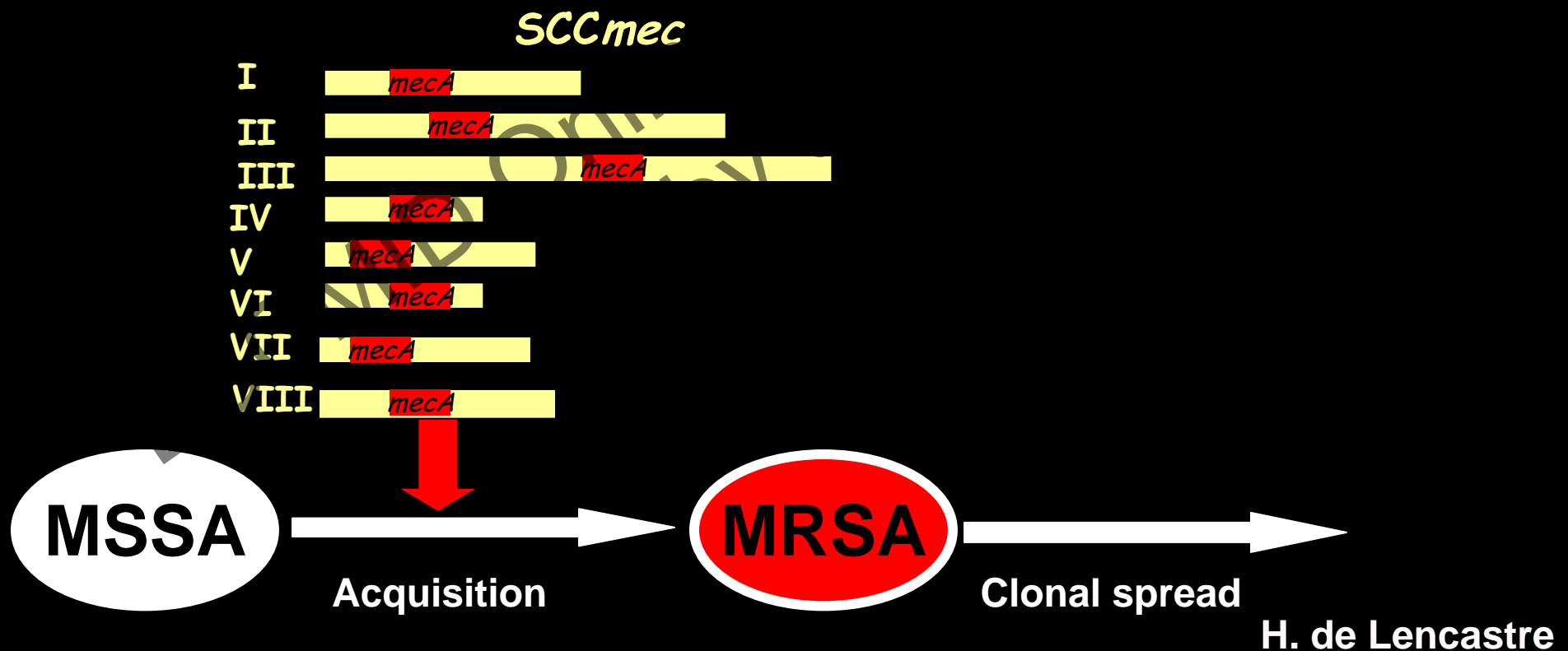
CA-MRSA

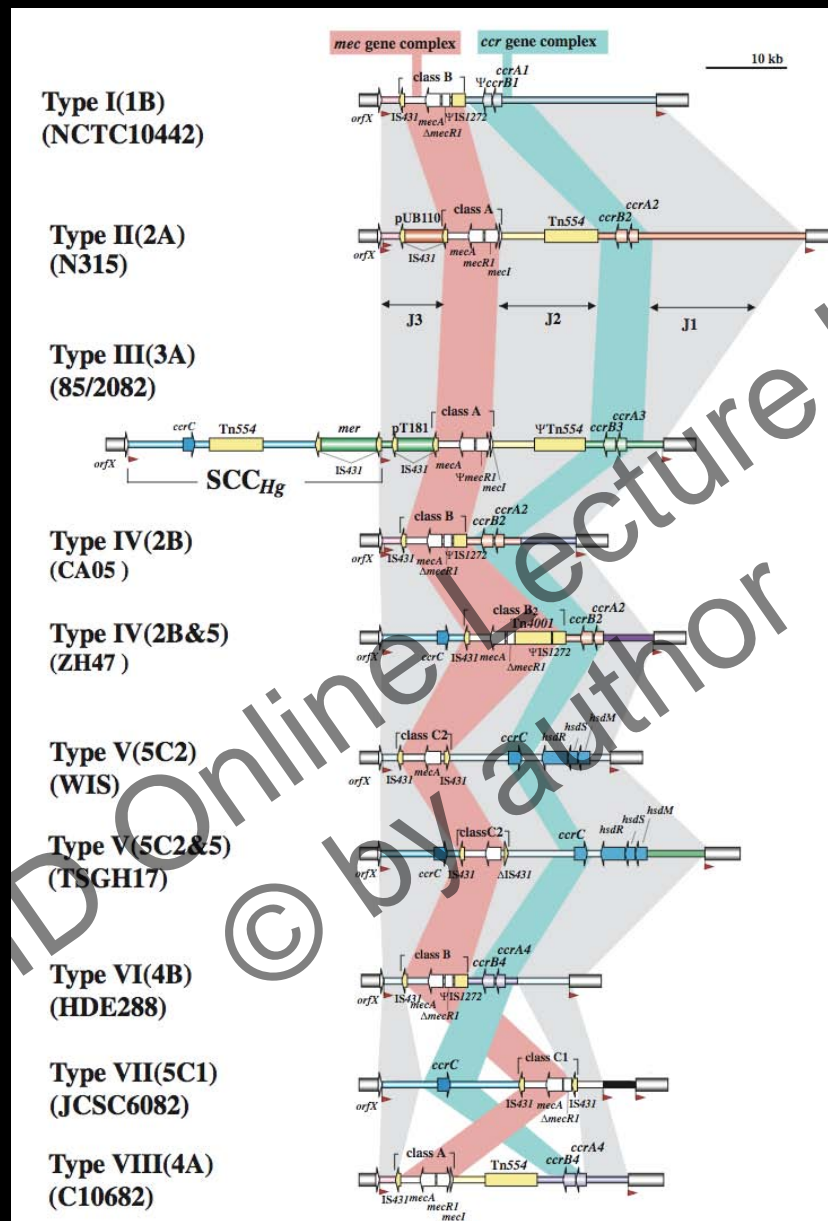
FA-MRSA

Animal husbandry

Key features and steps in MRSA evolution

- **resistance mechanism:** against all beta-lactams
- **resistance gene *mecA*:** not native to *S. aureus*
- **mobile form of *mecA*:** *SCCmec* – *mecA* embedded in exogenous DNA cassettes





