

# ***S. epidermidis* – insights in pathogenesis from genomics**

D. Ashley Robinson, Ph.D.

Department of Microbiology and Immunology  
University of Mississippi Medical Center

# Outline

- *S. epidermidis* and the diagnostic conundrum
- Use of population genetic structure to identify pathogenic variants of *S. epidermidis*
- Population genomic study of *S. epidermidis* ST2

# *S. epidermidis*: commensal or pathogen?

- *S. epidermidis* is an abundant species of the microbial community that colonizes human skin
- For healthy persons, it is a commensal that can impede skin colonization and infection by more aggressive cutaneous pathogens
- For hospitalized and immunocompromised persons, especially those with indwelling medical devices (e.g., catheters, prosthetics), it is a pathogen
- It is the most commonly isolated coagulase-negative staphylococci from clinical specimens, accounting for 21% of CLABSI's and 11% of all healthcare-associated infections in the US

*S. epidermidis*: contaminant or true infection?



# Microbiological approaches for assessing *S. epidermidis* pathogenic potential

- Biomarkers: specific genes and phenotypes
  - *mecA*, *SCCmec*, multidrug resistance
  - *ica*, *aap*, biofilm
  - IS256
- Population structure: specific clones and groups of related clones
  - multilocus sequence types
  - clonal complexes, genetic clusters
- Genomics: potential for unbiased, comprehensive list of pathogen biomarkers, and maximally resolved population structure

