Comparative genomics reveals molecular evolution of Q fever pathogen

February 2 2009

Scientists from the National Institute of Allergy and Infectious Diseases, Texas A&M Health Center, and the Virginia Bioinformatics Institute at Virginia Tech have uncovered genetic clues about why some strains of the pathogen *Coxiella burnetii* are more virulent than others.

The researchers compared the sequences of four different strains of *C. burnetii*, an intracellular bacterium that can cause acute and chronic Q fever in humans, to build up a comprehensive picture of the genetic architecture and content of the different genomes. The scientists examined *C. burnetii* strains of differing virulence to unveil clues on the genetic features associated with pathogenicity.

Q fever is considered one of the most infectious diseases in the world since inhalation of a single bacterium alone is sufficient to kick-start infection. Infection in humans typically results from contact with infected animals such as cattle, goats, and sheep. The *C. burnetii* bacterium targets macrophages — white blood cells in the body that usually provide protection against invading pathogens. The pathogen has the remarkable ability to replicate in a lysosome-like vacuole of macrophages, an extremely harsh intracellular environment that usually protects the body from infection by breaking down invading pathogens. The chronic form of Q fever in humans is rare but can lead to heart infections that are usually deadly if untreated.

Dr. Robert Heinzen, head of the Coxiella Pathogenesis Section at the National Institute of Allergy and Infectious Disease, remarked: "Our

results suggest that mobile genetic elements have played a major role in the evolution and function of the *C. burnetii* genome. Recombination between insertion sequence elements or jumping genes appears to have brought about large-scale generation of non-functional genes, a change that may be associated with a more pathogenic lifestyle."

In the study, the researchers sequenced the genomes of three strains of the bacteria and made a four-way comparison of *C. burnetii* genomic sequences. Strain virulence was associated with a smaller genome. The loss of genes was due in part to the formation of pseudogenes, evolutionary remnants of earlier genes that no longer code for functional proteins.

Kelly Williams, research investigator at VBI, commented: "A principle of our and many modern studies was first enunciated in the title of a 1965 paper by Emile Zuckerkandl and Linus Pauling, 'Molecules as documents of evolutionary history'. Genomes are the ultimate molecular documents, filled with stories that fascinate and instruct, and we can now speed-read them."

VBI Executive and Scientific Director Bruno Sobral, a co-author on the paper, remarked: "2009 is the 200th anniversary of the birth of Darwin. That's a very suitable time to step back and think about how new technologies are giving us ever more powerful ways to investigate the history and mechanism of evolution. We hope the work in the current study serves as a resource for both the Coxiella and wider infectious disease research communities interested in the evolution of pathogen virulence."

Dr. Heinzen concluded: "The results of this study provide a solid foundation upon which we can test a number of hypotheses related to *C. burnetii* gene function and virulence. This information will prove invaluable as we proceed to dissect, at a molecular level, events

associated with Q fever pathogenesis."

"Comparative genomics reveal extensive transposon-mediated genomic plasticity and diversity among potential effector proteins within the genus Coxiella" was published in the February issue of *Infection and Immunity* 77(2): 642-656.

Source: Virginia Tech