Chlamydia that avoids diagnosis

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New sequencing and analysis of six strains Chlamydia will result in improved diagnosis of the sexually transmitted infection. This study provides remarkable insights into a new strain of Chlamydia that was identified in Sweden in 2006 after spreading rapidly across the country by evading most established diagnostic tests.

The results also reveal more about the evolution of the Chlamydia trachomatis bacterium, which is the most common cause of sexually transmitted infections (STIs) globally. The long-term effects of an undetected Chlamydia infection include infertility and ectopic pregnancy. Long-term eye infection by Chlamydia is also the leading cause of preventable blindness in the developing world.

As part of a long-standing collaboration between the Wellcome Trust Sanger Institute and University of Southampton, the team of researchers focused on six strains of Chlamydia. Of particular interest to the team was the new Swedish strain provided by collaborators at Malmo University Hospital, Sweden.

The genome of the Swedish strain features an evolutionary 'hiccup' that allowed it to go undetected in Sweden for several months. Indeed, doctors thought that the numbers of cases of Chlamydia were falling, when the opposite was true. Through non-diagnosis, this version of Chlamydia spread silently. The reason: a deletion of the region of genetic information used to diagnose the presence of Chlamydia.

"The medical and research communities need to heed this warning," says

Dr Helena Seth-Smith, investigator at the Sanger Institute and lead author on the study. "Chlamydia infections appeared to be in decline in Sweden, but this could not have been further from the truth. The loss of a segment of genetic code made the tests completely powerless to detect this particular strain of Chlamydia. This type of evolution to evade diagnosis could occur in other infectious bacteria."

"We have found more stable genetic targets - these should be the regions against which we design diagnostic tests."

The deletion - 377 letters of genetic code - occurred on the plasmid of the bacterium. Plasmids are small, circular molecules of DNA that are located outside the chromosome. Chlamydial plasmids have been shown to vary little between different strains of Chlamydia, and are present in larger quantities than the chromosome. This makes them ideal candidate targets for diagnostic tools. Clinical tests have focused on one region of the bacterial plasmid - a gene of unknown function which is largely deleted in the new Swedish strain.

"We have confidently placed great reliance on nucleic acid based diagnostic tests for many years," explains Professor Ian Clarke, University of Southampton, senior author on the study, "but we must always be alert to changes in the biology of this organism. Chlamydia are notoriously difficult to study in the laboratory and genomics can make a vital contribution to adding to our understanding of this insidious parasite."

After careful analysis of the newly sequenced plasmids of these strains, the team have identified the regions of the plasmid that vary least between strains. "These are thought to be important in the stability of the plasmid, and so tests on these regions should prove more reliable," explained co author Dr. Pete Marsh from the Southampton Health Protection Agency."

"This is a truly remarkable turn of events," explains Dr Nicholas Thomson, principal investigator at the Sanger Institute. "It is an example today of evolution in action: we believe that diagnostic tests that target one region of the Chlamydial plasmid have allowed the Swedish strain, very quickly, to become the dominant strain in that country."

"Paradoxically, the efforts of humans to control the spread of the disease may well have been the cause that shaped the development and spread of this new strain."

Chlamydia is a bacterial parasite that only grows within human cells: as a result there is not a great deal of exchange of genetic material between strains. The stability of the link between the bacterial chromosome and the plasmid DNA was also established in this study, reinforcing confidence in the plasmid as the target for diagnostic tests.

More information: Seth-Smith H. et al. (2009) Co-evolution of genomes and plasmids within Chlamydia trachomatis and the emergence in Sweden of a new variant strain. *BMC Genomics*.

Source: Wellcome Trust Sanger Institute