Perceived Discrimination and Immunological Aging: A Systematic Review of Cellular and Molecular Markers

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Objective: Perceived discrimination is a chronic social stressor that increases the risk of disease. While prior research has linked discrimination to adverse biological health outcomes, the cellular and molecular mechanisms underlying these associations remain understudied.

Methods: We conducted a systematic review and identified 32 empirical studies that met the inclusion criteria examining the relationship between self-reported discrimination experiences and markers of immunological aging, focusing on telomere length, gene expression profiles, and immune cell composition.

Results: Findings consistently showed discrimination to be associated with accelerated telomere shortening; altered transcriptional activity, particularly within proinflammatory and antiviral pathways aligned with the Conserved Transcriptional Response to Adversity; and shifts in immune cell populations indicative of immune aging and heightened inflammatory activity. Despite this growing evidence, the dominance of cross-sectional designs, limited racial/ethnic diversity in study populations, and narrow focus on select immune markers restrict generalizability and mechanistic clarity.

Conclusion: We emphasize the need for longitudinal research, broader immune phenotyping, and rigorous modeling of behavioral and physiological mediators to elucidate how discrimination drives chronic immune dysregulation. Advancing this field is essential for understanding the biopsychosocial pathways linking discrimination to disease.

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INTRODUCTION

Perceived discrimination (hereafter, discrimination) is a chronic social stressor that can be characterized by a feeling of lack of control, persistent uncertainty, and the constant anticipation of unfair treatment. This stressor is a critical determinant of health and health inequities across racialized and structurally excluded populations.[1–3] Decades of research have documented associations between discrimination and adverse health outcomes, including cardiovascular disease, metabolic dysfunction, depression, and premature mortality.[3–6] These well-documented associations have spurred growing interest in examining how discrimination becomes affects biological processes.

The Weathering Hypothesis posits that repeated exposure to discrimination and other social, economic, and political adversities accelerates biological deterioration, resulting in premature aging and early onset of disease, particularly among racialized populations. This hypothesis has often been operationalized through global indicators of dysregulation of multiple physiological systems (eg, high C-reactive protein, obesity, hypertension, etc.),[7,8] and research consistently shows that exposure to discrimination is associated with such multisystem dysregulation.[9] Yet physiological dysregulation can be viewed as a downstream expression of more proximal biological disruptions. An immunological aging perspective directs attention to upstream processes by identifying cellular-level changes that embody weathering before they are observable in broader physiological outcomes. Immunological aging is reflected in features such as cellular senescence, stress-related gene expression profiles, and shifts in immune cell proliferation and composition. Together, these processes capture how discrimination gradually compromise immune resilience, leading to diminished capacity for repair, heightened susceptibility to infection, and increased risk of chronic disease.

Growing recognition suggests that discrimination may compromise immune function at the cellular level through leukocyte telomere attrition.[10–12] Telomeres are

protective DNA-protein structures that cap the ends of chromosomes and naturally shorten with each cell division. Given their progressive shortening over time, telomeres serve as markers of cellular aging, with accelerated shortening reflecting biological weathering, a phenomenon that highlights how chronic social and environmental stressors drive premature aging, increased disease, and early mortality.[13–15] Sustained activation of stress-related systems, such as the hypothalamic pituitary adrenal (HPA) axis and the sympathetic nervous system (SNS), can accelerate this process by increasing oxidative stress and reducing the activity of telomerase, the enzyme that helps maintain telomere length.[16] In this framework, discrimination functions as a repeated social threat that gradually wears down the body's regulatory systems, including those involved in immune maintenance and repair.[17–19] Past reviews have reported associations between discrimination experiences and shortened telomere length.[20,21] However, telomere length is only one aspect of cellular health. Discrimination may also alter the composition and function of immune cells in ways that reflect deeper disruptions to immunological aging and resilience.

