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“Expression of *Chlamydia trachomatis* Topoisomerase I Can Compliment conditional-lethal DNA topoisomerase I mutation in *Escherichia coli*”

Abstract

Chlamydia trachomatis is responsible for the most commonly reported Sexually transmitted bacterial infections worldwide. Over 70% of women with *C. trachomatis* genital tract infections are asymptomatic, often leading to pelvic inflammatory disease (PID) and infertility. Despite ongoing control efforts, new cases reported in the US have risen from ~0.7 million in 2000 to ~1.8 million in 2019. It is unclear how Ct causes disease, but it likely relies on its ability to adapt to, survive in, and replicate within the intracellular niche.

Bacterial topoisomerase I (TopA) is an essential enzyme affecting bacterial viability. TopA has a key role in removing excess negative supercoils in chromosomal DNA by relaxing the supercoils and is widely characterized in *Escherichia coli*. *C. trachomatis* TopA is distinct in that it consists of regions homologous to bacterial TopA, as well as the eukaryotic SWIB domain. The function of chlamydial TopA has not been well-studied, in part, due to the lack, until recently, of genetic tools with *C. trachomatis*.

In this study, plasmids expressing full-length of *C. trachomatis* TopA in temperature-sensitive *E. coli* strain VS111-K2 were used to investigate whether *Chlamydia topA* is functional. The empty vector containing the strain was used as the control. Through plate assay and the growth curve examination, we show that the expression of the *C. trachomatis topA* gene can correct the growth deficiency of a conditional-lethal *E. coli topA* mutant, permitting the normal growth at 30°C, 37°C and 42°C. These results indicate that despite differences in their primary structures between the *E. coli* and *C. trachomatis* TopA enzymes, the *C. trachomatis* TopA is able to restore the growth phenotype and likely have a common feature that is known as interconversion of DNA supercoiling. Future studies are required to clarify whether the DNA relaxation activity of the chlamydial TopA is responsible for its role in restoring the viability of *E. coli* VS111-K2 cell. This system may be useful in the identification of a functional domain and screening of drugs acting on chlamydial TopA.