Abstract EF-04 Table 1 Association between cumulative average ultraviolet-B radiation and risk of incident SLE, overall and by subtypes characterized by anti-Ro/La antibodies (+Anti-Ro/La) and cutaneous manifestations, among participants in nurses' health study and nurses' health study II (1976–2014)

	Cumulative Average Ultraviolet-B Radiation (mW/m^2)			
	T1	T2	T3	p-trend
SLE overall (n=286)				
Cases/Person-Years	86/22856321	97/20171088	103/25959040	
MV-Adjusted HR (95% CI)[a]	1.00 (ref)	1.19 (0.89–1.60)	1.27 (0.94–1.70)	0.17
SLE with±Anti Ro/La (n=38)				
Cases/Person-Years	10/22855418	10/20169348	18/25958172	
MV-Adjusted HR (95% CI)[a]	1.00 (ref)	0.99 (0.40–2.42)	1.75 (0.79–3.87)	0.10
SLE with Malar Rash (n=131)				
Cases/Person-Years	33/22855609	46/20169693	52/25958442	
MV-Adjusted HR (95% CI)[a]	1.00 (ref)	1.44 (0.92–2.26)	**1.68 (1.08–2.62)**	**0.04**
SLE with Photosensitivity (n=164)				
Cases/Person-Years	49/22855817	57/20170566	58/25958484	
MV-Adjusted HR (95% CI)[a]	1.00 (ref)	1.23 (0.83–1.81)	1.29 (0.87–1.90)	0.29
SLE with±Anti Ro/La and/or Malar Rash and/or Photosensitivity (n=224)				
Cases/Person-Years	64/22856035	75/20170825	85/25958826	
MV-Adjusted HR (95% CI)[a]	1.00 (ref)	1.24 (0.89–1.75)	**1.44 (1.03–2.00)**	**0.05**

Tertiles T1 (lowest), T2 (middle), T3 (highest). Tertile range: T1: 2–171 mW/m^2 ; T2: 171–183 mW/m^2; T3:183–285 mW/m^2.
[a]Adjusted for age (months), race (white, non-white), questionnaire cycle, cohort, body mass index (20 to <25, 25 to <30,>30), cigarette smoking (never/past/current), alcohol intake (0,>0 to<5 grams per day)
HR=hazard ratio; CI=confidence interval; MV=multivariable; P-trend derived by treating median value of each category as a continuous variable
p for heterogeneity between the cohorts>0.05 for all analyses

prospective cohort of women, examining SLE risk overall and by subtypes defined by presence of anti-Ro/La antibodies (+anti Ro/La) and/or cutaneous manifestations most associated with UV exposure in SLE patients.

Methods The Nurses' Health Study (NHS) enrolled 121,701 U.S. female nurses in 1976; NHSII enrolled 116,430 in 1989. Biennial questionnaires collected lifestyle, environmental, and medical data. Residential addresses were geocoded. Incident SLE was confirmed by medical record review. National Aeronautics and Space Administration Total Ozone Mapping Spectrometer and Ozone Monitoring Instrument gridded remote sensing images scaled to a 1 km spatial resolution predicted average July noon-time erythemal UV-B (mW/m^2) annually starting in 1980. Participants without UV-B data at baseline were excluded. Hazard ratios (HR) and 95% confidence intervals (CI) were estimated using Cox regression models across tertiles of cohort-specific, time-varying cumulative average UV-B through one cycle prior to SLE onset. We examined SLE risk overall and stratified by presence of anti-Ro/La or cutaneous manifestations (malar rash and/or photosensitivity) at diagnosis through 2014 (NHS) or 2013 (NHSII), controlling for potential confounders. We also conducted a 'lagged' analysis by ending the exposure window two cycles prior to SLE diagnosis, as SLE symptoms may develop insidiously pre-diagnosis.

Results Mean age at SLE diagnosis was 49.3 (10.4) years among 286 SLE cases in NHS/NHSII. At SLE diagnosis, 13% of women had +anti Ro/La whereas 80% had either +anti Ro/La or at least one cutaneous manifestation. Compared to the lowest tertile of UV-B exposure, risk of overall SLE, SLE with +anti Ro/La, or SLE with photosensitivity in the highest UV-B tertile were increased, but not statistically significant in the main analysis (table 1) or in lagged analyses. However, women in the highest UV-B tertile had statistically significantly increased risks of SLE with malar rash (HR 1.68 [95% CI 1.08 to 2.62]) (table 1), but this was no longer significant in the lagged analysis (HR 1.39 [95% CI 0.92 to 2.10]).

Conclusions Increasing cumulative UV-B exposure was not associated with risk of developing overall SLE. However, among women at risk for SLE, living in areas with higher UV-B exposure was associated with increased risk of developing SLE presenting with malar rash. Further studies are warranted to determine whether high UV-B exposure may play a role in triggering SLE onset with malar rash.

EF-05 ANDROGENS REGULATE MICROBIOTA COMPOSITION, FUNCTION AND PROTECTIVE PROPERTIES IN LUPUS-PRONE MICE

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Background Dysbiosis (alterations in microbiota composition) is associated with autoimmune diseases, including lupus. Factors that are thought to influence gut microbiota include diet, age and more recently, sex. Like humans, female NZBxNZWF1 (BWF1) mice spontaneously develop lupus-like disease, and exhibit much greater incidence of disease than males. Castration of male BWF1 mice increases disease onset/incidence and decreases survival suggesting that male sex steroids, androgens, play an important role in protection of males from disease.

