



EVOLUTION OF INVASIVE AND COLONIZING PEDIATRIC *STAPHYLOCOCCUS AUREUS* ISOLATES

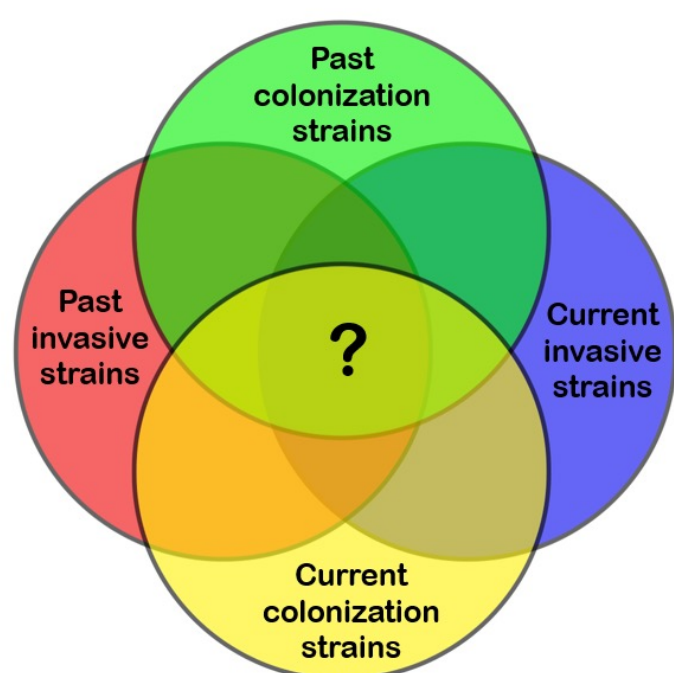
Margaret Free, Nicole Soper, Shristi Shrestha, Jean-Philippe Cartailier, Isaac Thomsen

Vanderbilt University Medical Center and the Monroe Carell Jr. Children's Hospital at Vanderbilt

INTRODUCTION

- Staphylococcus aureus* is the most common bacterial pathogen isolated in children hospitalized with invasive bloodstream and musculoskeletal infections.
- A major barrier to vaccine or novel therapeutic development against *S. aureus* is its constant evolution. Many recent and current vaccine candidates target antigens that appeared vital to its pathogenesis, only to see these factors recede from circulating invasive strains.
- Characterization of clinically relevant *S. aureus* strains over time is necessary to find targets for novel therapeutics. Efforts toward new interventions should target factors that remain prevalent in invasive strains over time.

