Recontruction of Burkholderia mallei adaptation to intracellular lifestyle

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Burkholderia is a genus of Gram-negative, ubiquitous bacteria that includes a large number of human, animal, and plant pathogens. Their genomes consist of two replicons: a primary chromosome and a chromid, an essential circular replicon evolved from plasmid. B. mallei relatively recently separated from the ancestral species of extracellular pathogen B. pseudomallei and transited to intracellular parasitism [1]. Thus, this species is a model organism for studying the genome architecture and the changes accompanying the transition to intracellular parasitism. The genome of the intracellular parasites are highly plastic due to the accumulation of numerous copies of mobile elements. In this work we investigated the evolutionary processes during this adaptation and the role of different families of IS elements and genome rearrangements in B. mallei strains and the ancestral B. pseudomallei.

In this work we used the Parebrick toolkit[2], which allows us to detect large-scale genomic features in clodely related strains and identify parallel rearrangements in a bacterial population. The tool takes synteny blocks and a phylogenetic tree as input and outputs rearrangement events allowing to detect horizontally moved blocks or their additional copies and inversions of blocks.

We worked with complete genomes from the RefSeq database; 31 B. mallei strains and 81 B. pseudomallei strains. We used the PanACoTA pipeline [3] to download and annotate the genomes, find the orthogroups and construct the species' phylogenetic tree based on concatenated alignment of common single-copy genes. Mobile elements were predicted and classified using the IsSaga server [4]. Genomic rearrangements were studied using the Parebrick tool.

Genomes of B. pseudomallei consist of two chromosomes, their sizes are 4 and 3.2 Mb, respectively. We found 30 different types of IS elements, their variety is higher in the secondary chromosomes. Genome reduction in B. mallei is 12.5% for the first chromosome and 31% for the second chromosome. Moreover, a variety of IS elements in B. mallei is also reduced to 9 types. In turn, IS elements are much more active in B. mallei . The average number of copies in the first chromosomes increases from 31 in B. pseudomallei to 120 in B. mallei in the first chromosomes and from 31 to 58 in the second chromosomes.

The analysis of deletions showed that they occured more often on the second chromosome resulting higher chromosome reduction. We estimated the size of B. mallei chromosomes in the end point of adaptation, the length of the chromosomes core-fractions is 2.8 mb and 1 mb for the first and the second chromosome. The comparison of the results of the core-genome construction by blocks and by genes revealed the advantages of pan-block-omics approach for bacterial micro-evolution. Pan-blockomics curves show have the same trends as the classic pan-genomic ones but includes more types of genomic reatures resulting in higher genome coverage.

In summary, our results show that an adaptation to intracellular lifestyle is accompanied by 1) decrease of IS elements variety; 2) growth of copy number of specific IS families. Accumulation of multiple identical repeats explains the high rate of genome reduction. 3) Reduction rate is higher on the second chromosome. 4) Parallel deletions occurred more often in the second

chromosome. 5) The pan-blockomic approach provides a basis for presize reconstruction of bacterial micro-evolution.

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