Methods Intact female and male, or castrated and sham-castrated male BWF1 mice were used in this study. Cecal contents (microbiota) from different groups were transferred into female BWF1 mice shortly after weaning (~26 days) and either disease or *in vitro* cell function (cell culture, flow cytometry) was evaluated. Feces were collected from adult mice and analyzed for either microbiota composition (deep sequencing of 16S gene) or metabolomic profiles (mass spectrometry).

Results We have found that the composition of gut microbiota and metabolomic/lipidomic profiles differ between mature female and male BWF1 mice. Transfer of male microbiota to female BWF1 mice suppresses disease and increases survival. Further, we found that male microbiota may protect, in part, via an effect on tolerogenic $CD103^+$ dendritic cells (CD103DC) that induce peripheral Tregs (pTregs) through TGF and retinoic acid (RA) production. Female BWF1 CD103DC have a decreased ability to induce pTregs and express retinaldehyde dehydrogenase, (RALDH2), an enzyme involved in RA synthesis. Transfer of male microbiota to female BWF1 mice reconstitutes both RALDH2 expression and the ability of the CD103DC to induce pTregs. Interestingly, castration of male mice significantly alters gut microbiota composition and metabolomic/lipidomic profiles by comparison to males, diminishes CD103DC function and decreases the ability of the microbiota to protect female mice from disease. The mechanisms underlying male microbiota-mediated protection from disease are unknown, but may be mediated through the production of metabolites. We have identified several metabolites that are increased in male compared to both female and castrated male feces that function as retinoid X receptor agonists and enhance RALDH2 activity and increase pTregs *in vivo*.

Conclusions Our data suggest that androgens alter the composition and function of the gut microbiota in males, and the metabolites produced by the male microbiota may have potential for development into therapeutic strategies for the treatment of disease.

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EF-06 ANTI-NUCLEAR ANTIBODIES (ANA) AND AIR POLLUTION: ULTRAFINE PARTICLES AND OZONE

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Background Previous studies suggest links between air pollution (i.e. fine particulate matter, PM2.5) and serum antibodies related to rheumatic diseases. No one has yet examined associations between anti-nuclear antibodies (ANA) and ultrafine particles (UFP) or ozone (O3), both of which can enter through the lungs and may have the potential to trigger systemic effects.

Methods Our analyses were based within the CARTaGENE general population cohort (n=20,000) based in the province of Quebec, Canada. We determined baseline ANA (HEp-2000, Immuno Concepts) on a random sample. Air pollutant exposures were assigned by linking subjects' residential postal codes with estimated levels (determined by hybrid approaches including satellite imagery and modelling). We performed multivariable logistic regression models for the outcome of positive ANA, assessing for independent effects of UFP (available for Montreal only) and O3 in separate models, adjusting for age, sex, smoking, and self-reported ancestry.

Results ANA positivity of at least 1:160 occurred in 713 (20%) of 3578 randomly selected patients tested. The ANA positive subjects were more likely than ANA negative subjects to be female (63% vs 49%) while the average age (55.4 vs 54.0) and percent never-smokers (37% vs 40%) were similar. There was missing information on covariates for 232 subjects, which therefore were not included in the model estimates.

There was a trend for higher average UFP: exposure in ANA positive subjects (24 606 particles/cm^3, standard deviation, SD 4979) versus ANA negative (24328, SD 5078), while average ozone levels were very similar (22.5 vs 22.6 µg/m). The multivariable model (table 1) for UFP showed a trend to higher levels in the ANA positive group (1.008, 95% CI 0.982 to 1.034) while in the multivariable model for O3 the OR was very close to the null value (0.996, 95% CI 0.965 to 1.029). In all models, risk factors for ANA positivity included older age and female sex, with trends for lower ANA positivity in French Canadians.

Conclusions We saw a non-significant trend towards higher UFP levels in ANA positive versus negative subjects, while O3 levels seemed very similar in the two groups. Expected trends for more ANA positivity with older age and female sex was seen. Further study of UFP levels with a larger sample size is in progress. If confirmed, these results may strengthen the hypothesis that air pollution is an environmental trigger of immune system activation.

Abstract EF-06 Table 1 Pollution variables and ANA positivity: odds ratios with 95% confidence intervals

Single pollutant model, Ozone, n=3346	Adjusted odds ratio	95%	CI
O3 (µg/m^3)	0.996	0.965	1.029
Age (continuous)	1.024	1.013	1.036
Female	1.778	1.492	2.118
Current (versus never or past) smoker	1.038	0.833	1.294
French Canadian Caucasian	0.843	0.703	1.012
Montreal	0.980	0.793	1.211
Ultrafine particules, n=1371 (Montreal)	**Adjusted Odds Ratio**	**95%**	**CI**
UFP (1000 particles/cm^3)	1.008	0.982	1.034
Age (continuous)	1.028	1.011	1.045
Female	2.054	1.558	2.708
Current (versus never or past) smoker	1.119	0.802	1.561
French Canadian Caucasian	0.749	0.571	0.982
Montreal	NA	NA	NA

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