Types
mec complex
ccr complex

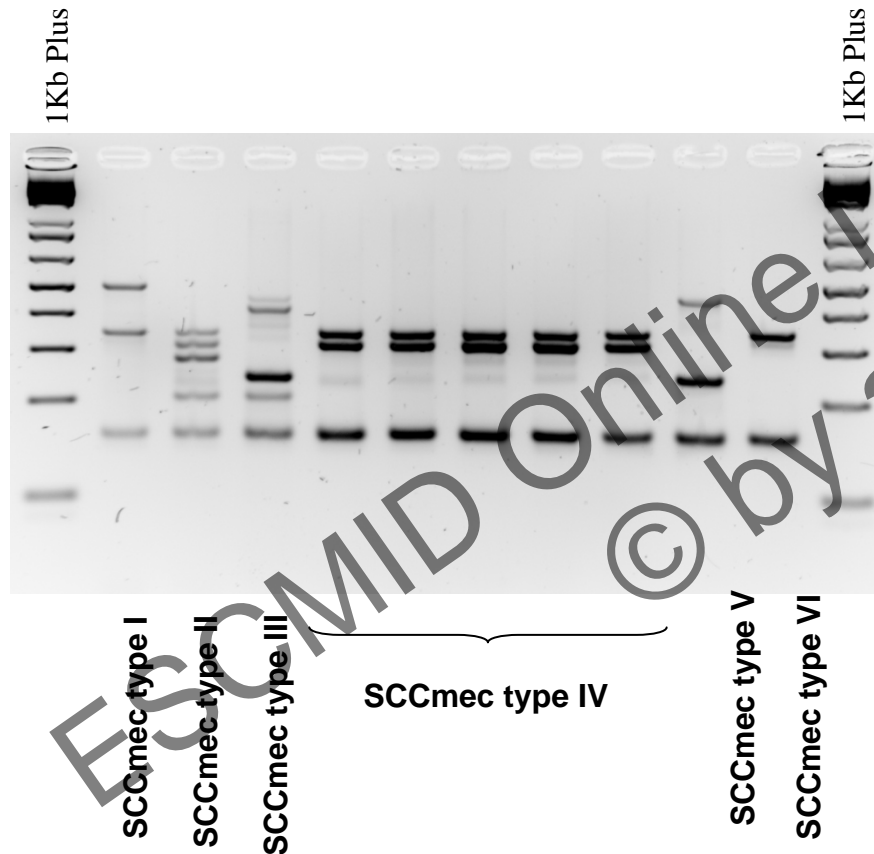
Sub-types
Structure J regions

"International Working Group on the Classification of Staphylococcal Cassette Chromosome Elements (IWG-SCC)" 2009. **Classification of Staphylococcal Cassette Chromosome *mec* (SCC*mec*): Guidelines for Reporting Novel SCC*mec* Elements.** (AAC 2009)

SCCmec typing system

2. SCCmec multiplex PCR update strategy

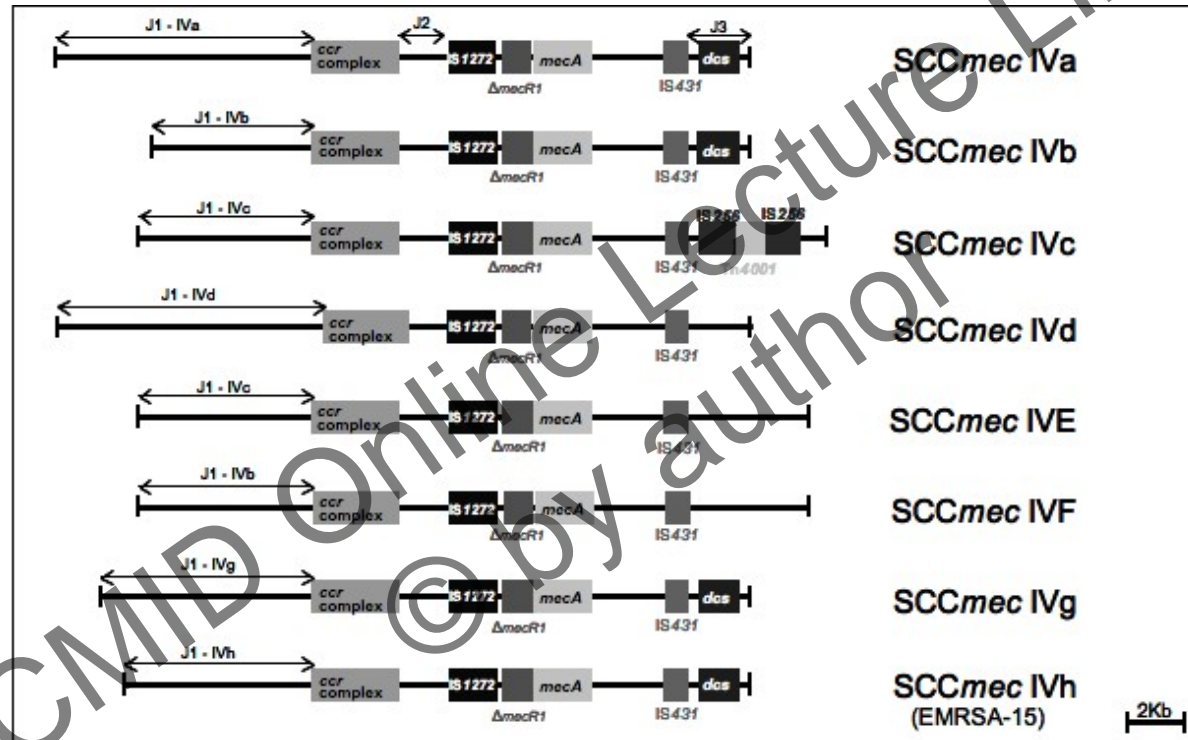
Advantages:



