Chlamydia protein has an odd structure, scientists find

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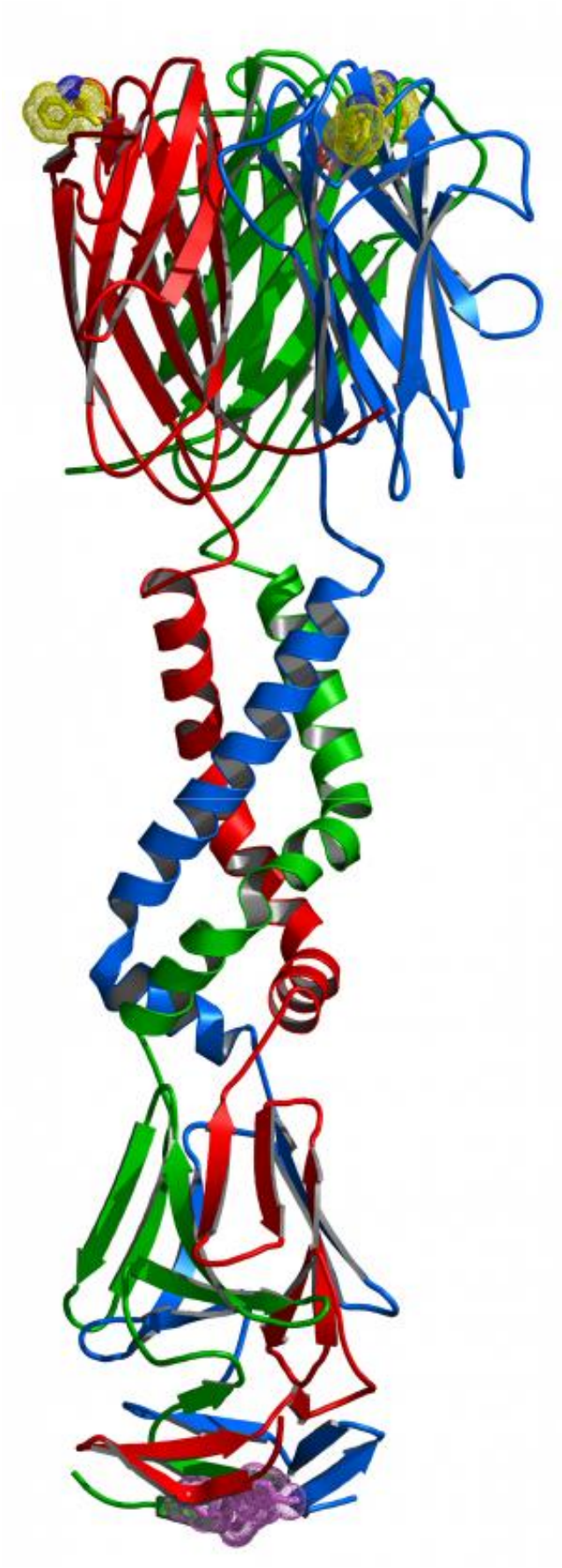
A protein secreted by the chlamydia bug has a very unusual structure, according to scientists in the School of Medicine at The University of Texas Health Science Center San Antonio. The discovery of the protein's shape could lead to novel strategies for diagnosing and treating chlamydia, a sexually transmitted disease that infects an estimated 2.8 million people in the U.S. each year.

The protein, Pgp3, is secreted by *Chlamydia trachomatis*, the bacterium that causes chlamydia. Pgp3's shape is very distinguishable—sort of like an Eiffel Tower of proteins. "From a structural standpoint, the protein is very odd indeed," said X-ray crystallographer P. John Hart, Ph.D., the Ewing Halsell President's Council Distinguished Chair in the Department of Biochemistry at the San Antonio medical school. "This long and slender molecule contains a fusion of structural motifs that resemble those typically found in viral and not bacterial proteins." Dr. Hart is co-lead author of the research, which is described in the *Journal of Biological Chemistry*.

The Pgp3 protein is a chlamydial virulence factor that is hypothesized to enhance the bug's ability to initially infect its human host and then evade host defenses. "Although my lab has worked on this protein for many years and gained a great deal of knowledge on it, we still don't know what roles it may play in chlamydial pathogenesis (disease development)," said co-lead author Guangming Zhong, M.D., Ph.D., professor of microbiology at the Health Science Center. "With the structural information uncovered in this paper, we can now test many

hypotheses."

This is the second chlamydial virulence factor that Dr. Zhong's laboratory has identified; the first was a protein called CPAF. Structural studies have played an important role in understanding CPAF's functions in chlamydial infections, Dr. Zhong said.



This is a ribbon diagram of the elongated, full-length structure of Pgp3, a protein secreted by *Chlamydia trachomatis*, the bacterium that causes chlamydia. Pgp3's shape is very distinguishable -- sort of like an Eiffel Tower of proteins. Image courtesy of researchers in the School of Medicine at The University of Texas Health Science Center San Antonio.

Chlamydia's toll

According to the U.S. Centers for Disease Control and Prevention (CDC), more than 1.4 million new cases of chlamydia were reported in 2011 across the 50 states and the District of Columbia. But the CDC says as many cases go unreported because most people with chlamydia have no symptoms and do not seek testing. If left untreated, chlamydia can permanently damage a woman's reproductive system. This can lead to ectopic pregnancy, pelvic inflammatory disease and infertility.

The disease burden of chlamydia worldwide is magnitudes greater, with new cases numbering in the dozens of millions per year. The World Health Organization estimates that 499 million new cases occur annually of four curable sexually transmitted diseases—chlamydia, syphilis, gonorrhea and trichomoniasis. This estimate is for cases in adults aged 15-49.

Chlamydia infection induces inflammatory pathology in humans, and Pgp3 may contribute to the pathology by activating inflammation via one of its structural features uncovered in the crystal structure, said Dr. Zhong, who has worked with Dr. Hart on the Pgp3 project for nearly four years.

More information: Structure of the Chlamydia trachomatis Immunodominant Antigen Pgp3, *Journal of Biological Chemistry*, 2013.

Provided by University of Texas Health Science Center at San Antonio