Relationship between gamma-interferon and interleukin-17 in *Chlamydia trachomatis* reactive arthritis

Sirs,

Reactive arthritis (ReA) is triggered by urethritis or enteritis causing pathogens (1). The presence of IL-17 has been reported in ReA joints following a history of diarrhea (2) but the presence of IL-17 in *C. trachomatis* ReA joints has never been investigated. The objective of the study described herein was to determine the levels of IL-17 and IL-17-modulating cytokines in the synovial fluid (SF) from *C. trachomatis* ReA, rheumatoid arthritis (RA) taken as inflammatory control, and osteoarthritis (OA) as non-inflammatory control patients:

(i) *C. trachomatis* ReA (n=13) was defined by the presence of asymmetrical mono/oligoarthritis and evidence of *C. trachomatis* infection (positive culture or DNA amplification)(median age, 26 years; interquartile range (IQR) 21-33, 2 were females, median number of SF leucocytes, 13700/mm^3 (9400–23900), median duration of arthritis, 14 days (IQR 7–46) and median number of active joints, 2 (IQR 1–3.3)).

(ii) Rheumatoid arthritis (RA) (n=20) (median age, 67 years (IQR 54–79), 17 females, median number of SF leucocytes, 7700/mm^3 (IQR 5738–12613)).

(iii) Osteoarthritis (OA)(n=17)(median age, 73 years (IQR 64–78), 11 females, median number of SF leucocytes, 300/mm^3 (IQR 150-463)).

The levels of cytokine concentrations in SF were determined by sandwich ELISA techniques. In *C. trachomatis* ReA patients, the SF concentrations of IFN-γ and IL-17 were significantly higher than in OA patients (median 13.6 pg/ml, IQR 2.33–31.3 *vs.* median 0 pg/ml, IQR 0–1.76 $p<0.005$ and median 5.7 pg/ml, IQR 0–25.4 *vs.* median 0 pg/ml, IQR 0–0, $p<0.005$, respectively). No significant difference was found between *C. trachomatis* ReA and RA patients (Fig. 1). A positive correlation (Rho=0.74, $p=0.011$) was found between the levels of IFN-γ and IL-17 in SF of *C. trachomatis* ReA patients. The levels of cytokines modulating IFN-γ and IL-17 expression such as IL-1β, IL-6, IL-12p70 and IL-23(p19/p40), (3, 4) were also determined. The concentrations of IL-1β in the SF of *C. trachomatis* ReA (median 6.5 pg/ml, IQR 1.6–15.2) were significantly higher than in OA patients (median 0 pg/ml, IQR 0-0.1, $p<0.0001$) (Fig. 1). A positive correlation (Rho=0.70, $p=0.02$) was found between the levels of IL-1β and IL-17 in SF of *C. trachomatis* ReA patients. There was no significant difference between ReA and OA regarding the other cytokines, mainly because of wide interindividual variations