Through its downstream effects on the SNS and the HPA axis, amygdala activation initiates a cascade of physiological changes that modulate immune function. Specifically, SNS activation prompts the release of norepinephrine, which binds to beta-adrenergic receptors on immune cells, enhancing the transcription of proinflammatory and antiviral genes.[19] Studies have identified a "Conserved Transcriptional Response to Adversity" (CTRA) in leukocytes, characterized by upregulation of proinflammatory genes and downregulation of genes involved in antiviral responses and antibody production.[19,22] This stress-related gene expression profile has been observed in individuals reporting higher discrimination levels, suggesting that discrimination can be embodied through gene regulation pathways.[18,23,24] In addition to shaping gene expression in existing cells, activation of the sympathetic nervous system can stimulate myelopoiesis in the bone marrow, which may lead to increased production and mobilization of monocytes and dendritic cells.[19] Supporting this framework, Chen et al.[25] found elevated numbers of classical monocytes among African American adolescents with higher reported discrimination. Nevertheless, monocytes and dendritic cells may not be the only immune cells responsive to social threats such as discrimination. Chronic HPA axis activation can cause other immune cells to become resistant to glucocorticoid signaling, a phenomenon known as glucocorticoid resistance. This condition can lead to both immune dysfunction and, in some cases, altered immune cell distributions,[26] indicating broader shifts in immune system balance. Klopack et al[27] found that lifetime discrimination was associated with a higher percentage of terminally differentiated CD4 and CD8 T cells, suggesting accelerated immune aging consistent with the theory of weathering. These molecular and cellular changes may serve as upstream pathways linking discrimination to immunosenescence. Yet, despite their theoretical plausibility and empirical support, these pathways have not been extensively explored nor have their biological mechanisms been determined, leaving a significant gap in our understanding.

To date, no comprehensive review has systematically evaluated the current empirical evidence linking perceived discrimination to immune cell function, immune cell composition, and cellular markers of inflammation and aging. A systematic synthesis is needed to assess whether and how discrimination influences immunological aging at the cellular level and whether these effects are consistent across populations, methodologies, and immune parameters. The current review addresses this gap by systematically identifying and synthesizing empirical studies that examine the relationship between perceived discrimination and cellular markers of immunological aging. Our primary objective is to assess the extent to which discrimination is associated with cellular-level immune processes, including telomere length, gene expression, and immune cell subset composition and abundance. To complement the synthesis, we highlight critical gaps in the existing literature, particularly the study designs, sample characteristics, mechanistic analyses, and analyses of immune function. In doing so, we aim to outline a clear roadmap for future research to advance understanding of the precise cellular and molecular mechanisms by which discrimination becomes imprinted on physiological processes in ways that ultimately account for the health and disease risks associated with discrimination.

METHODS

This systematic review evaluated the association between discrimination and cell-mediated immune biology, focusing on biomarkers of cellular immune regulation and related mechanisms. Eligible studies investigated alterations in cell-mediated immunity linked to discrimination exposure (general or specific, eg, racial or gender-based). The protocol for this systematic review was registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the registration number CRD420251041621.

Inclusion and Exclusion Criteria

Inclusion criteria required studies to (1) be peer-reviewed publications in English, with no restrictions on publication date, (2) examine cellular immune processes (eg, production of white blood cells, gene expression related to immune function, or indicators of immune cell aging), (3) assess discrimination as the primary exposure, and (4) involve human participants, regardless of health status. Studies were excluded if they focused solely on systemic signaling proteins (eg, interleukins, C-reactive protein) or epigenetic clocks without including direct measures of immunological aging as outcomes.

Search Strategy

A systematic research was conducted using multiple electronic databases, including PubMed, Scopus, Web of

Science, as well as manual searches on Google Scholar. We solely focused on studies that assessed discrimination, defined as self-reported unfair or differential treatment directed at individuals. Nevertheless, to ensure comprehensive coverage, we also included terms such as institutional racism and related concepts, as some scholars conceptualize self-reported discrimination as an indicator of broader institutional or structural discrimination. Key Words and MeSh terms used included terms related to discrimination (eg, "perceived discrimination," "institutional racism," "microaggression") and immune regulation (eg, "immune cell," "leukocyte," "white blood cell"). The full strategy can be found in Table S1, Supplemental Digital Content, http://links.lww.com/PSYMED/B145.

Study Selection Process

All identified records were imported into Covidence software for systematic screening. Two reviewers independently performed title/abstract screening, followed by full-text review of potentially eligible articles. Discrepancies were resolved through consensus or consultation with a third reviewer. Data extraction was conducted using a standardized form, capturing study design, sample characteristics, exposure and outcome measures, effect estimates, and adjusted covariates. The study selection process is summarized in a PRISMA flow diagram (Figure 1), which documents the number of records screened, excluded, and retained at each stage.