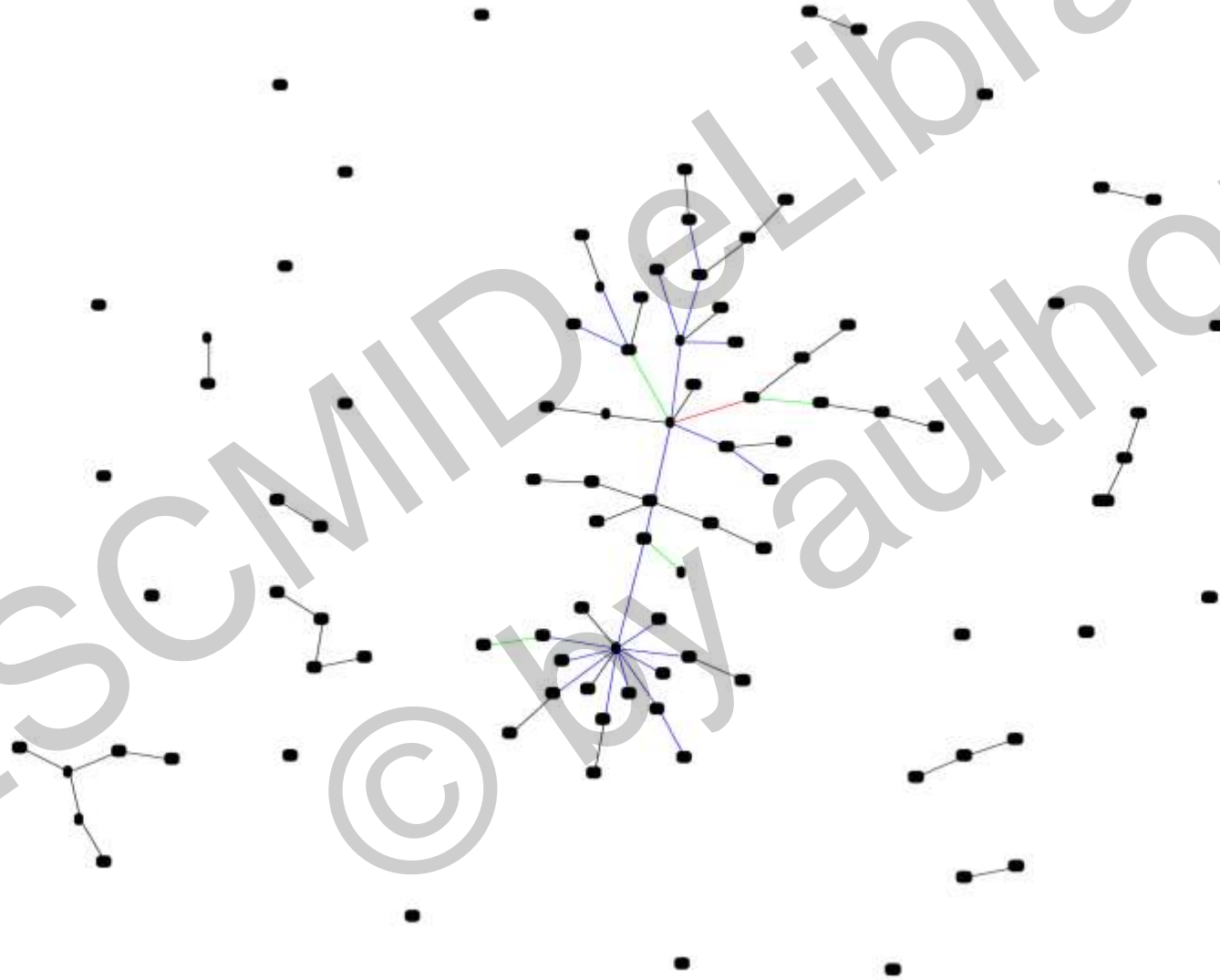
# Population structure: MLST and eBURST

- Consensus MLST scheme of the 7 most discriminatory loci from 3 earlier MLST schemes
  - Thomas et al. 2007. J Clin Microbiol 45:616, hosted at [pubmlst.org](http://pubmlst.org)
- Several STs frequently occur in clinical specimens
  - ST2
  - ST5
  - ST23
- eBURST clustering of STs, based on allele sharing at 7 loci
  - Kozitskaya et al. 2005. J Clin Microbiol 43:4751
  - Miragaia et al. 2008. J Bacteriol 189:2540
  - most strains of clinical significance and/or those with pathogen biomarkers, cluster together in a single clonal complex