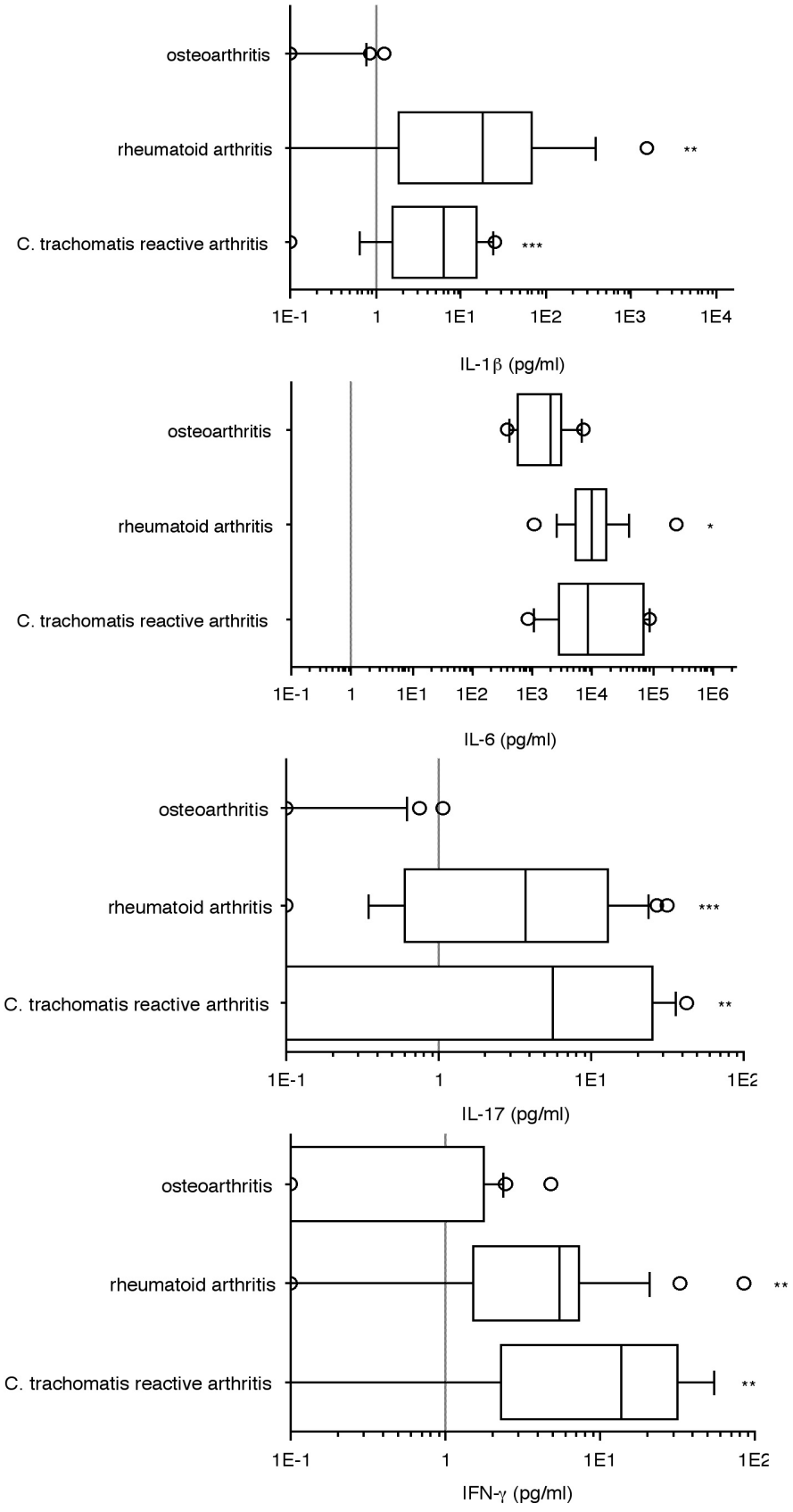

Fig. 1. Levels of IFN-γ, IL-17, IL-6, and IL-1β in the SF of patients with *C. trachomatis* ReA, RA and OA. Levels were determined by ELISA. Horizontal bars within boxes show the median, boxes show the interquartile range and vertical bars show the 95% confidence interval (values above and below these levels were plotted separately). Comparison between two groups was made only when the Kruskal-Wallis test yielded statistically significant results. **$p<0.005$; ***$p<0.0001$ compared with OA patients (Mann-Whitney test).

in IL-6 concentrations and non detectable levels of IL-12p70 and IL-23 (data not shown).

This is the first study reporting the presence of IL-17 in the SF of patients with *C. trachomatis* ReA. Both IFN-γ and IL-17 were detected and a positive correlation was found between their levels indicating possible similar regulation by the local cytokine milieu in *C. trachomatis* ReA joints.

The role of IFN-γ and IL-17 in the SF from *C. trachomatis* ReA patients is unclear. IFN-γ is well known for its antichlamydial activity but its median concentration (13.6 pg/ml) was lower than values reported to be efficient *in vitro*. Indeed, high levels of IFN-γ (2 ng/ml) promoted the destruction of *Chlamydia* whereas lower levels (0.2 ng/ml) induced the formation of persistent forms (5). However it is difficult to extrapolate results obtained *in vitro* to the environment of an arthritic joint. The same remark is valid for IL-17 concentrations found in SF from *C. trachomatis* ReA patients. IL-17 is well known for its role in joint destruction (6) but recent findings indicate that IL-17 may also contribute to protection against intracellular bacteria (7, 8).

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