503 INTESTINAL PERMEABILITY CORRELATES WITH DISEASE ACTIVITY AND DNA METHYLATION CHANGES IN LUPUS PATIENTS

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Objective Systemic lupus erythematosus (SLE or lupus) is a chronic autoimmune disease that can involve multiple organ systems. Although the exact cause of SLE is unknown, several studies have suggested that increased intestinal permeability may play a role in the pathogenesis of the disease. The aim of this study was to elucidate the relationship between intestinal permeability and disease activity in lupus patients.

Methods A total of 25 female lupus patients were included in this study. Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) scores were used as an indicator of disease activity. Plasma zonulin levels were measured, using an ELISA, as a marker of intestinal permeability. In addition, genome-wide DNA methylation patterns were assessed for 19 of the lupus patients using the Infinium MethylationEPIC array. Linear regression and Pearson's correlations were used to evaluate the correlation between zonulin concentrations and SLEDAI scores, as well as the relationship of DNA methylation levels with zonulin concentrations adjusting for age and race.

Results Intestinal permeability, as reflected by plasma zonulin levels, was positively correlated with disease activity in SLE patients (p-value = $7.60x10^{-3}$, r = 0.53). The analysis of DNA methylation levels showed 5 significant CpG sites (FDR-adjusted p-value < 0.05) and 20 suggestive CpG sites (p-value < $1x10^{-5}$) associated with zonulin levels. Among significant associations, the CpG site in the *LRIG1* gene (cg14159396, FDR-adjusted p-value = $3.77x10^{-2}$) suggested progressive demethylation levels with increasing intestinal permeability in lupus patients. Interestingly, the protein encoded by this gene has been proposed to play a role in the control of intestinal epithelium homeostasis.

Conclusion Our data suggest a significant correlation between increased intestinal permeability and disease activity in lupus patients. Further, increased intestinal permeability might be associated with epigenetic changes that could play a role in the pathogenesis of SLE.

Environmental Triggers

504 HAIR CHEMICAL USE AND SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE-CONTROL STUDY

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Background Systemic lupus erythematosus (SLE) is a complex chronic autoimmune disease of unknown etiology. Previous studies of beauty products as potential triggers of SLE development have shown conflicting results. Increasing awareness of parabens and estrogenic chemicals in beauty products prompted us to revisit this topic. Our study examines the relationship between hair chemical use and SLE, investigating their role in the risk of SLE development and severity of disease.

Methods Patients with SLE (n = 388) within an ongoing longitudinal registry at a single center were selected based on diagnosis of SLE, female gender, and age ≥18. Controls (total n = 178; unrelated n = 116) were from the same population-based cohort, recruited via patient family members and 'bring a friend' methods. All participants completed a questionnaire on hair chemical use (including dyes, permanents, straighteners) administered at one of their study visits. Disease damage, using the SLICC-Damage Index, and other SLE manifestations were obtained through in-person interviews and chart review and recorded as part of the research registry. Social vulnerability index (SVI) was calculated to identify the relative vulnerability of the participants' communities, using US Census tract data and current addresses.

Results Patients with SLE were overall more likely to use hair chemicals than controls (OR=1.77; 95% CI=1.16–2.68), **table 1**. This difference did not persist when the cohort was limited to Black patients and controls (OR=1.77; 95% CI=1.16–2.68) due to low numbers of White participants. Prior use of hair chemicals was not associated with the development of SLE (OR 0.85; 95% CI 0.44–1.62).

Among the patients with SLE, lupus nephritis was more likely to develop among those who used hair chemicals prior to their diagnosis, but this difference was no longer statistically significant after controlling for covariates (OR=1.67;95% CI=0.97 – 2.94), **table 2**. Overall disease damage scores did not differ (p=0.64). However, when comparing SLE

Abstract 504 Table 1 Characteristics of study population (patients with SLE and controls). *All p-values are compared to patients with SLE

Characteristics	SLE		Compared to SLE: All Controls				Compared to SLE: Unrelated Controls			
	n= 388 (%)		n=178 (%)		p-value*		n= 116 (%)		p-value*	
Black	276	(71.1)	126	(70.8)	0.93	NS	67	(57.8)	**<0.01**	
Prior hair chemical use	222	(57.2)	92	(51.7)	0.22	NS	50	(43.1)	**0.01**	
Hair chemical usage, any (%)	271	(69.8)	92	(51.7)	**<0.01**		50	(43.1)	**<0.01**	
Insured (any)	354	(91.2)	153	(86.0)	0.25	NS	99	(85.3)	0.33	NS
High school graduate	331	(85.3)	149	(83.7)	0.67	NS	102	(87.9)	0.18	NS
Years followed in cohort	9.8	±4.7	8.6	±5.0	**<0.01**		7.6	±4.4	**<0.01**	
Current age (end of 2022)	49.2	±15.2	47.1	±15.8	0.13	NS	46.1	±14.0	0.05	NS