Whole genome analysis of Chlamydia trachomatis highlights risks with current method of tracking

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In a study released today in *Nature Genetics*, researchers have found that *Chlamydia* has evolved more actively than was previously thought. Using whole genome sequencing the researchers show that the exchange of DNA between different strains of *Chlamydia* to form new strains is much more common than expected.

The team highlights that current clinical testing methods do not capture the variation between *Chlamydia* strains. Changes to the genome structure are not the aim of current diagnostics for *Chlamydia*. The researchers are working with hospitals to use their results to improve *Chlamydia* testing in terms of detecting variation between *Chlamydia* strains.

Chlamydia trachomatis is the most common sexually transmitted infection (STI) both in the UK and globally, with approximately 100 million new cases worldwide each year. It is also the most common cause of infectious blindness, or trachoma, in the developing world. Relatively little is known about the evolution of the different strains of *Chlamydia* that are causing infection.

"Scientists recently discovered that if two *Chlamydia* strains co-infect the same person at the same time, they can swap DNA by a process called recombination." explains Dr Simon Harris, lead author from the Wellcome Trust Sanger Institute. "This was originally thought only to

affect a few 'hotspots' within the genome. We were very surprised to find recombination is far more widespread than previously thought."

The team found there appeared to be no barriers to the swapping of DNA when circumstances allow, even between bacterial strains associated with infecting different parts of the body.

"Despite this being the most important sexually transmitted infection in the world, until now it's clear that there are major gaps in our knowledge of the strains that are currently circulating, their evolution and natural history," says Professor Ian Clarke, senior author from the University of Southampton, Faculty of Medicine.

Clinical diagnosis of *Chlamydia* infections simply returns a positive or negative result, providing no information about the nature of the infecting strain. This makes it impossible to determine whether a person who tests positive again after antibiotic treatment has picked up a second infection or if their treatment has failed. The significance of this is that although antibiotic resistant *Chlamydia* has never been seen in patients, it can occur in the laboratory. If resistance did occur in the general population, it would not be detected by current diagnostic procedures.

"Until now a person treated with antibiotics with a reoccurring infection of C. trachomatis was assumed to have been re-infected" says Dr Nicholas Thomson, senior author from the Wellcome Trust Sanger Institute. "The current gaps in our understanding of the population makeup of *Chlamydia* limit our ability to implement health policies, because we do not fully understand how *Chlamydia* spreads within our population."

This study is not just important for the treatment of the sexually transmitted strains of *Chlamydia* but also for the treatment of African *Chlamydia* strains that can cause infectious blindness, or trachoma. The

team sequenced strains of African *Chlamydia* and found that these strains are also using recombination to fool the human immune system.

"For many years various groups have observed co-circulating strains of *Chlamydia* causing trachoma. In our study we have shown that some strains appear to have swapped only their surface coat" says Dr Martin Holland from the London School of Hygiene & Tropical Medicine. "This provides real clues as to how this bacterium is able to avoid the human immune system and cause disease"

This study shows that whole genome sequencing is the resolution required to understand in fine detail the spread of Chlamydia through a population. Scientists at the Sanger Institute are currently working with hospitals to bring this technology into the clinical setting. The challenge that researchers face is to provide enough DNA from routine samples to generate a whole genome sequence.

More information: Harris et al 'Whole-genome analysis of diverse Chlamydia trachomatis strains identifies phylogenetic relationships masked by current clinical typing' Published online on *Nature Genetics* 11 March 2012; DOI: 10.1038/ng.2214

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