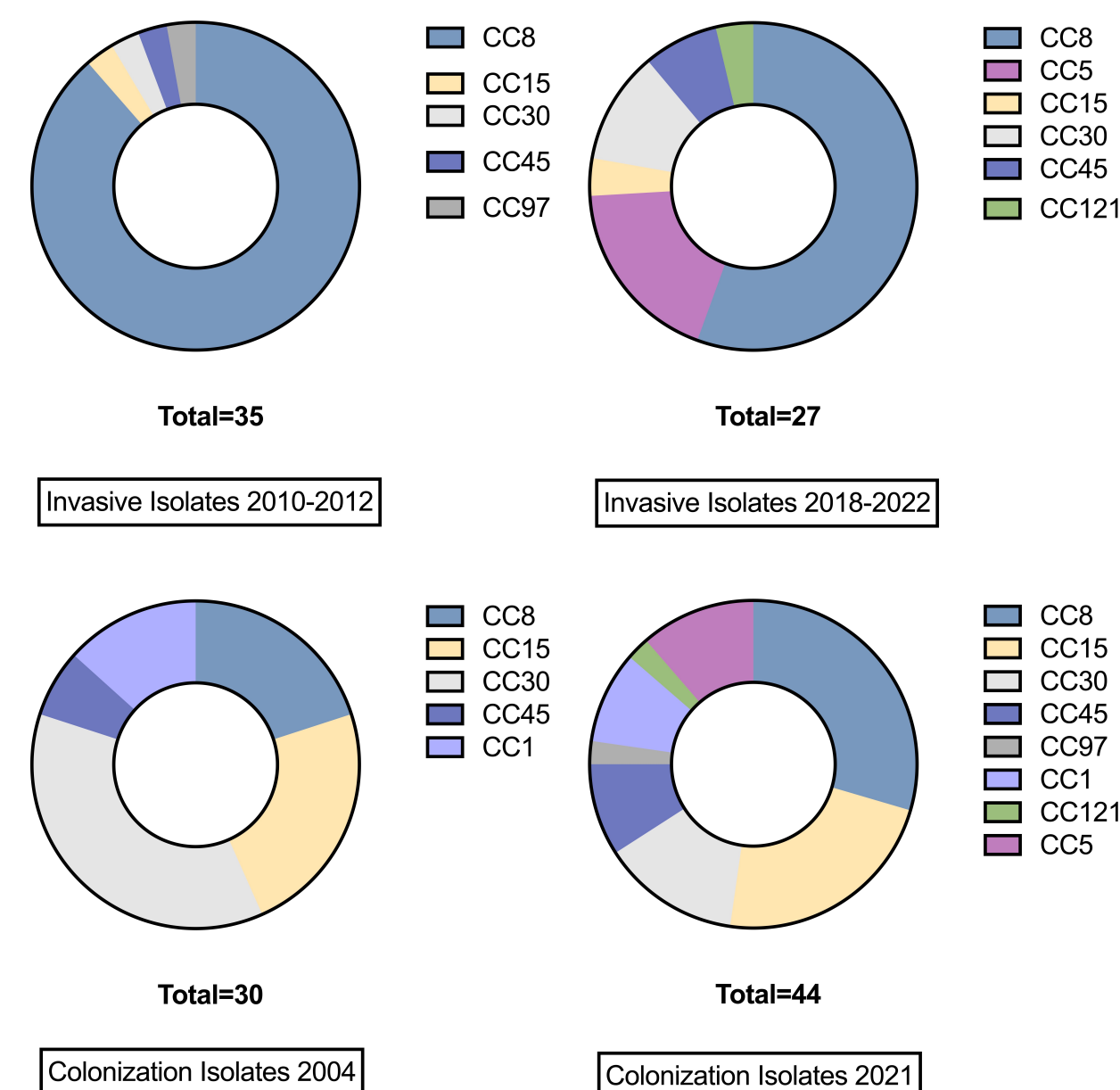
METHODS



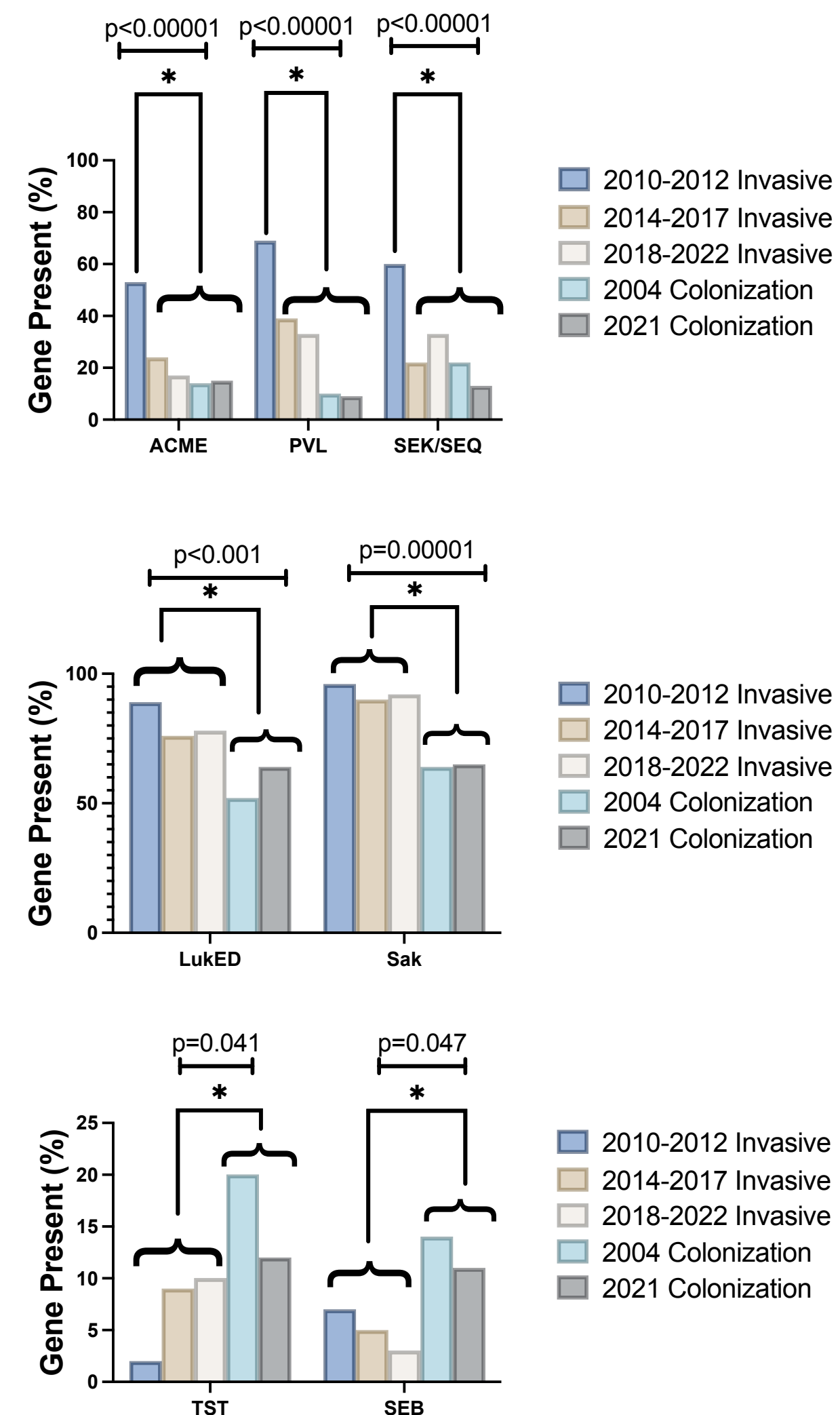
- We obtained 146 colonizing and 120 invasive *S. aureus* isolates from children admitted to the Monroe Carell, Jr. Children's Hospital at Vanderbilt from 2010 to 2022.
- Whole genome sequences are obtained using the Illumina sequencing platform.
- Virulence factors and sequence typing are determined using Geneious software and through PubMLST, an open-access curated database.

RESULTS I: INVASIVE AND COLONIZING STRAIN LINEAGE

- 9 unique clonal complexes were identified among 174 isolates.
- CC8 remains the most common invasive clonal complex, though is significantly less frequent now than in 2010-2012.
- Diversity of invasive strains has increased substantially, with the emergence of CC5 and CC121 lineages causing invasive disease in children.
- Some lineages (e.g. CC1) are exclusive to colonization strains.



RESULTS II: VIRULENCE FACTOR PREVALENCE



- The prevalence of ACME, PVL, and SEK/SEQ has decreased significantly in invasive *S. aureus* strains since 2010, from 53-70% to 21-35% for current isolates.
- The leukocidin LukED and surface protein staphylokinase (Sak) are strongly associated with invasive strains compared to colonization strains.
- Conversely, TST and SEB were seen more commonly in colonization strains (12-15%) vs invasive strains (5-7%).
- The genes encoding HlgA-C, LukAB, IsdA, IsdB, sbi, Efb, ClfA, and ClfB were identified in all strains tested.

CONCLUSIONS

- Significant shifts have occurred over the past decade with regarding to the predominant circulating *S. aureus* strains and their virulence factor repertoire.
- The once-dominant CC8 (USA300) clone has receded, and with that has come a significant reduction in some factors once thought crucial for pathogenesis.
- These findings also have implications for infection prevention and control practices, as eradication of colonizing strains with low potential for pathogenicity may allow replacement by more virulent strains.

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