✓ Discrimination of the SCCmec types I, II, III, IV, V and VI (2-5 bands)

✓ This technique probes, in addition to *mecA* gene, eight loci scattered through the SCCmec element (*ccrC*, *ccrB2*, *mecl*, J1 of SCCmec types I, II, III and V; J3 of SCCmec types I, II, III, IV and VI)

3. SCCmec IV multiplex PCR strategy



Milheiriço *et al.*, JAC 2007

- ✓ Rapid assignment of all major subtypes of SCCmec type IV described so far and also the new subtype IVh characteristic of EMRSA-15

Epidemic Waves of MRSA

Wave 1: 1960 through late 1976

MRSA born multiresistant

Archaic clone

STs 250, ST247, ST8, ST254

SCCmec I

UK, Denmark, Egypt, Poland ...

1st epidemic wave of MRSA

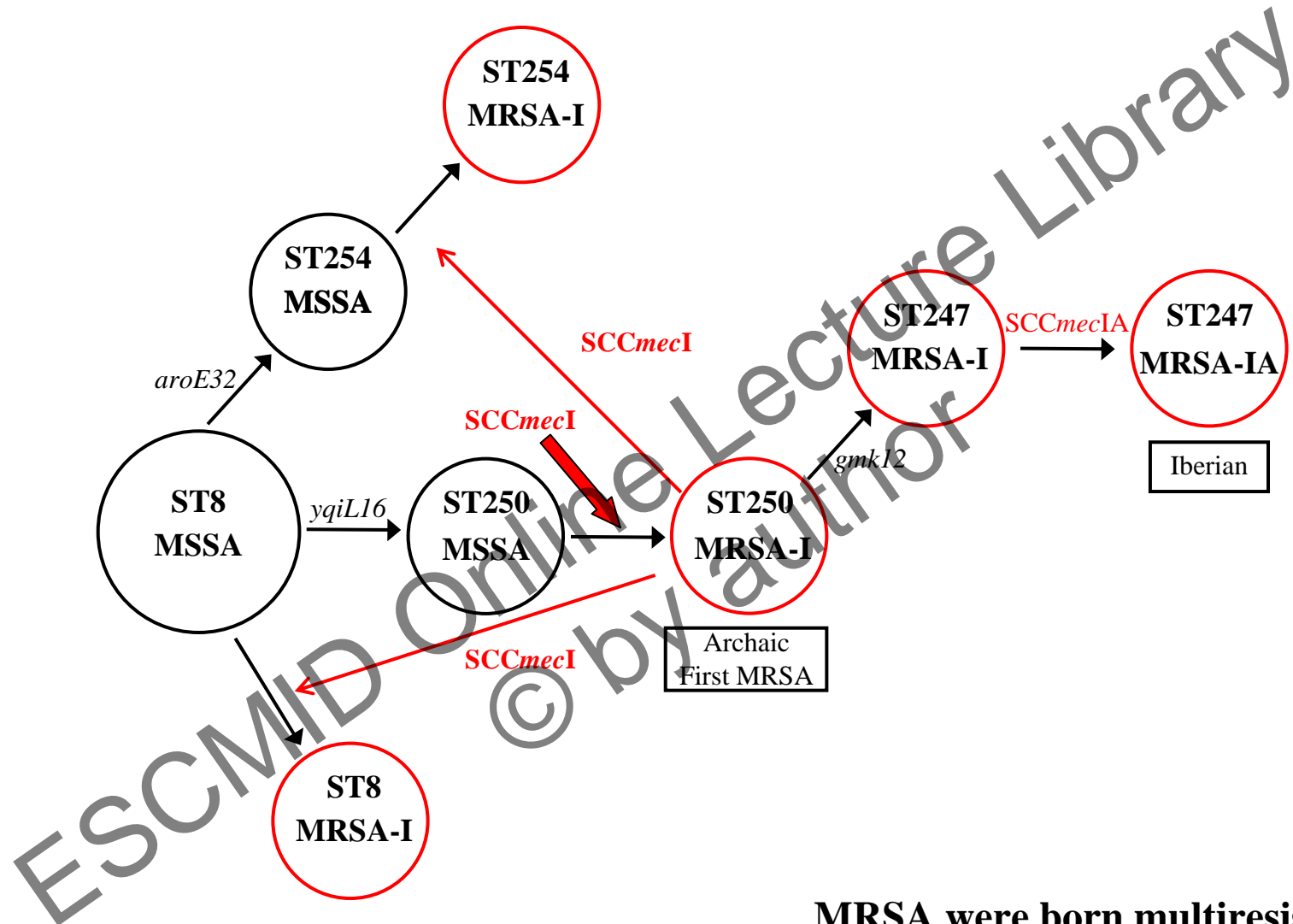
MSSA with genetic backgrounds of future MRSA clones existed but only one – ST250 – became a major MRSA clone during the first 17 years

SCC*mec* type I



H. de Lencastre

Donations of SCCmecI from ST250 occurred only within CC8!



MRSA were born multiresistant

Crisostomo et al (2001). PNAS 98:9865-70.

