



SHORT REPORT OPEN ACCESS

Measuring Dynamic Inflammation Regulation in Low-Resource Settings: Results From a Sample of Adults in the Dominican Republic

Keegan C. Krause¹ | Sayira Paola Mueses Jiménez² | Franceska Duperval^{3,4} | Farah St. Juste⁴ | Aaron A. Miller¹ | Thomas W. McDade^{1,5}

¹Department of Anthropology, Northwestern University, Evanston, Illinois, USA | ²Instituto de Medicina Tropical y Salud Global, Universidad Iberoamericana, Santo Domingo, Dominican Republic | ³Clínica Dr. Lambert S. Emmanuel, Puerto Plata, Dominican Republic | ⁴Community Research Partner, HABITAT Project, Puerto Plata, Dominican Republic | ⁵Institute for Policy Research, Northwestern University, Evanston, Illinois, USA

Correspondence: Keegan C. Krause (kckrause@u.northwestern.edu)

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ABSTRACT

Introduction: Inflammatory signaling mediates several homeostatic mechanisms that shape health, and quantifying inflammation regulation patterns using ex vivo cell culture systems—response to activation and sensitivity to inhibition—improves upon baseline measures of chronic inflammation. The purpose of this report is to demonstrate the feasibility of implementing an ex vivo cell culture system in a low-resource setting in the Dominican Republic.

Methods: This study implements an ex vivo cell culture system to measure stimulated inflammation and glucocorticoid (GC) sensitivity using finger stick capillary blood collected from 202 adults in the Dominican Republic (age: 18–61 years).

Results: Median cytokine responses (pg/mL) to incubation with lipopolysaccharide (LPS) were robust for IL6 (58.0), IL1 β (21.3), and TNF α (23.1). Median cytokine responses to incubation with LPS and GC—capturing sensitivity to inhibition—were attenuated for IL6 (20.2), IL1 β (8.4), and TNF α (7.0).

Conclusion: Minimally invasive cell culture protocols offer novel research opportunities for measuring inflammation regulation and health in low-resource settings across diverse eco-social milieus.

1 | Introduction

Inflammatory signals are integral to homeostatic mechanisms, and dysregulated inflammation signaling is implicated in bio-social pathways for eco-social contexts to modulate population health (Lam et al. 2022; McDade 2023). Baseline measures of cytokines and acute phase proteins quantified in dried blood spots (DBS)—drops of capillary blood collected on filter paper after finger stick—offer insight into chronic low-grade inflammation with low participant burden. Alternatively, ex vivo cell culture technology—stimulating leukocytes with lipo-polysaccharide (LPS) and synthetic glucocorticoid (GC)—that simulates acute inflammatory responses and their inhibition, provide more nuanced measures of inflammation regulation processes that

interface with neuroendocrine function (McDade et al. 2024; Chen et al. 2024).

We previously reported on the validation of a portable cell culture system that requires only a few drops of capillary blood in Belgian school-based settings (McDade et al. 2024; Michels et al. 2025). Here, we present results from the first field-based implementation of this protocol in a low-resource community setting. Finger stick whole blood was collected from adults living in the Dominican Republic (DR), immediately incubated with LPS and LPS combined with GC, and subsequently transferred to filter paper. This report describes overall inflammatory response patterns and viability of adapting this protocol to resource-limited community settings with adults.

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2 | Materials and Methods

2.1 | Study Design

The Health and Belonging in Tourism and Trade (HABITAT) Project is a mixed methods study of social belonging and health initiated in September 2024 in Puerto Plata province, DR. Data was collected from 202 Dominican and Haitian adults in private rooms in two community clinics from July–September 2025. The protocol was approved by Northwestern University (US), Universidad Iberoamericana (DR), and Consejo Nacional de Bioética en Salud (CONABIOS) (DR) ethics committees. Written informed consent was received from all participants.

2.2 | Portable Cell Culture System and Cytokine Quantification

Following a previously validated cell culture protocol (McDade et al. 2021), this study utilized three conditions: LPS (InvivoGen, #tlrl-eklps) in normal saline with heparin (2.083 ng LPS in 40 μ L total volume); LPS and GC (Millipore/Sigma, H0888-1G) in normal saline with heparin (2.083 ng LPS and 8.657 10⁵ M hydrocortisone in 40 μ L total volume); and a control (40 μ L normal saline with heparin). Each condition was prepared in bulk, aliquoted into 2.0 mL sterile vials (Corning, 430659), and stored at -30°C before shipping in a dry vapor shipper (MVE Doble 28) to Universidad Iberoamericana in Santo Domingo, DR. Vials were then transported in the dry vapor shipper to Puerto Plata, DR where vials were stored at approximately -20°C .

Finger stick capillary blood was collected using sterile, single-use lancets (BD Microtainer, 366954). 30 μ L aliquots were transferred to each condition and incubated 4 h at 37°C in portable mini dry baths (Benchmark Scientific BSH200) powered by lithium battery packs. Contents of each vial were transferred to filter paper (Whatman #903) on site or transported while incubating to an off-site pipetting station. Uncultured whole blood was transferred to filter paper for C-reactive protein (CRP) quantification. Samples were dried overnight and stored at -20°C until completion of the study. Samples were transported overnight to Northwestern University for quantification in a single batch and stored at -30°C prior to analysis.