Quality Assessment

Study quality was evaluated using the National Heart, Lung, and Blood Institute (NHLBI) Quality Assessment Tool of Observational Cohort and Cross-Sectional Studies. This validated tool systematically assesses risk of bias across 14 critical domains, including research question specification, population characterization, exposure and outcome measurement validity, temporal sequencing, confounding control, and statistical methods. Quality ratings (good, moderate, poor) were assigned through rigorous qualitative synthesis considering both design strengths and limitations. Cross-sectional studies were eligible for "good" rating when demonstrating: (1) use of objective biomarkers with established laboratory protocols (eg, qPCR for telomere length, flow cytometry for immune markers), (2) comprehensive adjustment for socioeconomic and biological confounders, and (3) conceptual alignment with biologically plausible mechanisms supported by prior longitudinal evidence. Longitudinal designs received particular emphasis for their ability to establish temporality, though exceptional cross-sectional studies with lifetime exposure measures and sensitivity analyses were appropriately weighted. Please see Table 1 for the NHLBI quality assessment.

RESULTS

Study Selection and Characteristics

This systematic review included 32 empirical studies examining the relationship between experiences of discrimination and cellular aspects of immune biology (including cell population dynamics, cellular aging, and cellular gene regulation; see Table 2). The majority of studies employed cross-sectional designs ($k = 20$), with 11 longitudinal studies and 1 article including both designs. Study sample sizes ranged from 20 to over 5000 participants. Most research was conducted in the United States, and analyses primarily focused on White and Black Americans. Several studies also focused on sexual and gender minority (SGM) individuals or people living with HIV. Perceived discrimination was assessed using a range of validated self-report instruments, including the Everyday Discrimination Scale (EDS),[6] the Experiences of Discrimination (EOD) scale,[28] and context-specific adaptations. Discrimination types captured included racial, gender-based, sexual orientation-based, and intersecting forms of discrimination.

Associations Between Discrimination and Leukocyte Telomere Length

Eleven studies assessed the relationship between experiences of discrimination and leukocyte telomere length (LTL), a widely used biomarker of cellular aging derived from peripheral blood leukocytes. Overall, findings indicated that higher exposure to discrimination, particularly racial or intersectional discrimination, was associated with shorter LTL, although effect sizes and statistical significance varied by population and methodological factors. For instance, Liu and Kawachi[11] found that everyday discrimination was associated with shorter LTL in Black participants ($\beta = -0.23$; 95% CI = −0.44, −0.01), though this association was not significant in White individuals ($\beta = 0.05$; 95% CI = −0.01, 0.10). Similarly, Chae et al[29] reported that cumulative exposure to discrimination across life domains (eg, employment, housing) predicted significant telomere attrition over 10 years in the CARDIA study ($\beta = -0.019$, $p = .015$), adjusting for baseline LTL. Gender-specific effects emerged in Sullivan et al,[30] where each 10-unit increase in everyday discrimination corresponded to 200 base pairs shorter LTL in African American ($\beta = -0.19$; 95% CI = −0.35, −0.04) and White women ($\beta = -0.19$; 95% CI = −0.37, −0.01), but not in men, even after adjusting for psychosocial factors.

Other studies identified psychosocial and contextual moderators. Lu et al[31] found that, among Black women, those who did not discuss their experiences of racism had significantly shorter LTL ($\beta = -0.11$; 95% CI = −0.21, −0.01; $p = .04$), suggesting coping style may influence biological aging. In addition, Lee et al,[32] found that high discrimination was associated with shorter LTL in older African American individuals ($\beta = -0.034$, $p = .017$), after controlling for sociodemographic factors. However, not all studies reported significant main effects. In a 10-year longitudinal analysis of the Multi-Ethnic Study of Atherosclerosis (MESA), Hailu et al[33] found no overall association between either major or everyday discrimination and changes in LTL after adjusting for sociodemographic characteristics. However, neighborhood social cohesion