Gomes, Westh, de Lencastre 2006. AAC, 50:3237-44

Epidemic Waves of MRSA

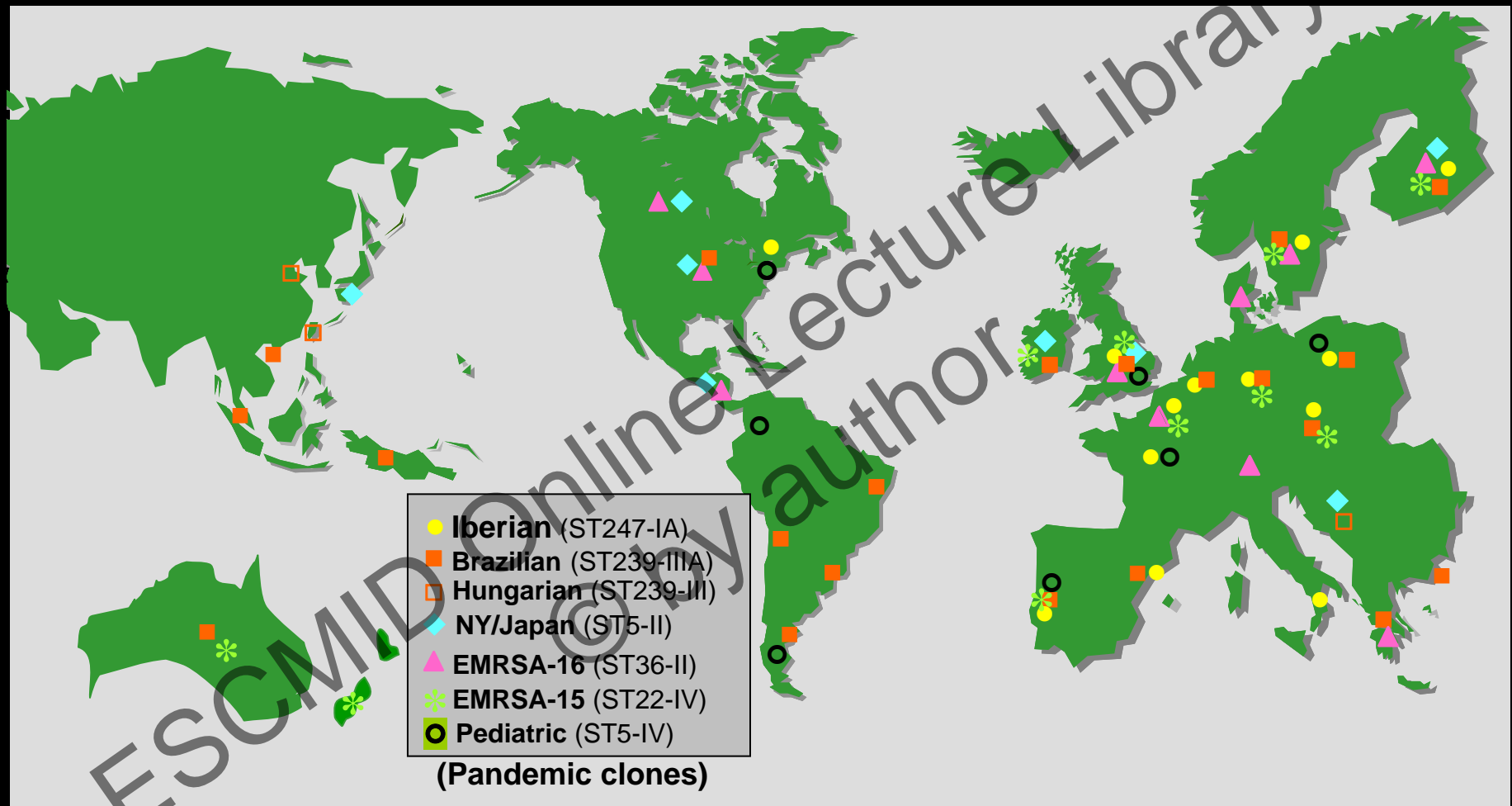
Wave 2: 1980 to present: expansion of 6 pandemic clones*

	<u>ST</u>	<u>SCCmec</u>
Iberian	247	IA
Brazilian	239	III
New York/Japan	5	II
Pediatric	5	IV or VI
EMRSA-15	22	IVh
EMRSA-16	36	II
Berlin	45	IV or V

* No birth dates known

* No birth certificates available

International surveillance



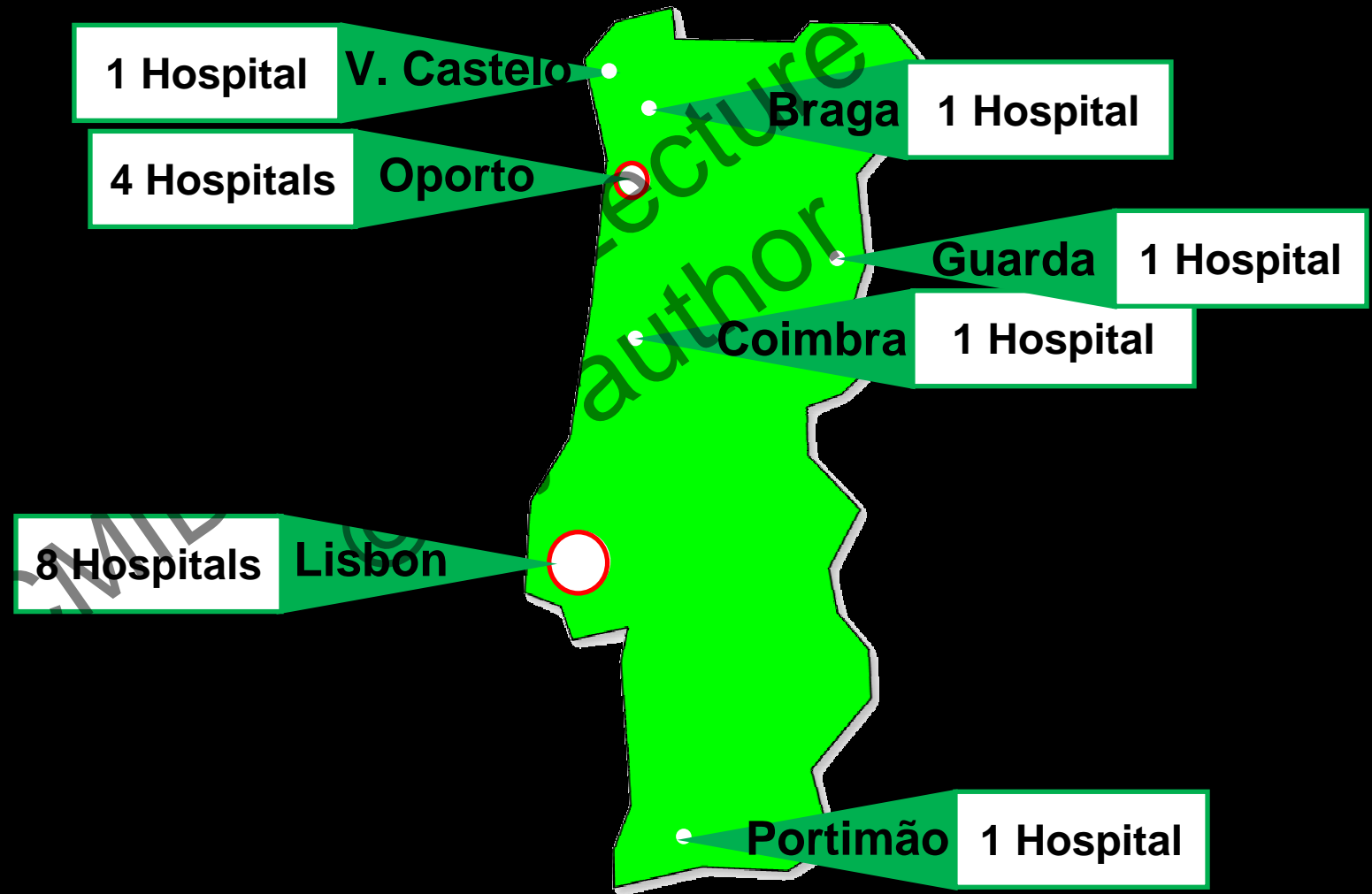
De Lencastre, H. and A. Tomasz. 2007. *In* Evolutionary Biology of Bacterial and Fungal Pathogens. Chapter 28, p.333-346. F. Baquero, C. Nombela, G. H. Cassell, and J. A. Gutierrez. ASM Press, Washington D. C.