# Clonal complexes: 2007 STs and goeBURST

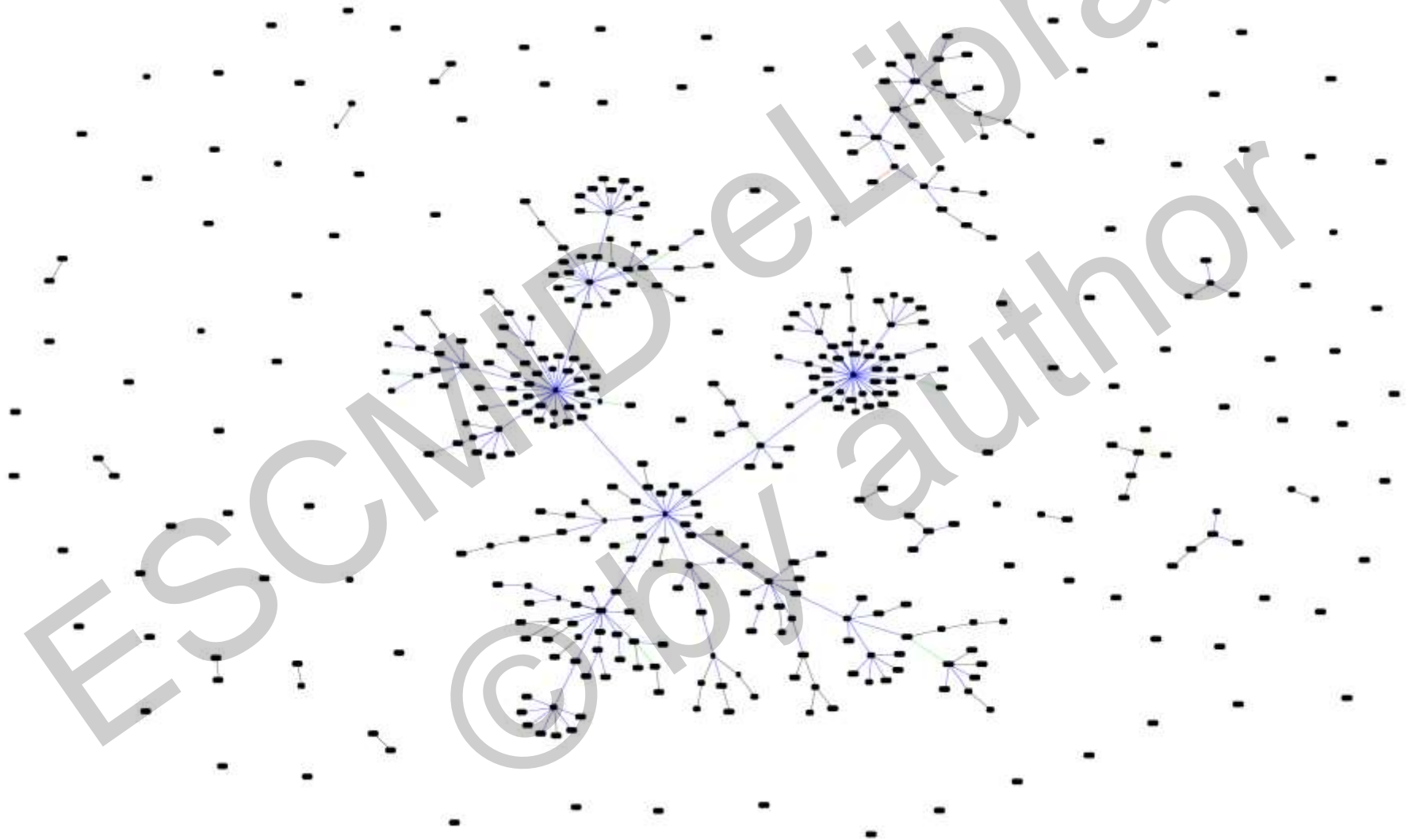


# Clonal complexes: 2008 STs and goeBURST





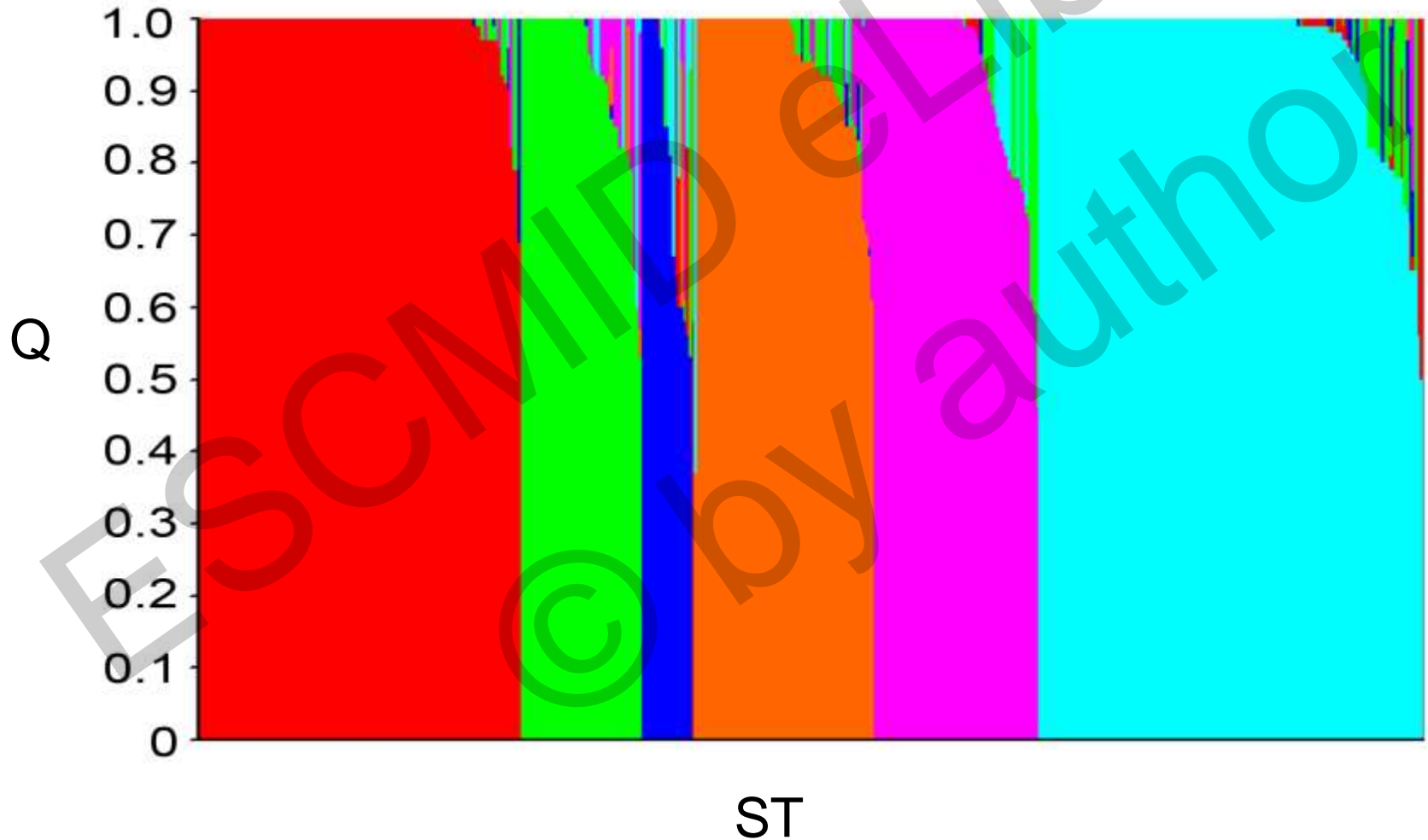
# Clonal complexes: 2012 STs and goeBURST