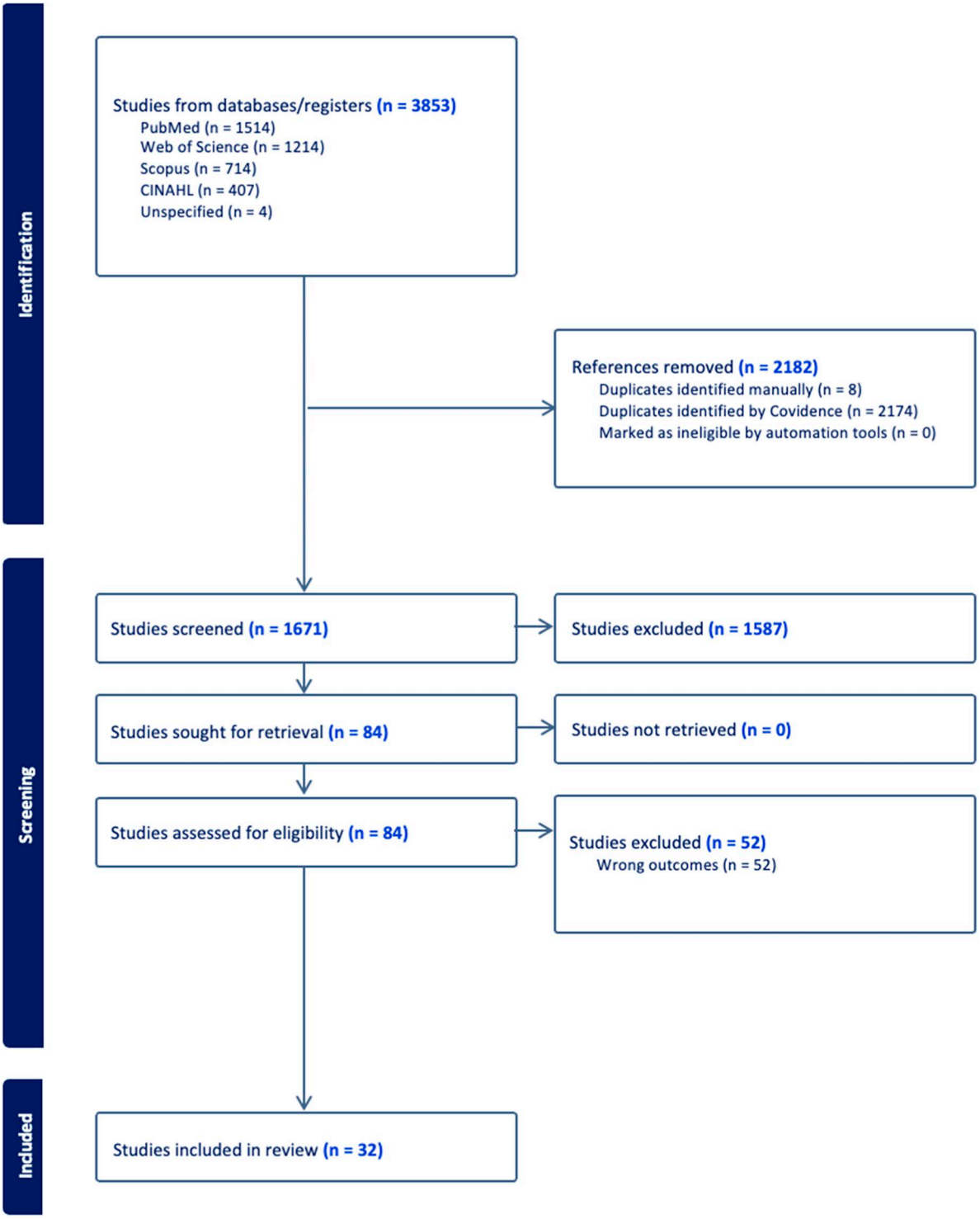

FIGURE 1. PRISMA flowchart. *Color image is available only in online version.*

significantly moderated this relationship. Among individuals living in low-cohesion neighborhoods, experiencing major discrimination in at least two life domains was associated with faster telomere attrition over time ($\beta = -0.03$; 95% CI = −0.06, −0.003). No interaction was found for everyday discrimination. Similarly, in a large cross-sectional analysis using data from MESA ($n = 1153$), Hailu et al[34] found no overall association be-

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TABLE 1. NLHBI Quality Assessment