Few epidemic MRSA clones spread worldwide

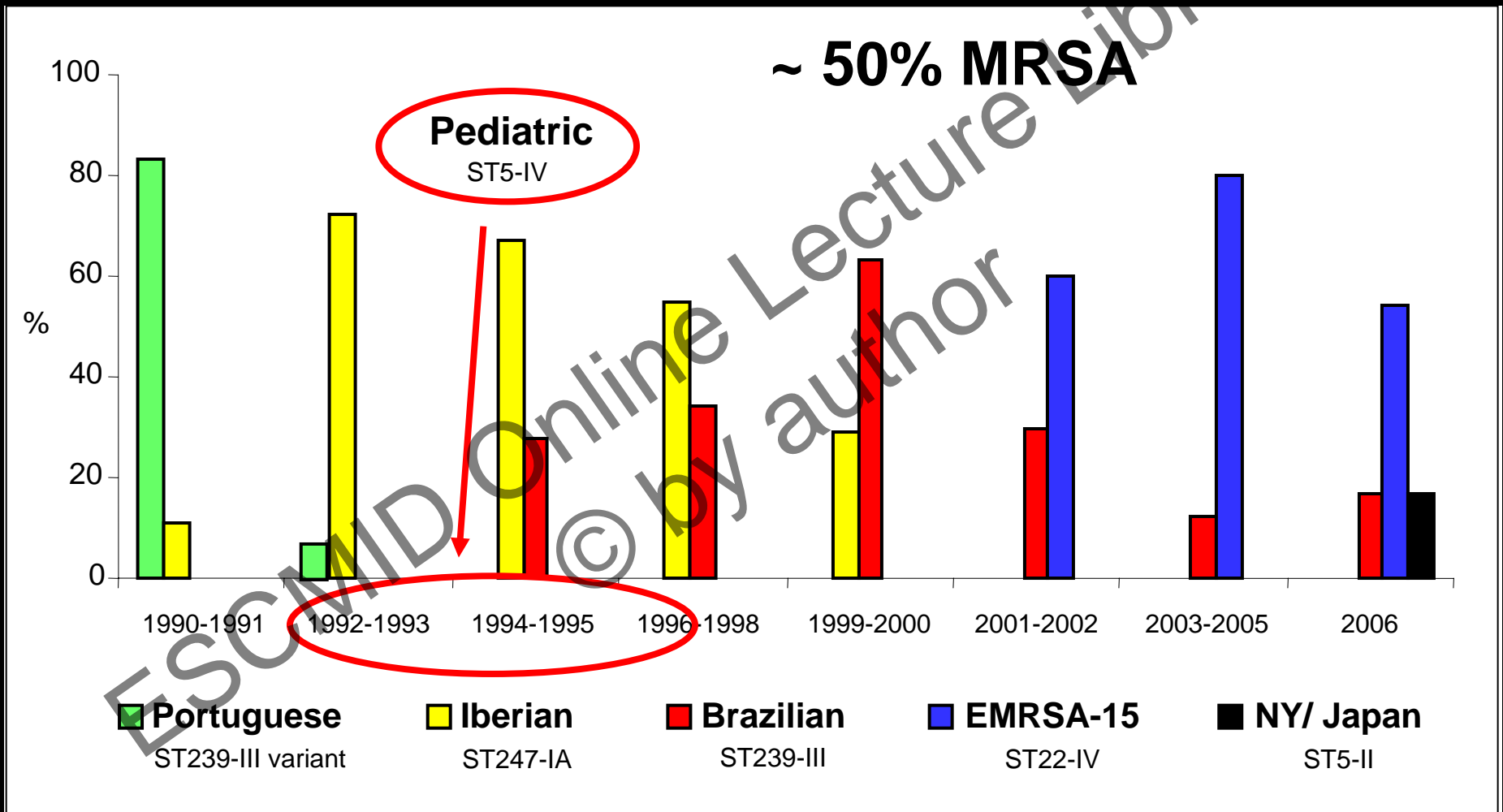
MRSA evolution over time 1990-2008



17 hospitals/ 7 cities



MRSA evolution over time 1990-2008



Adapted from Aires de Sousa, M. et al. 2008. JCM. 46:2912

Epidemic Waves of MRSA

Wave 3: Early late 1990s to present: **community acquired MRSA appears and spreads**

Settings:

Australia: aborigines populations

USA: Indian reservations

High degree of virulence:

1998 - 4 children without risk factors die in Minnesota in 24 h

Definition of CA-MRSA

CA-MRSA definition

MRSA strains isolated from patients in a community setting (community onset);

MRSA strains isolated from patients within 48 h of hospital admission (hospital onset);

Patients without previous history of MRSA infection or colonization, hospitalization, surgery, dialysis or residence in a long-term care facility within the previous year;

Patients without indwelling catheters or percutaneous devices at the time of culture

Types of CA-MRSA infections

Infection	Number	%
Skin infection or abscess	107	76%
UTI	19	14%
Pneumonia	5	4%
Blood	4	3%
Osteomyelitis or arthritis	3	2%
Intraabdominal infection	2	1%
Total	140	

Origin of CA-MRSA: assembly of new genotypes

**None of the HA-MRSA clones found among
CA-MRSA**

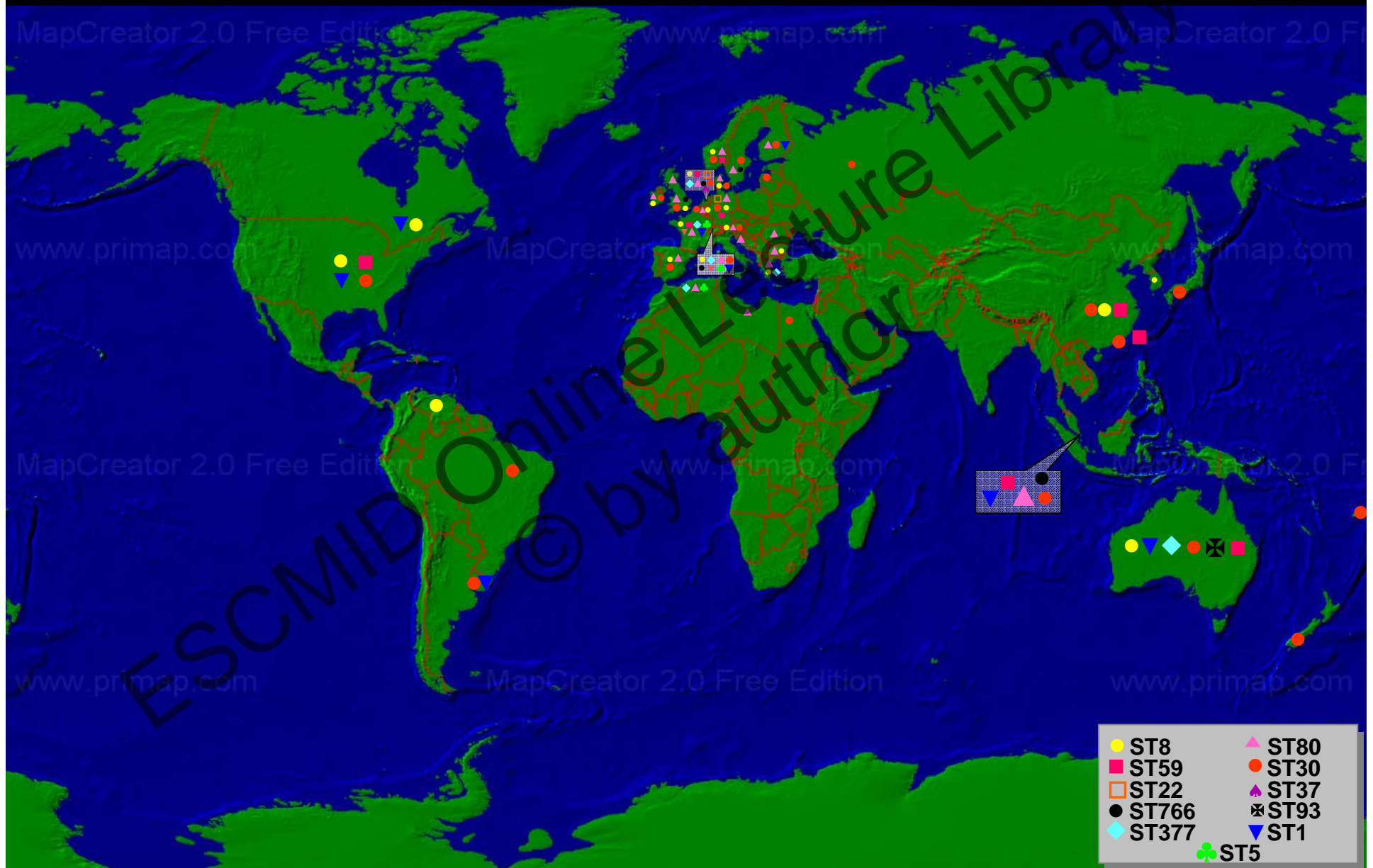
**Genetic backgrounds: frequent among MSSA
clones**

(ST1, ST8, ST30, ST80)

Methicillin resistance: *SCCmecIV* and *SCCmecV*

CA-MRSA were born susceptible or PenR

Global Distribution of Panton-Valentine Leukocidin-positive Methicillin-resistant *Staphylococcus aureus*, 2006



European Distribution of Panton-Valentine Leukocidin-positive Methicillin-resistant *Staphylococcus aureus*, 2006



H. de Lencastre

Main CA-MRSA clones in the USA

ST1-SCC*meclV*

USA400

ST59-SCC*meclV*

USA1000

ST8-SCC*meclV*

USA300

Prevalence of MRSA among 422 Emergency Department Patients with SSTI

MRSA 59%

This is NOT EUROPE

S. aureus isolated from 320 of 422 pts

7/13 (54%)

11/28 (39%)

4/20 (20%)

32/58 (55%)

24/47 (51%)

43/58 (74%)

17/25 (68%)

26/42 (62%)

18/30 (60%)

23/32 (72%)