# Population structure: MLST and population assignment

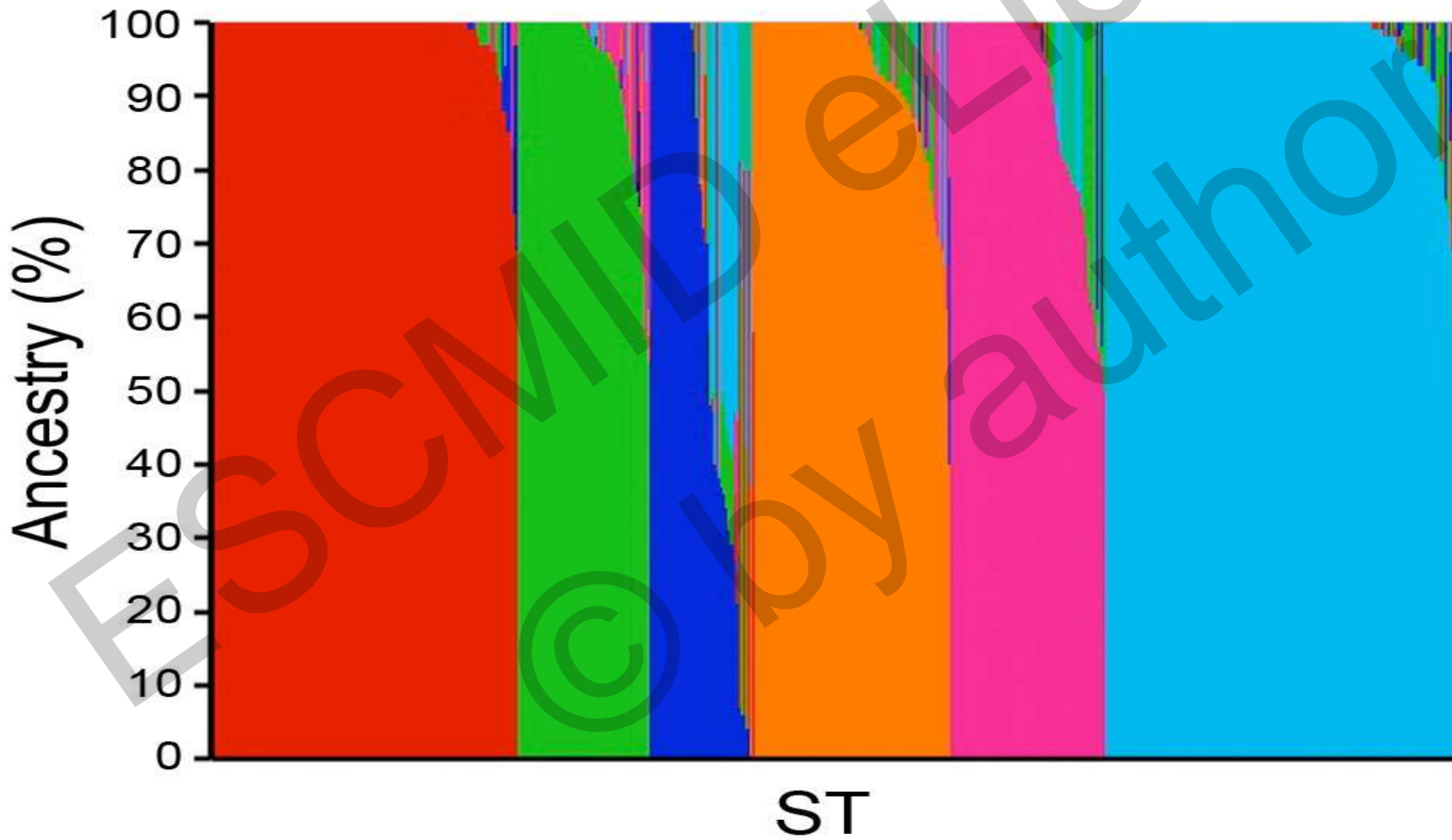
- Bayesian analysis with STRUCTURE and BAPs
  - model-based probabilistic assignment of STs to populations based on nucleotide allele frequencies
  - inference on number of populations and admixture between populations
- Initial study with analysis of MLST database and 129 isolates from clinical specimens
  - Thomas et al. 2014. Infect Genet Evol 22:257
- Second study with analysis of MLST database and 154 isolates from true infections, contaminants, and non-hospital carriage isolates
  - Tolo et al. 2016. J Clin Microbiol 54:1711