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Q12	Q13	Q14	Overall Assessment
Sullivan et al[30]	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	NR	NA	Y	Good
Aronoff et al (2023)	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	NR	NA	Y	Moderate
Kimani et al[35]	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	NR	NA	Y	Good
Kelso et al (2014)	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	NR	NA	Y	Moderate
Chen et al—1 (2023)	Y	Y	Y	Y	N	Y	Y	Y	Y	Y	Y	NR	Y	Y	Good
Chen et al—2 (2023)	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	NR	NA	Y	Moderate
Liu and Kawachi[11]	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	NR	NA	Y	Good
Santos et al[38]	Y	Y	NR	Y	N	CD	CD	Y	Y	Y	Y	NR	Y	Y	Good
Chae et al[10]	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	NR	NA	Y	Moderate
Chae et al (2014)	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	NR	NA	Y	Moderate
Hailu et al[34]	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	NR	NA	Y	Good
Zhao et al (2024)	Y	Y	NR	Y	N	Y	Y	Y	Y	N	Y	Y	CD	Y	Good
Troxel et al (2023)	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	Y	NA	Y	Moderate
Thames et al[18]	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	Y	NA	Y	Moderate
Li et al[36]	Y	Y	NR	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Good
Bird et al[43]	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y	Y	Y	Y	Good
Brown et al[23]	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y	NR	Y	Y	Good
Pacheco et al[39]	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	NR	NA	Y	Moderate
Alley et al (2025)	Y	Y	NR	Y	N	Y	Y	Y	Y	N	Y	NR	Y	Y	Moderate
Cuevas et al[24]	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	Y	NA	Y	Good
Carroll et al (2022)	Y	Y	NR	Y	N	Y	Y	Y	Y	N	Y	NR	Y	Y	Good
Hailu et al[33]	Y	Y	Y	Y	N	Y	Y	Y	Y	N	Y	NR	Y	Y	Good
Flentje et al (2018)	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	NR	NA	Y	Moderate
Harris et al. (2024)	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	NR	NA	Y	Moderate
Bogart et al (2013)	Y	Y	NR	Y	N	N	N	Y	Y	Y	Y	NA	NA	Y	Moderate
Lu et al (2020)	Y	Y	N	Y	N	Y	Y	Y	Y	Y	Y	Y	Y	Y	Good
Sluiter et al[44]	Y	Y	NR	Y	N	Y	Y	Y	Y	Y	Y	NR	Y	Y	Good
Gillespie and Anderson (2020)	Y	Y	NR	Y	N	Y	Y	Y	Y	N	Y	NR	Y	Y	Moderate
Chae et al[29]	Y	Y	NR	Y	Y	Y	Y	Y	Y	Y	Y	NR	Y	Y	Good
Szanton et al (2012)	Y	Y	NR	Y	N	N	N	Y	N	N	Y	NR	NA	Y	Moderate
Brown et al[37]	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	NR	NA	Y	Good
Klopack et al[27]	Y	Y	NR	Y	N	N	N	Y	Y	N	Y	NR	NA	Y	Good
Lee et al[32]	Y	Y	Y	Y	N	N	N	Y	Y	N	Y	NR	NA	Y	Good

Note. NLHBI = National Heart, Lung, and Blood Institute. Y = yes. NR = not recorded. N = no. NA = not applicable.

Q1: Was the research question or objective in this paper clearly stated? Q2: Was the study population clearly specified and defined? Q3: Was the participation rate of eligible persons at least 50%? Q4: Were all the subjects selected or recruited from the same or similar populations (including the same time period)? Were the inclusion and exclusion criteria for being in the study prespecified and applied uniformly to all participants? Q5: Was a sample size justification, power description, or variance and effects estimates provided? Q6: For the analyses in this paper, were the exposure(s) of interest measured before the outcomes(s) being measured? Q7: Was the timeframe sufficient so that one could reasonably expect to see an association between exposure and outcome if it existed? Q8: For exposures that can vary in amount or level, did the study examine different levels of exposure as related to the outcome (eg, categories of exposure, or exposure measured as a continuous variable)? Q9: Were the exposure measures (independent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? Q10: Was the exposure(s) assessed more than once over time? Q11: Were the outcome measures (dependent variables) clearly defined, valid, reliable, and implemented consistently across all study participants? Q12: Were the outcome assessors blinded to the exposure status of participants? Q13: Was the loss to follow-up after baseline 20% or less? Q14: Were key potential confounding variables measured and adjusted statistically for their impact on the relationship between exposure(s) and outcome (s)?

tween either everyday or major experiences of discrimination and LTL. Importantly, however, the study revealed that the relationship between everyday discrimination and telomere length was modified by social support. Specifically, among participants with low social support, those reporting moderate and high levels of everyday discrimination had telomeres that were 0.35 (95% CI = −0.54, −0.15) and 0.17 (95% CI = −0.34%, −0.01) units shorter, respectively, compared with those reporting no discrimination. No such associations were observed among individuals with moderate or high social support.