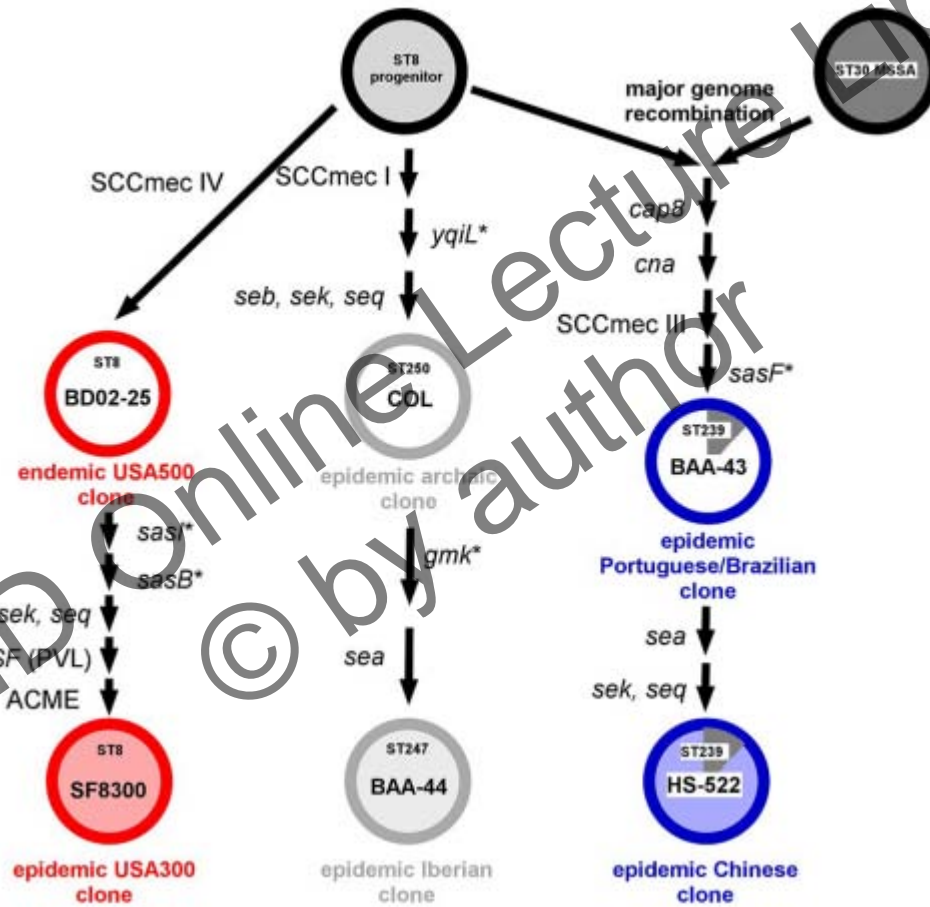
46/69 (67%)

MSSA 17%

Moran GJ et al. N Engl J Med 2006;355:666-74.

F. Vandenesch

The Secret of Success of USA300?

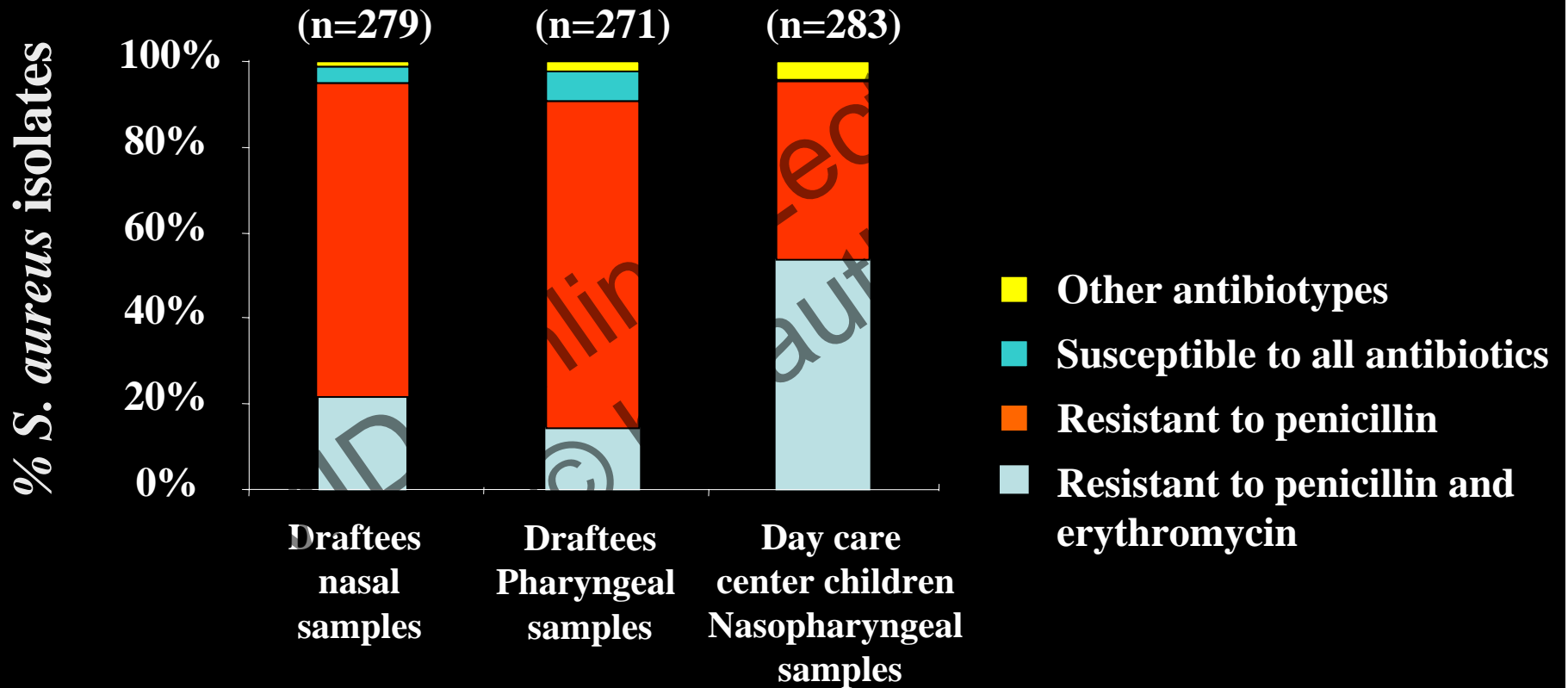


Li et al 2009 PNAS

**Is there an ecological reservoir of MRSA
among healthy carriers?**

Carriage of *S. aureus* by Healthy People in Portugal (Year 2001)