# Genetic clusters: 2012 STs and BAPs



(n=437 STs)

# Genetic clusters: 2015 STs and BAPs



(n=578 STs)

# Characteristics of genetic clusters

## Thomas et al. 2014

- GC5 abundant (34%) from clinical specimens, relatively recombinant, enriched for multidrug resistance, biofilm, *icaA*, IS256 and *sesD*
- GC1, GC6 abundant (24%, 38%), enriched for *aap*
- GC2 rare (2%)
- GC3 rare (2%), highly recombinant

# Characteristics of genetic clusters

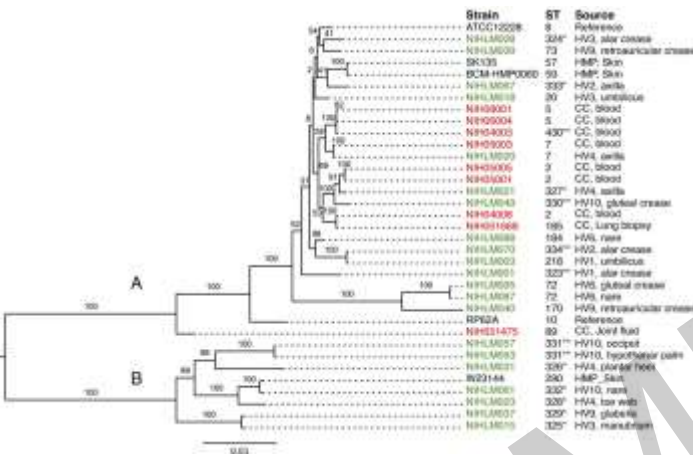
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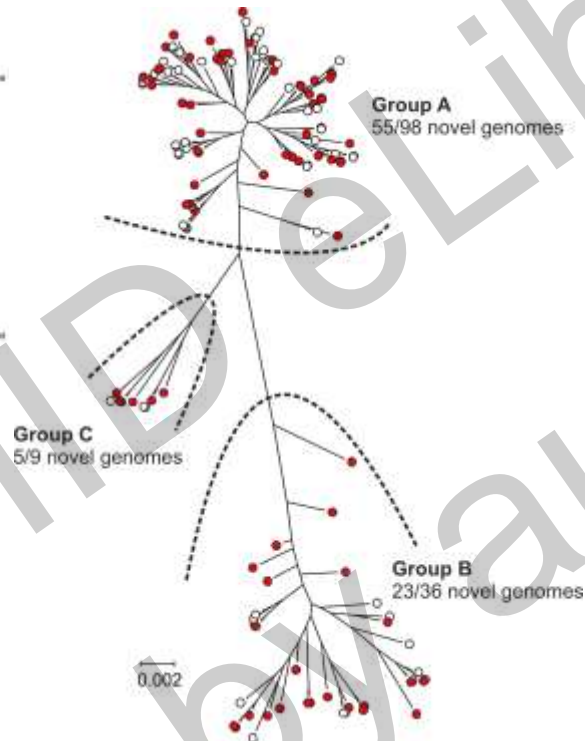
## Tolo et al. 2016

- GC5 isolated almost exclusively from hospital sources, relatively recombinant, enriched for *icaA*, IS256
- GC1, GC6 isolated from all sources
- GC2 and GC4 rare yet relatively diverse, not associated with non-hospital carriage source
- GC3 rare, highly recombinant
- 
- GCs can predict hospital and non-hospital isolation source with 80% accuracy (comparable to 5 biomarkers), alone they do not distinguish true infection from contaminant source