Associations Between Discrimination and Gene Expression and Epigenetic Alterations

Eight studies examined associations between discrimination and molecular biomarkers of immune and stress-related processes, specifically gene expression and epigenetic alterations. Results consistently indicated that individuals who reported higher levels of discrimination exhibited gene expression patterns consistent with a shift toward greater pro-inflammatory gene expression and/or reduced antiviral gene expression. For instance, Kimani et al[35] found that high discrimination exposure was associated with increased expression of genes regulated by the pro-inflammatory transcription factor, nuclear factor kappa B (NF-κB), showing a 1.24-fold increase compared with those reporting lower discrimination ($p = .06$). Simultaneously, these individuals exhibited downregulation of genes regulated by the antiviral interferon regulatory factor (IRF) pathway (0.67-fold difference, $p = .02$). Thames et al[18] found that African American individuals exhibited greater activity of the pro-inflammatory transcription factors NF-κB and AP-1 compared with European Americans, and that racial discrimination accounted for over 50 percent of this group difference. Li et al[36] reported a 3.1-fold increase in CTRA gene expression

TABLE 2. Summary of Included Articles

References	Study Design	Sample Size	Population Characteristics	Discrimination Measure(s) Used	Sample Timeframe	Immune Health Outcome(s) Measured	Results	Covariates
Alley et al (2025)	Longitudinal	250	Young Black/African American, Hispanic/Latino, or multiracial/ethnic in the Healthy Young Men (HYM) cohort study who self-identify as sexual minority men (SMM)	6 items assessed homophobia 10 items assessed racial discrimination	June 2016 to July 2019	CTRA expression	Experienced homophobia and racism were unrelated to CTRA gene expression and did not interact with HIV status to predict differences in gene expression	Sociodemographic characteristics Substance use
Aronoff et al[41]	Cross-sectional	3,319	African American adults with cardiovascular disease in the tri-county area of Jackson, Mississippi	The Jackson Heart Study Discrimination Instrument, which includes the Everyday Discrimination Scale, Lifetime Discrimination Scale, and the Perceived Burden of Lifetime Discrimination	2000-2004	Leukocyte cell counts DNA methylation	High perceived burden from lifetime discrimination burden was significantly associated with higher neutrophils and a higher neutrophil-lymphocyte ratio (NLR). High lifetime discrimination was significantly associated with lower neutrophils and a lower NLR compared with low lifetime discrimination. High perceived burden was also associated with lower lymphocytes among older men; analyses suggest this is attributable to differences in CD4 T cells.	Sociodemographic characteristics Health behaviors
Bird et al (2023)	Longitudinal	94	Black trauma survivors indicating severe/near-death experiences or scoring at risk for PTSD	Perceived Ethnic Discrimination Questionnaire	March 2016 to October 2019	CTRA expression	For individuals exposed to higher levels of lifetime racial discrimination, CTRA significantly increased between timepoints 1 and 2. CTRA did not increase significantly over time in individuals exposed to lower levels of lifetime racial discrimination.	Sociodemographic characteristics Health behaviors Trauma-related variables (PTSD, mechanism of injury, lifetime trauma)
Bogart et al (2013)	Cross-sectional	197	Black and Latino men who have sex with men on antiretroviral therapy	Major Discrimination Scale Schedule of Racist Events (Black participants only) Perceived Ethnic Discrimination Questionnaire—Community Version (Latino participants only) Internalized Homophobia Scale–Revised AIDS-related Stigma Scale	January 2007 to February 2009	CD4 count HIV viral load AIDS-related symptomology	Black participants who experienced more racial discrimination exhibited lower CD4 T cell counts and higher HIV viral load. Black men who have sex with men who experienced higher racial discrimination were more likely to visit the emergency department in the last 6 mo.	Sociodemographic characteristics Health behaviors
Brown et al[23]	Cross-sectional	1,264	Non-Hispanic Black, Hispanic, and non-Hispanic White MESA study participants	6 items adapted from the Detroit Area Study Discrimination Scale were used to capture lifetime discrimination	April 2010 to February 2012	CTRA expression	In global analyses, major or lifetime discrimination and chronic burden were significantly associated with CTRA expression.	Sociodemographic characteristics

