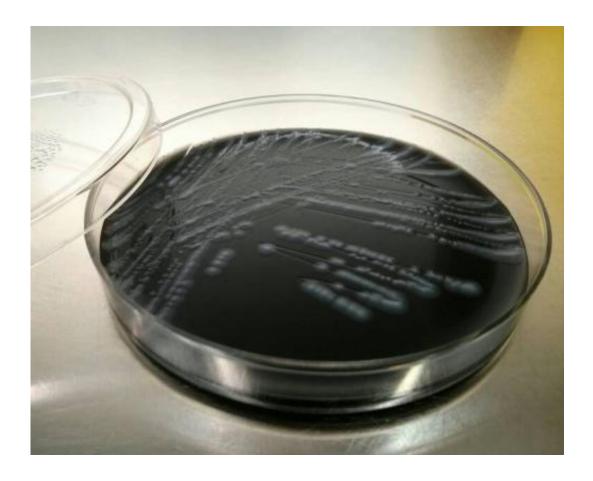


Valencian researchers state that the legionella outbreaks of Alcoy may have multiple sources

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Analysis of Legionella pneumophila

Researchers have carried out a genomic analysis of Legionella pneumophila strains of 13 legionellosis outbreaks produced in Alcoy



during the period from 1999 to 2010.

Legionella pneumophila is a strictly environmental pathogen, an opportunistic bacterium that inhabits aquatic and soil environments, spreading through the air and that can infect humans who have certain susceptibility characteristics, such as being over 65 years, having breathing problems or using cigarettes, among others. L. pneumophila is the causative agent of Legionnaire's disease, a potentially severe form of pneumonia, but it is not transmitted from person to person. Since the first identification of this bacterium as a human pathogen, outbreaks of legionellosis have been recurrent in many countries.

This research has been published in the article "Recombination drives genome evolution in outbreak-related Legionella pneumophlia isolates" in the prestigious journal *Nature Genetics*, and the study describes in detail the whole genome sequencing of 69 isolates from 13 of the 18 historical legionella outbreaks that occurred in Alcoy. Researchers have discovered that more than one strain is found in some of the outbreaks studied and that the genetic differences between these strains are such that there are likely different sources for one outbreak.

It is the first time that in-depth genomic analyses has been carried out with an environmental bacterium, as there are no similar studies in other environmental organisms due to the difficulty of studying isolates over such a long period of time. There are precedents for pathogenic bacteria transmitted between humans, but not in the case of an environmental bacterium like Legionella, which is not transmitted from human to human and whose infection derives from an environmental source.





Leonor Sánchez-Busó, Iñaki Comas and Fernando González-Candelas

The researcher Leonor Sánchez-Busó claims the need to understand how these Legionella outbreaks are produced in order to control them, and therefore, how having all the possible information, including genetic information, will allow us to know how the bacterium evolves at the individual and population level.

Mutations are the ultimate source of genetic variation, but not all the variants found are the result of structural or point mutations. Bacteria have developed specific strategies for incorporating and exchanging genes and plasmid segments of external sources. The processes of non-vertical transmission allow microorganisms to acquire new genes or variants which provide new adaptations such as resistance to environmental processes and to antibiotics both in the short and long term. "The ST578 type of L. pneumophila has caused outbreaks during more than 10 years in Alcoy, and in this study, based on massive



sequencing analysis, we observe that some of the outbreaks have not been caused by a single biological source. The results show that the evolution of this population of ST578 has been incited by the introduction of a variant with the same profile, from external sources of the city's water distribution network. "All this has occurred despite the remarkable success of prevention and control measures carried out by the health authorities that contributed to the absence of outbreaks between 2006 and 2009," explains Sánchez-Busó.

It has been shown that L. pneumophila has evolved very quickly in the period analysed (1999-2010) by the exchange of genes with other strains of Legionella. Different phenomena of recombination between them have occurred, and these exchanges of genetic material are responsible for 98% of the observed genetic changes. Moreover, these changes have occurred in a very short period of time for these types of processes. It should be noted that these recombination events don't affect the resistance of the Legionella as the <u>bacterium</u> is sensitive to current antibiotics and patients respond well to medical treatment.

The presence of Legionella cannot be prevented or eliminated from many potential sources but the risk of transmission in the community can be reduced and controlled if the necessary information is available. The study carried out over one year has shown that scientists have the tools necessary for doing the genomic research of an entire outbreak in just two days, at the time it is occurring, while the incubation process of legionella can take up to two weeks. Leonor Sánchez-Busó states that "this is the first work of high impact which shows the real genetic structure of Legionella outbreaks, and allows us to see that the application of the technique of massive sequencing to the study of these outbreaks should be applied not only retrospectively, but in real time for identifying and controlling outbreak sources when they are occurring, as well as for predicting the risk at short and long term."



More information: Leonor Sánchez-Busó, Iñaki Comas, Guillermo Jorques & Fernando González-Candelas. "Recombination drives genome evolution in outbreak-related Legionella pneumophila isolates." *Nature Genetics* (2014) DOI: 10.1038/ng.3114 Published online 05 October 2014

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