1001 *S. aureus* isolates but only 7 MRSA (< 0.1%)



2001: MRSA infections in Portuguese hospitals: 45-50%

Carriage of MRSA in the Community

Time/Place	Children	MRSA Carriage (%)	Major Sequence Types SCCmec types	Reference
2001-2002 Japan	880 (Day Care Centers)	4.3	ST5 ST8 (USA300) SCCmec II & IV	Hisata et al, JCM 2005
2005-2006 Taiwan	3046 – 2 months to 5 yrs (Health Care Visit)	7.3	ST59, ST239 SCCmec IV & V	Huang, Y.C. JCM 2007
2007-2008 Japan	136 (Day Care Centers)	3.7	-----	Ozaki et al JIC (Japan) 2009
2001-2002 USA	10,000 people (1 year up)	0.8 (MSSA 32%)	-----	
2003-2004 USA	10,000 people (1 year up)	1.5 (MSSA 28%)	ST5 (USA100) SCCmec II, IV or VI	Gorwitz et al JID 2008

Majority of MRSA isolates were HA-MRSA clones but some CA-MRSA also included

H. de Lencastre

Carriage of *S. aureus* by Healthy People in Portugal (2006-2009)

Year	Location	Total NP samples	<i>S. aureus</i> isolates (%)	% of MRSA among <i>S.aureus</i>
2006	Oeiras	571	92 (16)	3
2007	Oeiras	538	71 (13)	0
2009	Montemor-o-Novo	380	86 (23)	2
2009	Oeiras	611	119 (19)	0

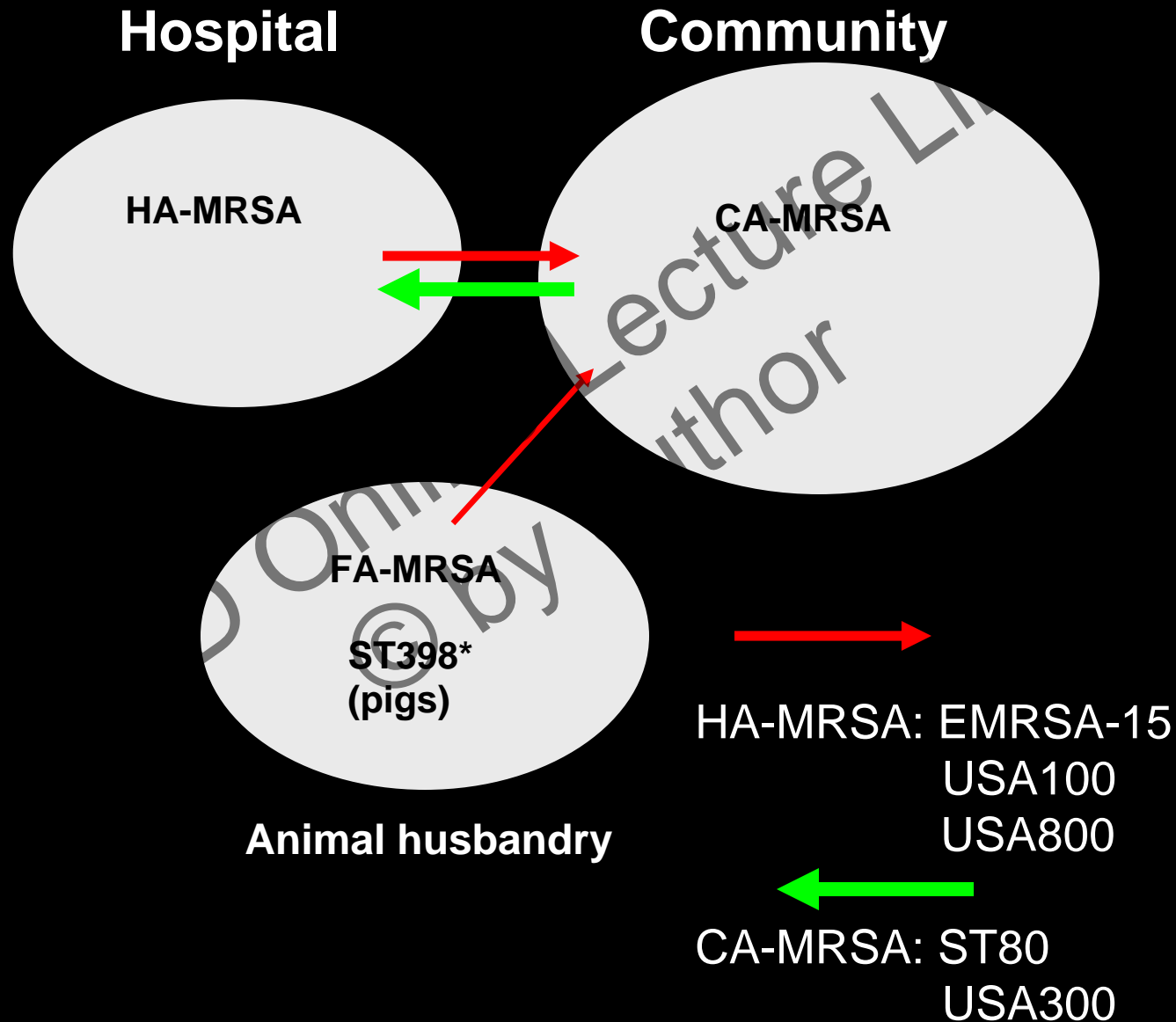
Tavares, Sá-Leão, Miragaia, de Lencastre (2009) unpublished

**Is there an ecological reservoir of CA-MRSA
among healthy carriers?**

(test colonization sites other than the nares?)

**Contrast with high rate of carriage of
drug resistant *S. pneumoniae* in healthy
children attending Day Care!**

Ecological sites for MRSA evolution



Acknowledgements

Marta Aires de Sousa

Duarte C. Oliveira

Nuno Faria

Catarina Milheiriço

Ines Crisostomo

Maria Miragaia

Teresa Conceicao

Ana Gomes

Débora Tavares

Raquel Sá-Leão

Alexander Tomasz

Henrik Westh