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Rheumatoid arthritis patients are free of filarial infection in filarial endemic area.

To the Editor:

We read with great interest the recent article by Pineda et al. (1) where the role of helminth product ES-62 on suppression of pathogenesis of collagen-induced arthritis (CIA) through IL-17 network has been elegantly demonstrated. Based on earlier reports (2, 3) and results of the current study, a possibility for the use of ES-62 in treatment of rheumatoid arthritis (RA) has been proposed as an innovative concept. Fred D. Finekelman in the editorial described limitations of ES-62, in the current form, as a therapeutic option for several reasons (4). Importantly, CIA is an imperfect model of human RA since the presentation is acute and chronic joint damage has not been envisaged. Although evidence points to an immunomodulatory and anti-inflammatory role for ES-62 and demonstrates its protective effect on experimental CIA, the proof of the concept can only be verified in human models

Odisha, India, is home to endemic lymphatic filariais and there are large numbers of patients with RA as well. Based on earlier evidence, we hypothesized that filarial infected subjects in endemic areas would be less prone to RA and/or individuals suffering from RA would be free of filarial infection. We conducted a pilot study to look into this association. Female RA patients (n=207), living in lymphatic filarial endemic areas (5, 6) were recruited from the inpatients and outpatients clinics of the Division of Clinical Immunology and Rheumatology, Department of Medicine, at S.C.B. Medical College Cuttack, Odisha, India. The mean age was 42.84 years (18-68 years) and the mean disease duration was 7.27 years. Since RA was more prevalent in females compared to males, only healthy female subjects (HC) (n=222) from identical areas were included (Table-1). None of the controls reported history of autoimmune

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disorder. About 5ml of blood was collected from each participant. Blood samples from HC were collected at night. The Institutional Ethical Committee approved the study protocol and informed written consent was obtained from each participant.

Parasitological status of HC was assessed by means of microscopic examination of Giemsa-stained blood smear. Further, circulating filarial antigen (CFA) in RA and HC was investigated by Og4C3 enzyme linked immunosorbent assay (ELISA) for specificity of the presence of filarial infection.(7). In an earlier study on patients with asymptomatic filarial infection who were followed up for 13 years (8) we had demonstrated that most of these individuals remain symptom free despite carrying the worm for long periods of time indicating its robustness in modulating immune response for its survival. As shown in Table-1, 40% of healthy controls (HC) in the present study displayed presence of filarial infection. Microfilaria was detected in blood smears of 18 subjects (8%) who were asymptomatic carriers. 32% (n=71) of HC showed CFA positivity (Og4C3 positivity) in the absence of circulating mf indicating presence of cryptic infection (6). Although prevalence of antigenemia was 40% in healthy controls, interestingly, none of the RA samples showed CFA positivity indicating a possible association between filarial infection and RA. This is the first observation highlighting a link between filariasis and RA in human subjects. In an area where filariasis and RA co-exist, there is an epidemiological opportunity to observe their association for validating the observation made in animal models. Suppression of CIA in experimental model by ES-62 could be extended to human RA in filarial endemic area. Healthy subjects infected with filariasis may be protected from RA. However, prospective studies on large samples from various filarial endemic areas would provide robust evidence on the link and an opportunity to study the immunological changes involved in there interaction.

Table-1. Baseline characteristics and filarial infectious status in healthy controls and rheumatoid arthritis.

	HC (n=222)	RA (n=207)
Sex (M/F)	0/222	17/190
Mean age in years (range)	31.05 (12-73)	42.84 (18-68)
Duration of disease in years (mean ± SD)	-	7.27 ± 5.47
Og4C3 positivity	89 (40%)	0

Note. HC: healthy control; RA: rheumatoid arthritis

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