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Hidden reservoirs of resistance: Contribution of plasmids to antibiotic resistance in *Staphylococcus aureus*

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Introduction

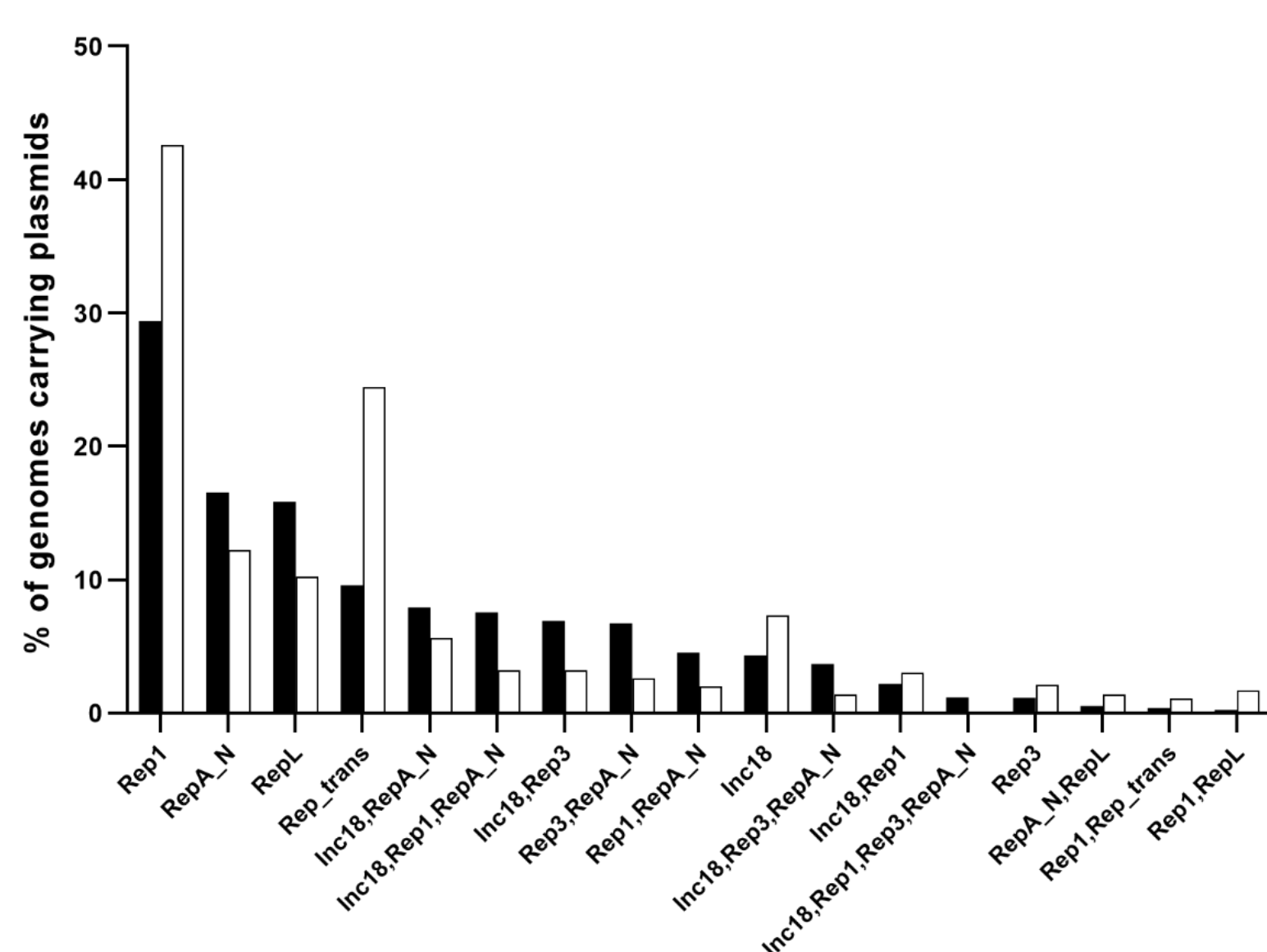
Staphylococcus aureus is a human and animal opportunistic pathogen that has demonstrated the capacity to develop resistance to a wide range of antibiotics. Its ability to acquire antibiotic resistance genes (ARGs) is closely associated with the large proportion of mobile genetic elements (MGEs) in its genome (between 15 to 20%) and its capacity to exchange genetic material with its environment. While plasmids have been shown to be key vectors for the dissemination of antibiotic resistance among Enterobacterales, their role in the spread of ARGs in *S. aureus* remains understudied.

