Characterization of a Persistent Chlamydial Infection and the Role of Toll-like Receptors in the IL-6 Secretion in Chlamydia Trachomatis-Infected Human Synovial Fibroblasts

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Abstract：*Chlamydia trachomatis* a urogenital pathogen is a trigger of reactive arthritis (ReA), which is able to induce interleukin-6 (IL-6) production in human fibroblast-like synovial cells (HFLS) *in vitro*, and the persistence of *chlamydia* might thus play an essential role in stimulating the synthesis of IL-6 in HFLS. In addition, a persistent infection has been established *in vitro* by treatment with gamma interferon(IFN-γ)or penicillin and by the deprivation of nutrients. This paper compared the mechanism of chlamydial persistence in *C. trachomatis*-infected HFLS to that of IFN-γ induced persistent infection in HeLa 229 cells. The secretion of IL-6 increased only slightly (～1,000 pg/ml) when HeLa 229 cells were treated with IFN-γ regardless of the degree of *C. trachomatis* infection or tryptophan depletion. On the other hand, pretreatment with an antagonistic inhibitor of indoleamine 2,3-dioxygenase, 1-methyltryptophan, had no inhibitory effect on the production of IL-6, and a large amount of IL-6 secretion (～45,000 pg/ml) was observed with the suppression of chlamydial growth in *C. trachomatis*-infected HFLS, i.e., abnormal inclusions could not return to their normal shape by the pretreatment with 1-methyltryptophan. These results indicated that IFN-γ-induced persistence might be different from the persistence of *chlamydia* in HLFS. The role of Toll-like receptors (TLRs) in IL-6 production in *C. trachomatis*-infected HFLS was also investigated. The blockade of TLR2 antibody diminished the infectivity but augmented the IL-6 production in *C. trachomatis*-infected HFLS ; however, TLR4 did not show any correlation with infectivity and IL-6 production. These results suggest that TLR2 is involved in both the process of chlamydial infection and the IL-6 production in HFLS.

Key words：**Reactive arthritis, Human fibroblast-like synovial cells(HFLS), Persistent chlamydial infection, Toll-Like Receptors**