Genetic Relatedness among Isolates of *Yersinia pestis* using Single Nucleotide Polymorphism Analysis.

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Background: *Yersinia pestis*, the causative agent of plague, possesses a highly conserved genome among different isolates. This pathogen is believed to have recently emerged as a highly uniform clone from the enteric pathogen, *Yersinia pseudotuberculosis*. The complete genome sequence of the orientalis biovar, CO-92 and the mediaevalis biovar, KIM10, confirm the high conservation of sequence identity between different strains of *Y. pestis*. We are currently sequencing two antiqua biovars of *Y. pestis*, Antiqua, isolated from the Republic of Congo and Nepal-516, isolated from Nepal. The aim of the current study was to identify polymorphic sequence that could be used to differentiate strains of *Y. pestis* and to study the evolutionary relatedness of strains that have been isolated from different parts of the world. **Methods**. Draft genome sequence of *Y. pestis* strains Antiqua and Nepal-516 have been completed to 12X coverage (> 100,000 sequence reads for each strain) and assembled into contiguous segments. Portions of the genome containing nearly identical sequence were compared with genome sequence from CO-92 and KIM10. Selected DNA polymorphisms were identified and confirmed by dideoxy sequencing among the four strains. **Results.** Initial analysis of 700 kb of nearly identical regions (15% of the genome) among the four sequenced strains revealed 70 confirmed single nucleotide polymorphisms (SNPs). The location of each SNP was mapped to the CO-92 genome and 51 were found to be within putative ORFs while 19 were located within intergenic regions. Specific SNPs were identified for each of the four strains in addition to 13 SNPs that distinguished Antiqua and CO-92 from Nepal-516 and KIM10. A random set of 49 validated SNPs was tested against an additional collection of 21 *Y. pestis* and two *Y. pseudotuberculosis* strains**.** Cluster analysis using Neighbor Joining demonstrated an association between the country of origin for each strain and its SNP pattern profile. **Conclusion:** SNP analysis provided insight into the evolution of the *Y. pestis* genome.