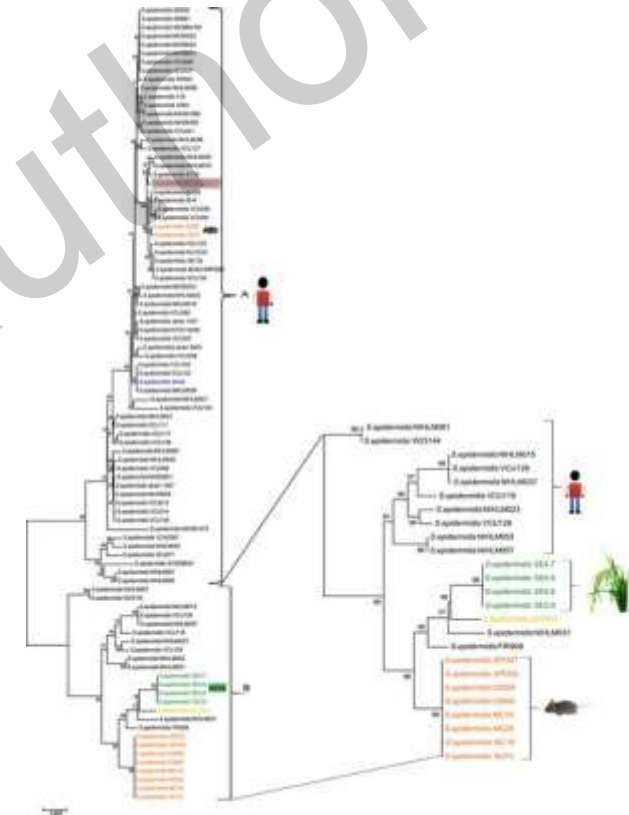
# Genomic views of *S. epidermidis* population structure



Conlan et al. 2012. Genome Biol 13:R64



Méric et al. 2015. Genome Biol Evol 7:1313



Chaudry & Patil. 2016. Sci Rep 6:19263



# Some strains of Genomic group B, Genetic cluster 4 are pathogenic

JOURNAL OF BACTERIOLOGY, Apr. 2011, p. 1854–1862

0021-9193/11/\$12.00 doi:10.1128/JB.00162-10

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## An Enterotoxin-Bearing Pathogenicity Island in *Staphylococcus epidermidis*<sup>∇†</sup>

Jyoti Madhusoodanan,<sup>1‡</sup> Keun Seok Seo,<sup>4‡¶</sup> Brian Remortel,<sup>5§</sup> Joo Youn Park,<sup>6</sup> Sun Young Hwang,<sup>4,7</sup> Lawrence K. Fox,<sup>6</sup> Yong Ho Park,<sup>7</sup> Claudia F. Deobald,<sup>4</sup> Dan Wang,<sup>8</sup> Song Liu,<sup>8</sup> Sean C. Daugherty,<sup>9</sup> Ann Lindley Gill,<sup>1,3||</sup> Gregory A. Bohach,<sup>4\*</sup> and Steven R. Gill<sup>1,2,3\*</sup>





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## Genotype and enterotoxigenicity of *Staphylococcus epidermidis* isolate from ready to eat meat products

Magdalena Podkowiak<sup>a</sup>,  , Keun Seok Seo<sup>b</sup>, Justyna Schubert<sup>a</sup>, Isaiah Tolo<sup>c</sup>, D. Ashley Robinson<sup>c</sup>, Jacek Bania<sup>a</sup>, Jarosław Bystron<sup>a</sup>



# Summary: *S. epidermidis* population structure in relation to pathogenic potential

- Genomic group A, Genetic clusters 1, 5, 6
  - the main source of true infections
  - the main carriers of pathogen biomarkers
  - genetic cluster 5 includes notable pathogens ST2 and ST23, and is relatively recombinant
- Genomic group B, Genetic clusters 2, 4
  - rarely isolated from clinical specimens
  - diverse, has a host range that is broader than humans
  - genetic cluster 4 includes some enterotoxin+ strains
- Genomic group C, Genetic cluster 3
  - rarely isolated, highly recombinant


# Population genomic study of *S. epidermidis* ST2

- ST2 is *S. epidermidis*' most prominent clone from clinical specimens:
  - Ahlstrand'14, Campanile'13, Cherifi'13, Cremniter'13, Du'13, Hellmark'13, Iorio'12, Kern'13, Kozitskaya'05, Li'09, Mendes'12, Sharma'14, Widerstrom'09, Widerstrom'12, Rolo'12
- ST2 is rare or absent from healthy people outside of hospitals:
  - Bispo'14, Cherifi'13, Du'13, Rolo'12
- ST2 isolates often have pathogen biomarkers
  - *mecA*+, *SCCmec*+ (but often non-typeable), multidrug-resistant, *ica*+, *aap*+, biofilm formers, like genetic cluster 5 to which they are assigned

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