								No associations were significant in linear regression analyses after accounting for multiple testing. Using elastic net regression, a small percentage of gene expressions were associated with at least one social factor.	
Brown et al[37]	Cross-sectional	1,264	Non-Hispanic Black, Hispanic, and -non-Hispanic White adults from the Multi-Ethnic Study of Atherosclerosis (MESA)	6 items adapted from the Detroit Area Study Discrimination Scale were used to capture lifetime discrimination	2010 - 2011	Proinflammatory biomarkers	Discrimination was significantly, positively associated with the chronic inflammation gene set, inflammatory response, immune response, and regulation of inflammatory response. Elastic net regression identified CX3CR1, VNN1, and CHAMPI as associated with chronic inflammation in addition to more across other gene sets. Linear regression showed some associations, but none remained significant after false discovery rate correction.	Sociodemographic characteristics
Carroll et al (2022)	Longitudinal	1,755	Women who self-identify as Black, White, or Hispanic and are at 1-24 mo after the birth of their first child	Abbreviated 6-item Major Experiences of Discrimination Scale Everyday Discrimination Scale with 1 additional item added	2013-2017	Leukocyte telomere length	Higher reports of lifetime discrimination were associated with shorter telomere lengths. Everyday discrimination was slightly higher among White participants. White mothers attributed discrimination to gender, age, and body size rather than racial discrimination.	Sociodemographic characteristics Health behaviors
Chae et al (2014)	Cross-sectional	92	African American men 30-50 y old from the Bay Area Heart Health Study without serious or unstable disease	Implicit Association Test Experiences of Discrimination Scale	February to May 2010	Leukocyte telomere length	Higher racial discrimination and implicit bias were associated with shorter leukocyte telomere length. Having a higher household income-to-poverty ratio was associated with longer leukocyte telomere length.	Sociodemographic characteristics Health behaviors
Chae et al (2015)	Cross-sectional	92	African American men 30-50 y old from the Bay Area Heart Health Study without serious or unstable disease	Experiences of Discrimination Scale	February - May 2010	Leukocyte telomere length	No effects of racial discrimination or depressive symptoms on leukocyte telomere length were observed, but analyses suggest a significant interaction between racial discrimination and	Sociodemographic characteristics Health behaviors Social desirability

TABLE 2. (*continued*)

References	Study Design	Sample Size	Population Characteristics	Discrimination Measure(s) Used	Sample Timeframe	Immune Health Outcome(s) Measured	Results	Covariates
							depressive symptoms. Among those with lower levels of depressive symptomology, racial discrimination was associated with shorter leukocyte telomere length.	
Chae et al (2020)[29]	Longitudinal	391	African American adults around 40 y old at year 15, followed to year 25 (around 50 y old)	Experiences of Discrimination Scale	2000-2001, 2010-2011	Leukocyte telomere length	Racial discrimination and implicit racial bias were significantly associated with shorter leukocyte telomere length. Those with stronger anti-Black implicit bias reporting higher levels of racial discrimination had the shortest leukocyte telomere length. Household income-to-poverty ratio was associated with leukocyte telomere length.	Sociodemographic characteristics Health behaviors Depressive symptomology Social desirability Leukocyte telomere length at baseline
Chen et al[25]	*Study 1* Longitudinal *Study 2* Cross-sectional	*Study 1* 419 *Study 2* 201	*Study 1* African American adolescents (ages 19-20) *Study 2* Eighth graders of color	Schedule of Racist Events	*Study 1* 2009-2010 *Study 2* 2015, 2017, 2019	*Study 1* Proinflammatory biomarkers *Study 2*: In vitro studies of immune cell functions Monocyte cell counts Proinflammatory biomarkers	*Study 1* High discrimination was linked with increased soluble urokinase plasminogen activator receptor over time. Significant between-youth variation was found for both soluble urokinase plasminogen activator receptor and C-reactive protein. Study 2 Discrimination scores did not differ by race, ethnicity, or gender. Greater proinflammatory biomarker expression was observed in adolescent boys of color in terms of higher cytokine response to stimuli, lower sensitivity to anti-inflammatory agents, higher classical monocyte counts, and increased low-grade inflammation.	*Study 1* Sociodemographic characteristics Health behaviors *Study 2* Sociodemographic characteristics Health behaviors *Supplemental analyses* Anxiety symptomology. Depressive symptomology Perceived stress
Cuevas et al (2022)	Cross-sectional	543	MIDUS study participants from the Refresher Cohort	Everyday Discrimination Scale	2011-2014	CTRA expression	Racially minoritized men exhibited stronger associations between daily discrimination and heightened indicators of	Sociodemographic characteristics

