

Global diversity of the *Chlamydia trachomatis* tryptophan operon reveals evolutionary trends among ocular and urogenital strains

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Chlamydia trachomatis (*Ct*) phylogeny reveals ocular, urogenital and LGV clades that are associated with, but not entirely restricted to specific tissues. *Ct* genomes have a nearly identical pangenome (>98%) where polymorphic regions [e.g., plasticity zone (PZ)] are informative for its evolution. The tryptophan synthase operon, *TrpRBA*, is located in the PZ, which is subject to high rates of mutation. The operon is thought to be retained in urogenital and LGV strains. In analyzing *trpRBA* from all publically available genomes, ocular strains before 1961 contained a truncated *trpA* of 210 bps at position 552, as did A strain sequences from the Solomon Islands in 2000. More recent Tanzanian and Chinese strains isolated in the 2000s-2015s contained only 136-496 bps. These data suggest that reductive evolution has resulted in loss of operon function. Furthermore, although ocular B strains prior to 1980 lacked *trpRBA*, several from Gambian and Tanzanian trachoma patients from the 1980-1990s have an ocular backbone with a near full-length *trpA* that is identical to ocular strains in the first two-thirds of the gene and thereafter to urogenital strains, suggesting homologous recombination with urogenital strains in the population. For ocular B and C strains from Australian Aborigines, *trpA* sequences were identical to urogenital D, E, F and J strains. Our findings suggest that *trpA* (and/or adjacent genomic regions) has undergone multiple mutation and recombination events, indicating disparate evolutionary strategies to either acquire the functional operon or lose it while maintaining its ability to scavenge the intracellular host environment for essential metabolites.