Cell culture samples were quantified for IL6, IL1 β , and TNF α using a previously validated multiplex assay (MSD #K151A9H) (McDade et al. 2021). Following previously reported methodology (McDade et al. 2024), samples were run in singleton, and calibrators and controls were assayed in duplicate. Inter-assay control CVs were <9.9% for IL6, <14.3% for IL1 β , and <13.3% for TNF α . CRP was assayed in duplicate using a previously validated high-sensitivity ELISA assay (McDade et al. 2004).

2.3 | Data Analysis

Prior to variable construction, cytokine and CRP values were natural-log transformed due to right skew. Following previously reported analyses (Chen et al. 2024; McDade et al. 2024), a composite inflammatory response variable was calculated by averaging z-scored IL-6, IL-1 β , and TNF- α concentrations from

the LPS condition (Cronbach's $\alpha = 0.935$). GC sensitivity was calculated for each cytokine by subtracting concentrations in the LPS + GC conditions from concentrations in the LPS conditions, dividing this difference by concentrations in the LPS condition. Cytokine-specific GC sensitivity scores were then z-scored and averaged (Cronbach's $\alpha = 0.860$).

Participants were screened for infection-related symptoms prior to study enrollment and excluded if symptoms were present within 2 weeks prior. Height was measured using a stadiometer (Seca 213i) and waist circumference was measured at the top of the iliac crest; waist-to-height ratios (WHtR) were calculated (waist/height) and z-scored. Participants reported inhaled nicotine use (smoking/e-cigarette). Descriptive statistics, Pearson correlations, and OLS regression were utilized to describe LPS and GC sensitivity patterns. Differences in WHtR by nationality were assessed using Welch's ANOVA. All variable transformations and statistical analyses were conducted with Stata for Mac, version 19 (StataCorp, College Station, TX).

3 | Results

Three participants were excluded: two due to high background/CRP values and one due to insufficient CRP sample; final analytic sample consisted of 199 observations. Mean age was 30.4 years (range: 18–61). Participants self-identified as 48.5% female; 43.5% Dominican, 44% Haitian, and 12.5% Dominico-Haitian. WHtR z-score had an approximate mean of 0 (SD = 1), and 34% of participants reported nicotine use.

Cytokine responses to the LPS condition were robust and attenuated for LPS with GC (Figure 1). Median GC sensitivity for IL6, IL1 β , and TNF α was 0.26, 0.28, and 0.49, respectively, and median un-transformed CRP was 0.672 mg/L. Composite LPS responses and GC sensitivity showed limited evidence of correlation (Pearson $R = -0.093$, $p = 0.191$). Baseline CRP was positively correlated with LPS response (Pearson $R = 0.227$, $p = 0.001$) and negatively correlated with GC sensitivity (Pearson $R = -0.194$, $p = 0.006$). Mean WHtR differed significantly by nationality (Welch's $F(2, 67.7) = 4.62$, $p = 0.000$) and was highest among Dominican (0.57) compared to Haitian (0.48) and Dominico-Haitian (0.49) participants.

Multivariable OLS regression models show a positive association of LPS response with WHtR and marginal associations with sex (Table 1). LPS response was not associated with age, nicotine use, or nationality. No associations were found between GC sensitivity and covariates in the unstratified model. However, models stratified by nationality show a negative association between GC sensitivity and WHtR only among Haitian participants ($B = -0.38$, $p = 0.033$), while the positive association between LPS response and WHtR remains only among Dominican participants ($B = 0.33$, $p = 0.005$) (results not shown).

4 | Discussion

This study is the first to demonstrate the viability of this “field-friendly” cell culture system to measure inflammation regulation patterns in low-resource community contexts. Materials

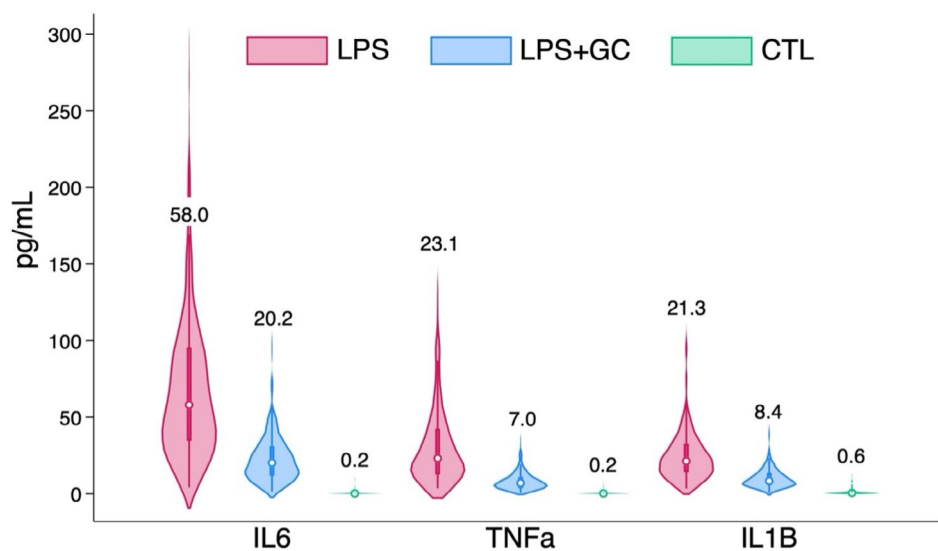


FIGURE 1 | Violin plots of cytokine responses to incubation with lipopolysaccharide (LPS), LPS with glucocorticoid (LPS+GC), and negative control (CTL). Plots indicate median and interquartile range and distribution as estimated by kernel density.