To address this gap, we identified the associations between plasmids and ARGs in 10,063 *S. aureus* genomes from humans and animals present in NCBI databases, along with 330 field strains collected by the French surveillance network in animals (Resapath).

What is the role of plasmids in the spread of antibiotic resistance in *Staphylococcus aureus*?

Diversity of plasmids in *S. aureus*

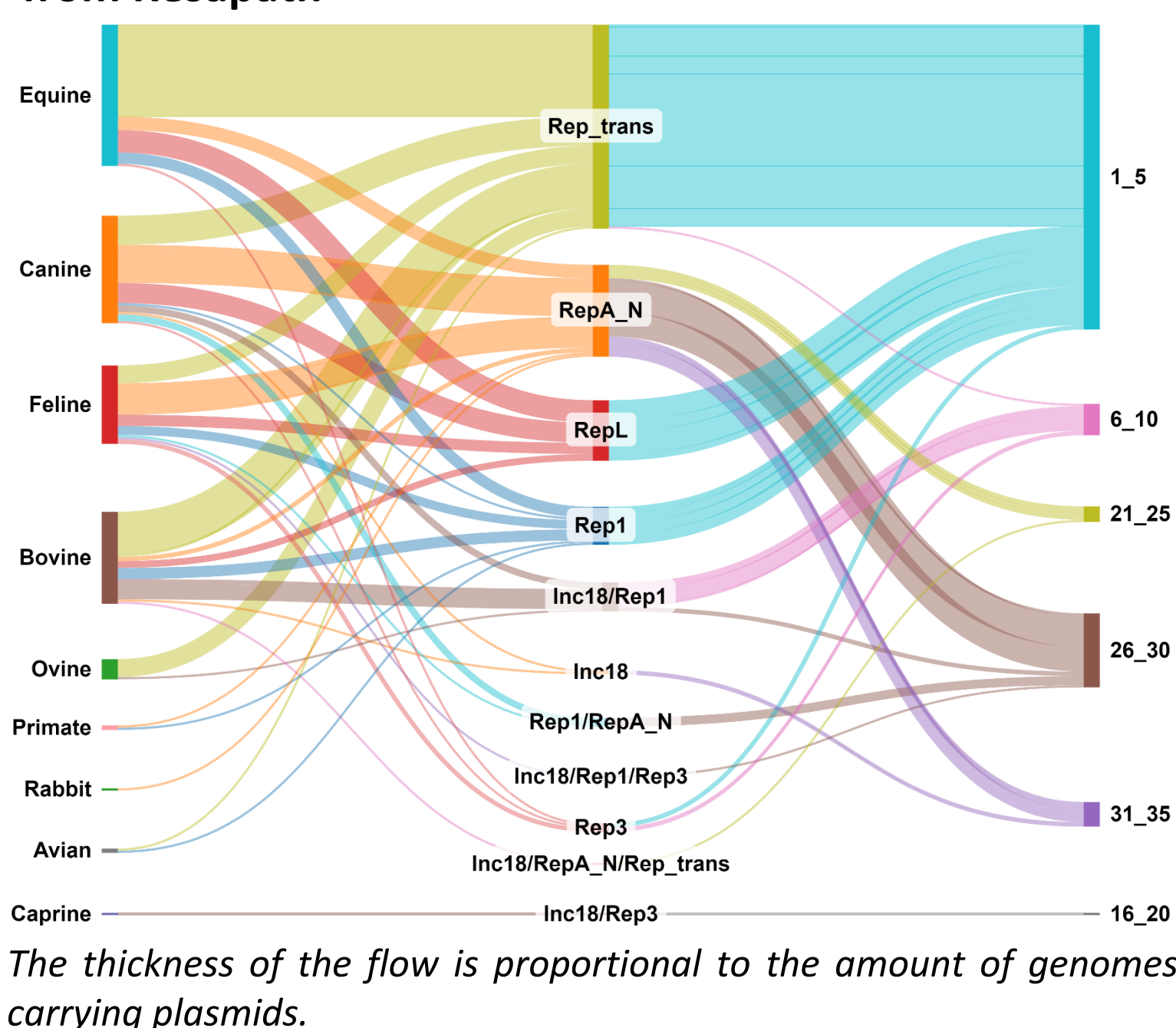
Occurrence of plasmids in *S. aureus* genomes of human (black) and animal (white) origin from NCBI database



