Genome sequencing reveals genetic diversity of the bacteria that cause Buruli ulcer

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A new study lays the groundwork for development of a cost-effective tool for studying the population structure and spread of *Mycobacterium ulcerans*, the causative agent of Buruli ulcer. Researchers at the Swiss Tropical Institute, Basel, Switzerland, and the Noguchi Memorial Institute for Medical Research, Legon, Ghana, developed SNP typing assays to systematically profile genetic diversity among M. ulcerans isolates by sequencing and comparing the genomes of selected strains.

The findings, published September 11 in the open-access journal *PLoS Pathogens*, show that bacterial strains from regions where Buruli ulcer is endemic are clonally related, but can be distinguished by a few single nucleotide polymorphisms (SNPs) spread over the genome. SNPs are DNA sequence variations occurring when point mutations persist in a population.

Buruli ulcer is a necrotizing skin disease that affects mostly children and youth in West Africa, but is also found in Asia, the Western Pacific, and Latin America. The causative organism is closely related to the mycobacteria that cause tuberculosis and leprosy, making Buruli ulcer the third most common mycobacterial disease. The mode of transmission of M. ulcerans is poorly understood, in part because standard molecular typing methods lack the resolution required for detailed micro-epidemiological analyses.

After publication of the first genome sequence, comparative sequencing of genomes from additional strains demonstrated that the more virulent classical lineage of M. ulcerans found in Africa diverged from the ancestral lineage found in Asia and in South America about 500,000 years ago. Although strains from different Buruli ulcer endemic regions of Africa are clonally related, the researchers' genome sequencing has now identified SNPs which diversify the isolates.

Based on the SNPs discovered, the researchers developed SNP typing assays and were able to differentiate a collection of M. ulcerans isolates into SNP haplotypes. Molecular fingerprinting of disease isolates based on these genetic markers allowed the researchers to trace transmission of variants within a confined Buruli ulcer endemic area of Ghana. These results suggest that transmission of Buruli ulcer is focal, i.e. local genetic variants are not quickly spread over long distances.

Sequencing of the genomes of more M. ulcerans isolates of worldwide origin will be required to develop a comprehensive fine typing method and gain further insight into the evolution of M. ulcerans. SNP-based molecular typing of isolates is now expected to help unravel the enigma of M. ulcerans transmission.

More information: Qi W, Ka ser M, Ro ltgen K, Yeboah-Manu D, Pluschke G (2009) Genomic Diversity and Evolution of Mycobacterium ulcerans Revealed by Next-Generation Sequencing. *PLoS Pathog* 5(9): e1000580. doi:10.1371/journal.ppat.1000580

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