TABLE 1 | Results of multivariable OLS regression models predicting composite cytokine response to LPS (left) and GC sensitivity (right) ($n = 199$).

	LPS response			GC sensitivity		
	<i>B</i>	SE	<i>p</i>	<i>B</i>	SE	<i>p</i>
WHtR (z-score)	0.25	0.09	0.007	-0.07	0.09	0.430
Sex (1 = male; 2 = female)	-0.26	0.15	0.085	0.11	0.15	0.467
Age (years)	0.00	0.01	0.992	-0.01	0.01	0.136
Nicotine use (1 = yes; 2 = no)	0.24	0.15	0.110	0.17	0.15	0.246
Nationality						
Dominican ^a	—	—	—	—	—	—
Dominico-Haitian	-0.09	0.22	0.693	0.10	0.21	0.645
Haitian	0.21	0.16	0.186	-0.02	0.15	0.913
Constant	-0.12	0.27	0.664	0.14	0.26	0.583
Model R^2 (adjusted)	0.048			0.004		

Abbreviation: WHtR, waist-to-height ratio.

^aReference category.

may be prepared and transported to a variety of settings and adapted to local resource availability using portable mini-incubators. Transfer of samples to filter paper facilitates easy and safe sample transport (McDade et al. 2007).

Concentrations of IL6, IL1 β , and TNF α generated robust responses to LPS with attenuated responses to GCs, tracking previous validation data (McDade et al. 2021). Higher baseline CRP was associated with increased LPS response and decreased GC sensitivity, indicating circulating acute phase proteins may track underlying inflammation regulation patterns.

Associations of WHtR with LPS response suggest increased adipose tissue is associated with a more pronounced inflammatory response, while no associations were present between GC sensitivity and WHtR in the full sample. However, models

stratified by nationality suggest potential physiological shifts in these relationships according to measures of adiposity: among Dominican participants (high mean adiposity), associations with LPS response became pronounced with no GC sensitivity association; among Haitian participants (low mean adiposity) associations with GC sensitivity emerge, with no LPS response association. While direct comparisons warrant caution, the latter results conform with our prior findings among Belgian adolescents with relatively low BMI (McDade et al. 2024), suggesting trade-offs in inflammation regulation patterns between high- and low-adiposity individuals.

Robust inflammatory responses associated with increased WHtR may reflect ample biosocial resources to stimulate innate immune activation under eco-social challenge, while reduced GC sensitivity may indicate synergy between adiposity

and endured adversity leading to neuroendocrine-mediated inflammatory dysregulation. As previously reported, Haitian HABITAT participants reported significantly higher social precarity composite scores (resource/job insecurity, loneliness, and fear of violence), which was independently associated with decreased GC sensitivity (Krause et al. 2026). These results implicate age-specific, socio-structural, and ecological contexts as important considerations for future cell culture research.

Limited correlation between LPS response and GC sensitivity suggests distinct inflammation regulation pathways, and increased LPS response does not increase risk of lower GC sensitivity in this sample. Using a single GC condition here is a limitation, and including a range of GC concentrations can provide enhanced inferential relationships between GC sensitivity and LPS response values (Lam et al. 2022). Further, the age range and sample size provide limited power for robust age-related analyses, and the amount of explained variance across all models was small, indicating potential for additional eco-social, behavioral, and genetic factors to contribute to inflammation regulation patterns. Nevertheless, this study demonstrates the feasibility of adapting this ex vivo cell culture technology to low-resource settings, improving measures of inflammation regulation and health across diverse eco-social milieus.

Author Contributions

Keegan C. Krause: conceptualization, data collection, data analysis, writing. **Sayira Paola Mueses Jiménez:** data collection, editing. **Franceska Duperval:** data collection, editing. **Farah St. Juste:** data collection, editing. **Aaron A. Miller:** data collection, editing. **Thomas W. McDade:** conceptualization, editing.

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Disclosure

Artificial intelligence was not used in the writing, editing, or for analyses in preparing this manuscript.

Ethics Statement

This study was reviewed and approved by the Institutional Review Boards (IRB) at Northwestern University (United States), Universidad Iberoamericana (Dominican Republic), and Consejo Nacional de Bioética en Salud (CONABIOS) (Dominican Republic).

Consent

All participants provided written informed consent prior to participation.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available upon request from the corresponding author. The data are not currently publicly available due to privacy or ethical restrictions.

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