

ONLINE SUPPLEMENTARY DATA

Supplementary Table 1. Association of LTL with incident RA risk by seropositivity status in the Nurses' Health Studies and the Women's Health Study combined^a

	Controls	Seronegative			Seropositive			p-het
		Cases	OR	95% CI	Cases	OR	95% CI	
Shortest tertile	271	33	1.00		43	1.00		
Intermediate	275	47	1.10 ^d	0.29 – 4.12	55	1.10	0.47 – 2.58	
Longest tertile	281	43	1.15	0.48 – 2.76	75	1.74	1.15 – 2.64	
Per standard deviation ^b			1.05	0.75 – 1.48		1.24	1.04 – 1.47	
P-trend ^c			0.76			0.01		0.37

Ca=cases; Co=controls; OR=odds ratio; CI=confidence interval; BMI=body mass index

^aMeta-analysis used to combine estimates from polytomous logistic regression analyses adjusted for the same covariates listed in Table 2.

^bNurses' Health Study LTL standard deviation = 0.26; Women's Health Study LTL standard deviation = 0.71

^cBased on per standard deviation analysis

^dSignificant heterogeneity between studies (p=0.02)

Supplementary Table 2. Association of LTL with incident RA risk by HLA-DRB1 status in the Nurses' Health Studies^a

	HLA_SE non-carrier			HLA_SE carrier			P-het
	Ca/Co	OR	95% CI	Ca/Co	OR	95% CI	
Shortest tertile	35/113	1.00		51/85	1.00		
Intermediate	46/111	2.56	1.42 – 4.63	40/80	1.22	0.68 – 2.18	
Longest tertile	20/120	1.88	1.02 – 3.47	31/75	1.56	0.88 – 2.78	
Per standard deviation ^b		1.25	0.99 – 1.58		1.14	0.91 – 1.42	
P-trend ^c		0.06			0.26		0.45

Ca=cases; Co=controls; OR=odds ratio; CI=confidence interval

^aUnconditional logistic regression analyses adjusted for the same covariates listed in Table 2

^bNurses' Health Study LTL standard deviation = 0.26

^cBased on per standard deviation analysis

<i>Supplementary Table 3. Past Studies of Leukocyte Telomere Length (LTL) in Rheumatoid Arthritis</i>							
First Author, year	Study Design	Number of RA cases	Number of Controls	Cell type	Telomere Assay used	Findings	Ref.
Koetz, 2000	Cross-sectional, case-control matched on age	51	42	CD4+ T cells	Southern blotting, hybridization with a telomere repeat-specific ³² P-end-labeled (CCCTAA) ₃ probe	In RA patients, LTL did not correlate with age. LTL appeared shorter in RA patients vs. controls <40 years of age.	9
Schonland, 2003	Cross-sectional, case-control, unadjusted	unspecified	37 HLA-DR4+; 37 HLA-DR4 - controls	CD4 + T cells and granulocytes	As above	HLA-DR4+ individuals and RA patients 20-40 years of age had shorter LTL vs. HLA-DR4 -	13
Steer, 2007	Cross-sectional, case-control, adjusted for age and sex	176	1151	WBC	Southern blotting, hybridization with a telomere repeat-specific digoxigenin 3'-end labeled (CCCTAA) ₃ probe	LTL shorter in RA than controls, but not related to RA duration or activity	34
Colmegna, 2008	Cross-sectional case-control, matched on age, sex and ethnicity	63	48	CD34+ hematopoietic precursor cells (HPCs)	Quantitative PCR	LTL shorter in RA patients vs. controls LTL in RA did not correlate with RA duration or treatment	14

Current study	Prospective, nested case control, matched on age, cohort, menopause and hormone use status, fasting, time of day of blood collection	296 (Pre-RA)	827	WBC	Quantitative PCR	LTL longer in pre-RA patients vs. controls; no heterogeneity by menopausal status, cytokine levels, age, BMI, seropositivity, HLA-DRB1 status, time since blood collection	
---------------	--	--------------	-----	-----	------------------	--	--

REFERENCES

1. Koetz K, Bryl E, Spickschen K, O'Fallon WM, Goronzy JJ, Weyand CM. T cell homeostasis in patients with rheumatoid arthritis. Proc Natl Acad Sci U S A 2000;97:9203-8.
2. Schonland SO, Lopez C, Widmann T, Zimmer J, Bryl E, Goronzy JJ, et al. Premature telomeric loss in rheumatoid arthritis is genetically determined and involves both myeloid and lymphoid cell lineages. Proc Natl Acad Sci U S A 2003;100:13471-6.
3. Steer SE, Williams FM, Kato B, Gardner JP, Norman PJ, Hall MA, et al. Reduced telomere length in rheumatoid arthritis is independent of disease activity and duration. Ann Rheum Dis 2007;66:476-80.
4. Colmegna I, Diaz-Borjon A, Fujii H, Schaefer L, Goronzy JJ, Weyand CM. Defective proliferative capacity and accelerated telomeric loss of hematopoietic progenitor cells in rheumatoid arthritis. Arthritis Rheum 2008;58:990-1000.