The Fe-S cluster biosynthesis in Enterococcus faecium is essential for anaerobic growth and gastrointestinal colonization.

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Presenter: Wu Zhen Yee **Date/Time:** 2025/2/27, 15:20 -16:10

Commentator: Jenn-Wei Chen Ph.D. **Location:** Room 601, Med College Building

Background:

E. faecium is a Gram-positive, opportunistic pathogen that has emerged as a major cause of hospital-acquired infections due to its remarkable resistance to antibiotics and its ability to persist in the host gastrointestinal (GI) tract. Successful colonization of the GI tract is a key step in its pathogenesis, providing a reservoir for infection and transmission. However, the metabolic adaptations that enable *E. faecium* to thrive in the oxygen-limited gut environment remain poorly understood.

Fe-S clusters are essential cofactors for key cellular functions, including metabolism and gene regulation. Their biosynthesis is crucial for bacterial survival, especially in anaerobic environments. In *Enterococcus faecium*, Fe-S cluster assembly likely supports growth and colonization in the oxygen-limited GI tract. Since Fe-S clusters are linked to anaerobic respiration, oxidative stress resistance, and virulence in other bacteria, understanding their role in *E. faecium* could offer insights into its survival mechanisms and potential antimicrobial targets.

Objective:

To determine the role of Fe-S cluster biosynthesis under anaerobic in *Enterococcus faecium*. By disrupting Fe-S cluster assembly, the research explores its impact on metabolism, survival, and persistence.

Results:

The author first constructed Tn-seq library to find out which genes are required during anaerobic condition. This study found that Fe-S cluster biosynthesis, *suf* protein and *pla* gene is essential for *Enterococcus faecium*'s anaerobic growth and gastrointestinal colonization. Disrupting key components of the Fe-S cluster assembly pathway led to severe growth defects under anaerobic conditions, indicating its critical role in metabolism. Additionally, mutants with impaired Fe-S cluster biosynthesis showed significantly reduced colonization in a murine gastrointestinal model, suggesting that this pathway is crucial for survival in the host environment. Transcriptome analysis showed that disrupting Fe-S cluster biosynthesis in *Enterococcus faecium* alters gene expression, downregulating pathways for energy metabolism and anaerobic respiration while upregulating stress response mechanisms. Finally, the animal experiment demonstrated that Fe-S cluster biosynthesis is crucial for *Enterococcus faecium*'s ability to colonize the gastrointestinal tract. Mutants with disrupted Fe-S cluster assembly showed significantly reduced bacterial loads in the gut, indicating that this pathway is essential for survival and persistence in the host environment.

Conclusion:

This study demonstrates that Fe-S cluster biosynthesis is essential for *Enterococcus faecium*'s anaerobic growth and gastrointestinal colonization. The disruption of Fe-S cluster assembly severely impairs bacterial survival under anaerobic conditions and reduces its ability to colonize the host gut, highlighting its critical role in metabolism and adaptation. These findings provide valuable insights into the physiological importance of Fe-S clusters in *E. faecium* and suggest that targeting this biosynthetic pathway could be a promising strategy for limiting its persistence and infection potential.