

Bioinformatics sheds light on evolutionary origin of Rickettsia virulence genes

March 12 2009

Scientists from the Virginia Bioinformatics Institute (VBI) at Virginia Tech, the University of Maryland School of Medicine, and the University of Louisville have revealed that genes for a specific type of molecular secretion system in Rickettsia, a structure that is linked in many cases to virulence, have been conserved over many years of evolution.

The scientists compared the [gene sequences](#) of 13 Rickettsia species to detect a highly conserved type IV secretion system. Type IV [secretion systems](#) are membrane-spanning transporters that can act as syringes that inject virulence factors into the cells of their hosts (eukaryotes). Once introduced, these virulence factors compromise the host and may result in harmful disease, for example Legionnaires' disease (Legionella pneumophila) and [Q fever](#) ([Coxiella burnetii](#)). However, these secretion systems have not been implicated in human diseases caused by Rickettsia, including [epidemic typhus](#) (*R. prowazekii*) and Rocky Mountain spotted fever (*R. rickettsii*). Type IV secretion systems are unique in their ability to transport [nucleic acids](#) and proteins into plant and animal cells. A possible role of the transporter that is not directly associated with virulence, such as [DNA transfer](#), has been overlooked in Rickettsia.

Dr. Joseph Gillespie, a bioinformatician at the Virginia Bioinformatics Institute and leader of the study, remarked: "We have used the Rickettsia genomic information steadily accumulated over the past 10 years as a starting point to look in detail at the origin and function of Rickettsia

virulence-like genes. The study reveals a highly conserved type IV secretion system across the 13 genomes investigated, some of which are, intriguingly, not known to cause disease in their invertebrate and vertebrate hosts."

In addition to the evolutionarily conserved nature of the Rickettsia type IV secretion system, informatics analysis revealed some unexpected properties, including [gene duplication](#) of nearly half of its components. Gene duplication is very rare in Rickettsia genomes. By digging a little further, the team also identified three additional genes that likely contribute to the secretion system. Gillespie noted: "Because Rickettsia live inside their hosts at all stages of their life cycle, we are very limited in how we can characterize their genes. Researchers often have little choice but to apply related information from other bacteria that are easier to study." This often entails labor-intensive manual work that cannot currently be substituted by automated gene prediction methods. "Sometimes, the brain beats the algorithm," Gillespie added.

One of the major revelations of the sequence comparison is that the ancestor organism of the Rickettsia most likely acquired a virulence-like genetic locus from distantly related bacteria. The team speculates that this may have taken place while the ancestor was residing in a protozoan host.

Principal Investigator Bruno Sobral remarked: "Virulent species of Rickettsia are of great interest both as emerging agents of infectious disease and potential bioterror agents. However, a lot of intense laboratory work has failed to provide information that characterizes their virulence factors. Our comparative genomics approach sheds light on the evolution of Rickettsia virulence and provides a solid foundation for the future laboratory assessment of the function of the Rickettsia type IV secretion system."

Dr. Gillespie concluded: "Additional experimental evidence from recent studies suggests that some of the components of the Rickettsia type IV secretion system are indeed expressed, regulated and secreted. It is too early yet to know with certainty the precise mechanism of how the system operates but we now have a solid foundation for future work."

More information: Joseph J. Gillespie, Nicole C. Ammerman, Sheila M. Dreher-Lesnicks, M. Sayeedur Rahman, Micah J. Worley, João C. Setubal, Bruno S. Sobral, Abdu F. Azad (2009) An anomalous type IV secretion system in Rickettsia is evolutionarily conserved. The paper is featured in the March 12, 2009 edition of the online publication *PLoS ONE*. [dx.plos.org/10.1371/journal.pone.0004833](https://doi.org/10.1371/journal.pone.0004833)

Source: Virginia Tech ([news](#) : [web](#))

Citation: Bioinformatics sheds light on evolutionary origin of Rickettsia virulence genes (2009, March 12) retrieved 27 April 2024 from <https://phys.org/news/2009-03-bioinformatics-evolutionary-rickettsia-virulence-genes.html>

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