Altered genomic methylation promotes *Staphylococcus aureus* persistence in hospital environment

Yuriko Yamazaki, Akiko Takaya & Yuumi Nakamura *Nature Communications* volume 15, Article number: 9619 (2024) Presenter: Yu-Hao Chen Date/Time: 2025/05/08, 16:20 -17:10 Commentator: Dr. Ching-Hao Teng Location: Room 601, Med College Building

Background:

Staphylococcus aureus is a major human pathogen which causes health problems worldwide, not only because of its pathogenicity but also the quick adaptation to antibiotic rich hospital environment. In S. aureus, the accessory gene regulator (Agr) system is both a quorum sensing system which bacteria use to communicate and coordinate based on population but also a major modulator for its virulence. Methicillin-resistant Staphylococcus aureus (MRSA), the major cause of outbreaks, is simply divided into community-associated (CA-MRSA) and healthcare-associated (HA-MRSA). In most cases, CA-MRSA is associated with more Agr-regulated virulence, whereas HA-MRSA exhibits defective Agr but somehow adapts to the more antibiotic hospital environment. In this paper, the authors want to discover the mechanisms how an outbreak CA-MRSA lineage adapts to the more antibiotic containing hospital environment.

Objective:

To find out how S. aureus easily adapts to hospital environments.

Results:

A novel Agr subclone was found in a CA-MRSA outbreak, which showed different expression level based on environments. This new "Environment-Adapted Agr" (EA-Agr) was found possibly evolved from the typical Agr positive strain, but showed increased persistence and plasmid acquisition comparing to Agr positive stain and better intracellular survival than mutant Agr. When infected in mice, better colonization and a lower inflammation level shown in EA-Agr also implies the persistence strategy it uses. As for mechanism, 3 genes were found having higher methylation level in the typical Agr positive while 2 of them later showed lower expression levels. The authors then found out that methylation was possibly done by *mraW*, a 5mc methyltransferase, and that mutant *mraW* in the typical Agr positive strain showed the phenotype of EA-Agr.

Conclusion:

In this research, a 5mC methyltransferase *mraW* was found to play a role in the adaptation of S. aureus under hospital environment. Without genomic methylation, expression level of pcrA and rpsD changes, leading to the new EA-Agr phenotype. Showing that epigenetics may play a role in the adaptation of S. aureus to the hospital environment.