

PLENARY SPEAKER

TITLE: Ultimate Origin of Leading Antibiotic Resistant Pathogens Revealed through Genomics: For Enterococci, it started long ago

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Enterococci are leading causes of multidrug resistant hospital infection. However, in nature, enterococci are among the most widely distributed core components of gut flora of animals, from invertebrates and insects to mammals. Despite being numerically minor constituents of animal gut microbiota, enterococci emerged among the vanguard of multidrug resistant hospital adapted pathogens. Interestingly this happened twice: in *Enterococcus faecalis*, and in the distantly related species *E. faecium*. This raises two questions: 1) What are the core properties of enterococci that make them universal components of gut consortia of animals? and 2) Why, among the great diversity of gut microbes, did enterococci repeatedly emerge to become leading causes of multidrug resistant hospital acquired infection? With antibiotic resistance now a leading global public health threat, there is a compelling need to understand the underlying biology and genetics that led to their hospital adaptation.

To accomplish this, we examined 25 enterococcal species, representing all major phylogenetic branches of the genus, in detail for phenotype, genotype, and where possible, correlated that with host association. We further compared traits of both commensal and multidrug resistant strains of the most common human associated species, *E. faecalis* and *E. faecium*. We found that the enterococci acquired the ability to withstand episodic desiccation and starvation, among other stressors, and that the formation of new enterococcal species occurs in parallel with the evolution of new host animals with new diets. Calibration of divergence times indicates that enterococci arose at about the time of terrestrialization of animals, and parallels their radiation, including fluctuations as occurred during the Permian Extinction. We infer that in adapting to cycles of deposition on land, the enterococci acquired traits that positioned them well for survival and adaptation to the modern hospital environment. We have identified the corresponding genes, and are now exploring the underlying mechanisms for their survival in hospitals.