In publicly available genomes,

- 86% and 81% of *S. aureus* genomes of human (Hm-SA) and animal (An-SA) origin, respectively carried at least one plasmid.
- Most abundant plasmids :
- Hm-SA: **Rep1**, **RepA_N** and **RepL**
- An-SA: **Rep1**, **Rep_trans** and **RepA_N**

Sankey diagram depicting plasmid families and size (in kb) depending on animal host in *S. aureus* collected from Resapath

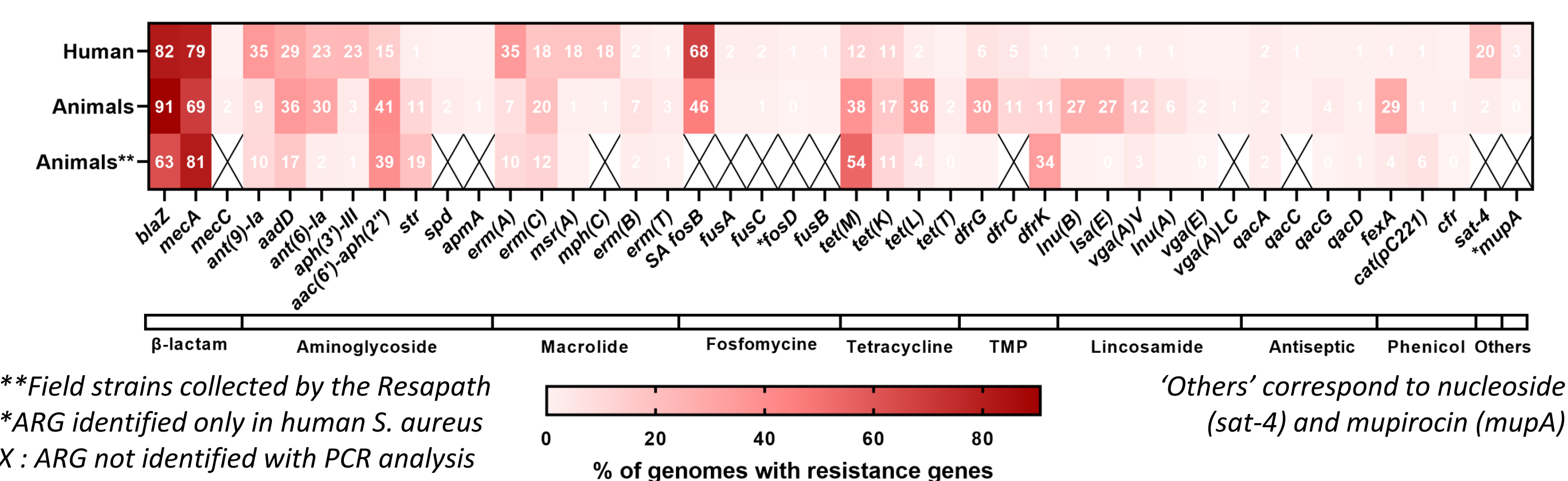


In animal field strains,

- 43% (143/330) strains carried at least one plasmid.
- Multiple families of plasmids were found in all animal hosts.
- Widespread families: **Rep_trans**, **RepA_N** and **RepL**
- Average size: small plasmids (≤ 5 kb)
- Plasmid family = specific range of size (except for RepA_N).

