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Oral Session

Emerging infectious diseases

BURKHOLDERIA PSEUDOMALLEI SEQUENCING IDENTIFIES GENOMIC CLADES AND EPIGENETIC BARRIERS RESTRICTING WIDESPREAD RECOMBINATION AND HORIZONTAL GENE TRANSFER

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OBJECTIVES: *Burkholderia pseudomallei* (Bp) is the causative agent of melioidosis, a serious infectious disease of human and animals. Our aim is to study population diversity, recombination and horizontal gene transfer in closely-related Bp isolates.

METHODS: We performed whole-genome sequencing (WGS) on 106 clinical, animal, and environmental strains from a restricted Asian locale. Whole-genome phylogenetic analysis resolved multiple genomic clades of Bp largely congruent with multi-locus sequence typing (MLST), and further highlighted additional subgroups belonging to the same ST.

RESULTS: We discovered widespread recombination in the Bp core genome, involving hundreds of regions associated with multiple haplotypes and functional enrichments which may contribute to virulence. Recombination within strains of the same clade was extensive; however, inter-clade crossover was rarely observed. Similarly, accessory genomic elements also exhibited a strongly clade specific pattern, suggesting mechanisms restricting gene flow between clades. Interrogation of accessory elements revealed that each genomic clade harbored a distinct complement of restriction-modification (RM) systems, predicted to result in clade-specific patterns of DNA methylation.

DISCUSSION: Our data suggests that RM systems borne on mobile elements may, in addition to preventing invasion of foreign DNA, also act as epigenetic barriers limiting the unimpeded exchange of genes and gene variants between individuals of the same species. Epigenetically defined genomic clades may thus represent functional units of genetic isolation in Bp, modulating intra-species genetic diversity and contributing to the emergence of new incipient species.