

# Pathway Complements of Four *Yersinia* Strains

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**Keywords:** *Yersinia*, gene networks, comparative genomics, evolution

## 1 Introduction.

*Yersinia pestis*, the causative agent of bubonic and pneumonic plague, is thought to have evolved relatively recently from *Y. pseudotuberculosis* [1]. The genomic sequence of the latter strain was recently published [2] and it forms, together with the three extant genomes from virulent [6, 3] and avirulent [7] strains of *Y. pestis*, a data set that should reveal much about the mechanisms and evolution of pathogenesis in *Y. pestis*. While interesting comparisons between the gene complements of these taxa have been made [2, 4, 8] in which researchers cataloged the loss or gain of function via lateral gene transfer, homologous recombination, and mutation, no comparisons incorporating data from all four strains have yet appeared. The lists of gene complement differences among these strains give many clues to how *Y. pestis* arose, but we feel the utility of such lists could be enhanced and their significance better understood if they were placed in a whole systems context, where the extended consequences of gene loss or gain could be seen. In order to integrate the gene gain/loss data with information about the metabolic and regulatory networks in these four strains, we built pathway genome databases (PGDBs) for them using the Pathway Tools software [5].

## 2 Methods and Results.

Sequence and annotation data were collected from GenBank and fed into the PathoLogic tool in the Pathway Tools software. The resulting PGDBs were enhanced by, firstly, ensuring that genes known to have been lost by mutation and so on were accounted for in the database. Secondly, based on literature searches, we made, whenever possible, functional assignments for genes that PathoLogic couldn't handle. This included unassigned genes, genes with ambiguous assignments, and transcriptional activators and other recognized regulatory genes. The resultant pathway repertoires were compared in the light of the hypothesis that since its emergence, *Y. pestis* has been undergoing a process of genomic streamlining. This process is thought to, at least in part, account for the remarkable differences in disease and mode of transmission between *Y. pseudotuberculosis* and *Y. pestis*. Of course, some of these differences also result from this change in lifestyle, as *Y. pestis* discards unnecessary functions and otherwise adapts to a host-associated lifestyle.

Although the Pathway Tools rely on a top-down approach to generating pathways from genomic sequence data, which precludes the detection of novel pathways, we feel that the 170 plus pathways detected are probably quite comprehensive, given the close evolutionary relationship between the genera *Escherichia* and *Yersinia*.

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We are currently developing bottom-up approaches to gene network inference that use probabilistic graphical methods to infer gene networks. Both approaches to these data place them in a context that enhances our understanding by allowing us to integrate data from different sources, visualize the effects of gene gain or loss on gene the cell's networks, and compare the gene networks among the strains of *Yersinia*.

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