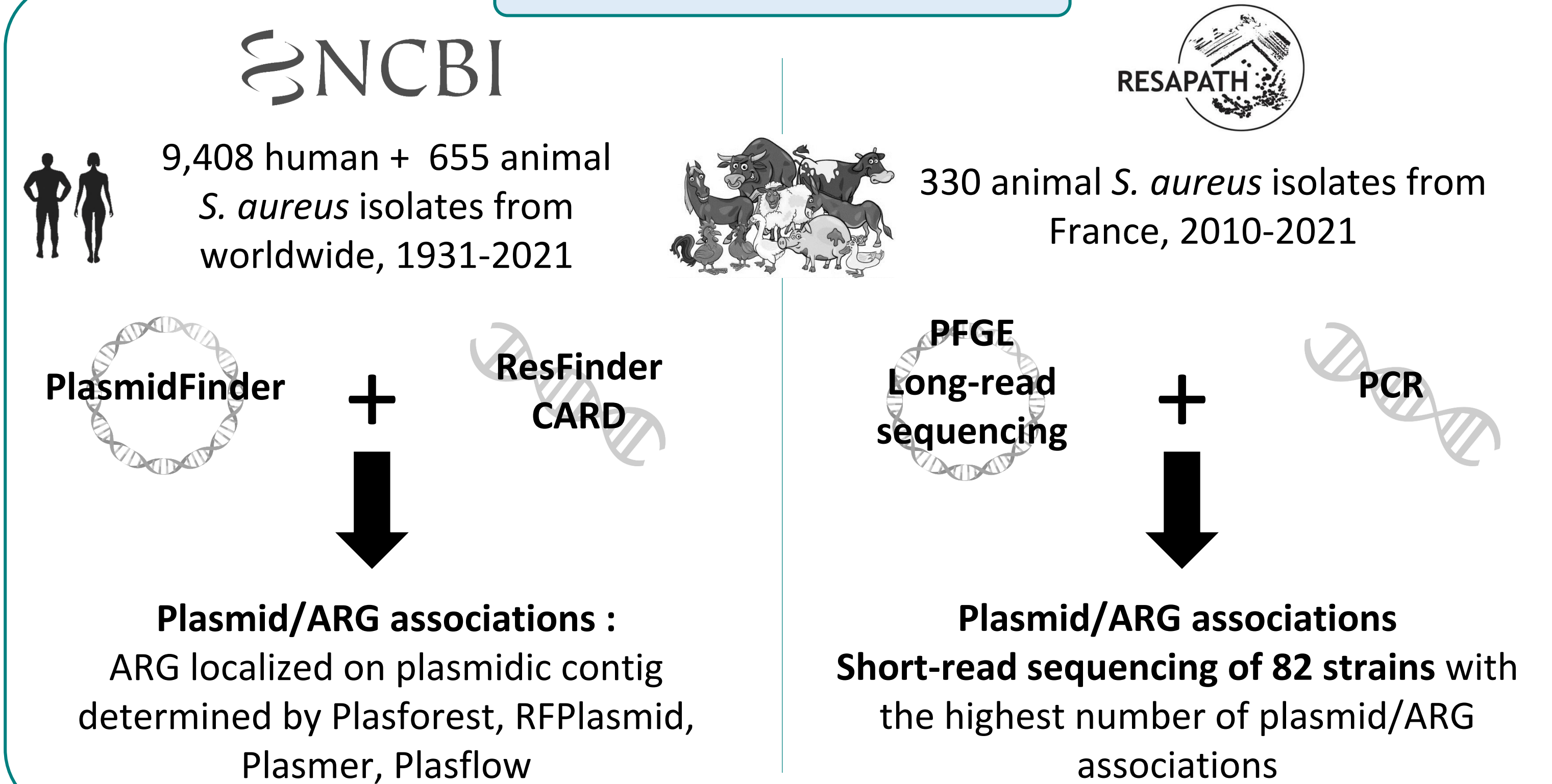
Richness of antibiotic resistance genes in *S. aureus*

Repartition of resistance genes in *S. aureus* of human and animal origin and from NCBI and Resapath



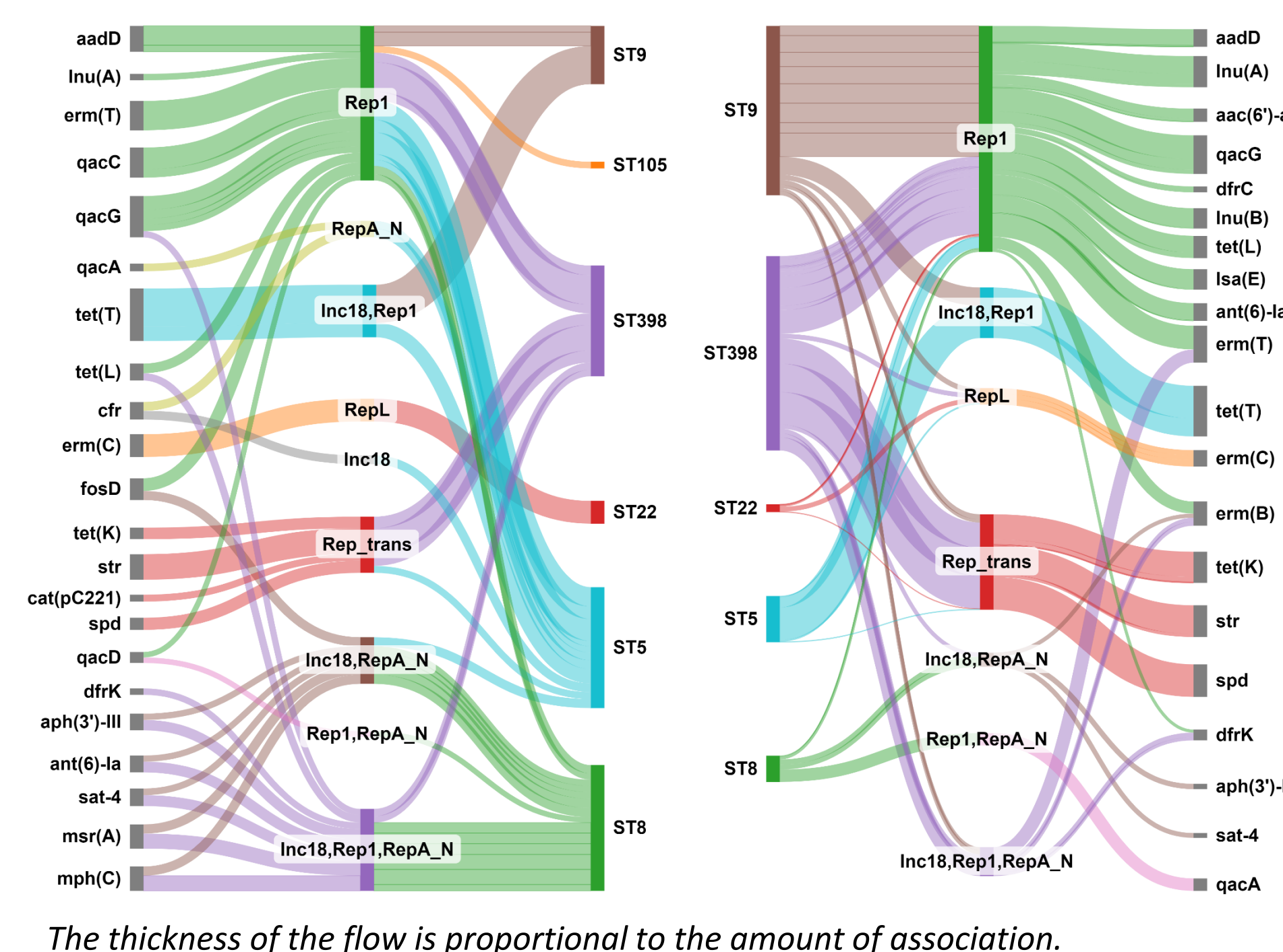
In publicly available genomes, only *S. aureus* with ARGs have been included in this study. However, in field strains, 92% of *S. aureus* (304/330) carried at least one ARG identified with PCR analysis. The genes identified mostly conferred resistance to **beta-lactams** and **aminoglycosides** in all *S. aureus* and to **tetracyclines** in An-SA.

Materials and methods



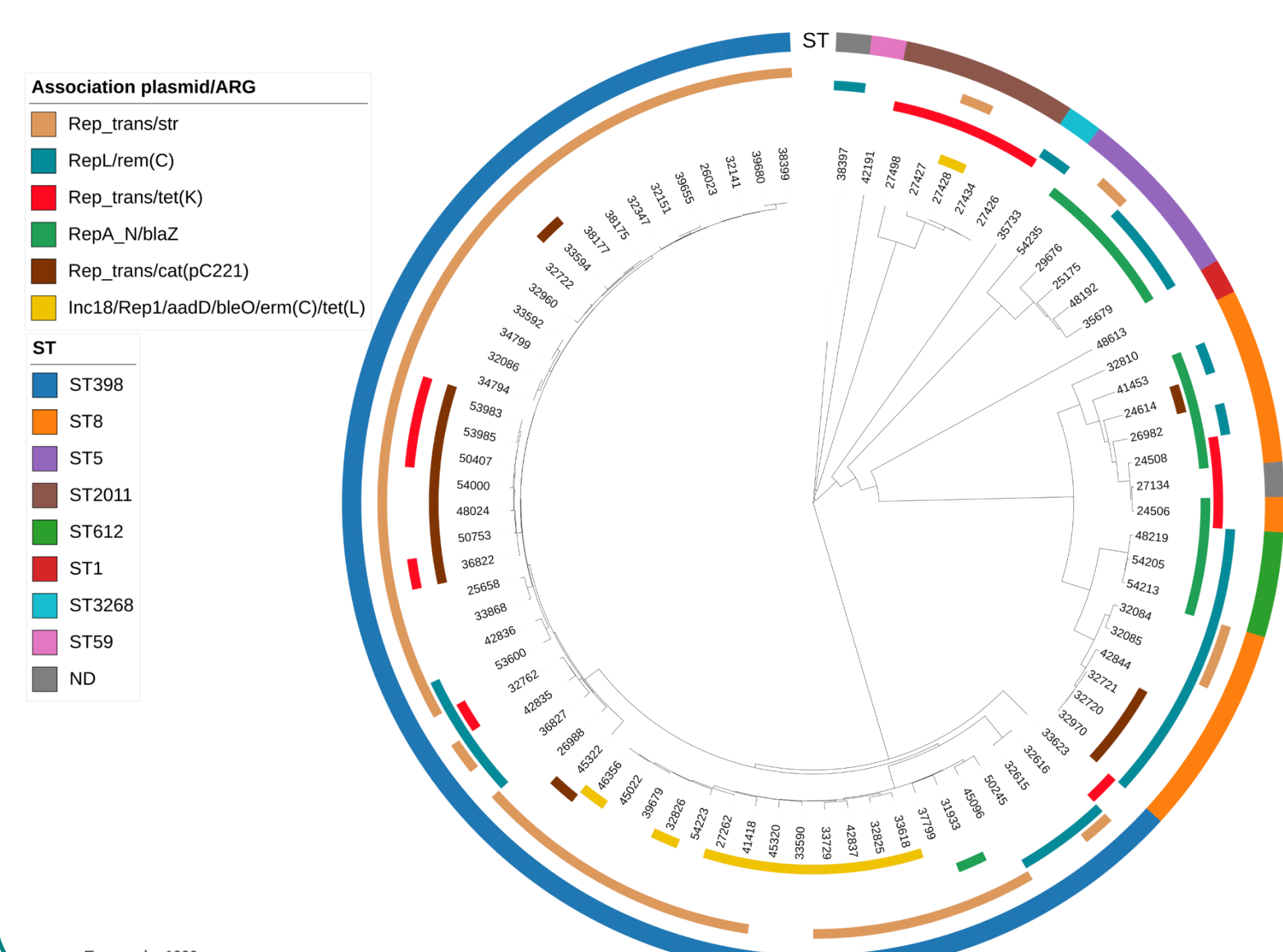
Plasmid carrying antibiotic resistance genes have no barriers in *S. aureus*

Sankey diagram depicting ARG/plasmid associations depending on ST in *S. aureus* of human (left) and animal (right) origin from the NCBI database



- ARG = one plasmid family
- Plasmid families most associated with ARG:
- **Rep1** in all *S. aureus*
- **Inc18/Rep1/RepA_N** in Hm-SA
- **Rep_trans** in An-SA
- Plasmid/ARG associations were found in multiple STs
- Dissemination through horizontal transfer within *S. aureus* genomes.

Neighbor-joining cgMLST-based tree showing the STs and the major plasmid/ARG associations per *S. aureus* strain from the Resapath



- The phylogenetic tree of the 82 field strains was built using pyMLST which compared the distance between 1,861 core genes.
- Dissemination of major ARG/plasmid associations through horizontal transfer:
- **RepL/erm(C)** → found in 7 different STs
- **Rep_trans/ARGs** and **RepA_N/blaZ** → found in 4 different STs

Conclusion

This study highlights the remarkable abundance and diversity of plasmids, ARGs and plasmid/ARG associations within *S. aureus* genomes. While it is known that *S. aureus* disseminates through clonal waves, our results showed that ARG-carrying plasmids can also spread through horizontal transfer. Therefore, *S. aureus* plasmids promote the dissemination of resistance genes without host specificity and antibiotic specificity. These findings highlight the critical need to elucidate the mechanisms governing the epidemic success of plasmids in *S. aureus*.

I'm looking for a post-doctoral position!
If you are interested in collaborating, feel free to contact me.
Scan the QR code for my CV!



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