								inflammation than white men. No evidence was found to suggest that daily discrimination was associated with proinflammatory gene expression in other subgroups.	
Flentje et al (2018)	Cross-sectional	38	Gay or bisexual individuals with HIV positive serostatus 18 y and older	Cultural Assessment of Risk for Suicide —Sexual Minority Stress Subscale	Not given	Leukocyte gene expression Proinflammatory biomarkers	Sexual minority stress was linked to the expression of genes related to inflammation, immune function, cancer risk, and cardiovascular function. Sexual minority stress was also linked with pathway perturbation of mechanisms related to immune health outcomes.	Sociodemographic characteristics Substance use Time since HIV diagnosis $CD4^+$ T cell count	
Gillespie and	Anderson (2018)		Longitudinal	91	Pregnant African American women recruited at 28-32 wk gestation from prenatal clinics	Experiences of Discrimination Scale	September 2013 to June 2015	Plasma cortisol Leukocyte sensitivity Cytokines Gestational age at birth	
Higher racial			discrimination was associated with lower leukocyte glucocorticoid sensitivity. Cortisol predicted early birth outcomes only in women with low to no reported discrimination.	Gestational age at blood draw Prepregnancy BMI					
Hailu et al (2019)	Cross-sectional	1,153	Participants free of clinical cardiovascular disease from the Multi-Ethnic Study of Atherosclerosis (MESA)	Everyday Discrimination Scale Major Experiences of Discrimination Scale	2000-2002	Leukocyte telomere length	No associations were found between leukocyte telomere length and discrimination. Among participants with low social support, moderate to high everyday discrimination was associated with shorter leukocyte telomere length.	Sociodemographic characteristics Health behaviors	
Hailu et al (2021)	Longitudinal	1,064	White, Black, or Hispanic participants with 2 waves of data from both study waves	Major Experiences of Discrimination Scale Everyday Discrimination Scale	2000-2002: Exam I 2010-2011: Exam V	Leukocyte telomere length	Major discrimination experiences from 2 or more domains were associated with faster telomere attrition over 10 years compared with no discrimination experiences. There were no associations found between Experiences of Discrimination scores and	Sociodemographic characteristics	

TABLE 2. (*continued*)

References	Study Design	Sample Size	Population Characteristics	Discrimination Measure(s) Used	Sample Timeframe	Immune Health Outcome(s) Measured	Results	Covariates
							neighborhood social cohesion.	
Harris et al (2025)	Cross-sectional	121	Black or White women with breast cancer	3 items from the Reaction to Race scale	February 2012 to September 2023	Tumor mutational burden Total RNA Serum immune oncologic markers	Higher discrimination exposure and neighborhood deprivation were associated with increased systemic inflammation and discrimination, dysfunctional local immune microenvironment profiles, and more aggressive tumor profiles.	Sociodemographic characteristics Health behaviors
Kelso et al (2014)	Cross-sectional	67	African American HIV+ women recruited from the CORE Center site of the Chicago Women's Interagency HIV Study (WIHS)	12 items each for racial discrimination and gender discrimination were adapted from the Detroit Area Study Discrimination Scale	Not given	CD4+ cell count	For those with higher levels of perceived racial discrimination, those with high critical consciousness had significantly larger CD4 T cell counts compared with those with low critical consciousness.	Sociodemographic characteristics Antiretroviral therapy adherence
Kimani et al[35]	Cross-sectional	20	Convenience sample of African Americans aged 18-50 y, fluent in English, born and raised in the U.S.	Everyday Discrimination Scale Race-based Traumatic Stress Symptom Scale Coping with Discrimination Scale	Not given	CTRA expression	Higher everyday discrimination was linked with poorer sleep, increased substance use, and lower resilience. Those reporting high everyday discrimination showed significantly greater proinflammatory gene expression and lower activity of antiviral control pathways compared with those reporting low everyday discrimination.	Sociodemographic characteristics
Klopack et al[27]	Cross-sectional	5,744	US adults from the Health and Retirement Study (HRS) 2016 Venous Blood Study (VBS)	Everyday Discrimination Scale 7 items on major stressful events related to discrimination throughout life	2014, 2016	T cell dysregulation	Experiencing life trauma and higher chronic stress were related to lower proportions of CD4 naïve T cells. Discrimination and chronic stress were associated with a greater proportion of terminally differentiated CD4 T cells. Stressful life events, high lifetime discrimination, and life trauma were linked with lower proportions of CD8 naïve cells. Stressful life events, high lifetime discrimination, and	Sociodemographic characteristics

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								chronic stress were associated with higher proportions of terminally differentiated CD8 T cells. High lifetime discrimination and chronic stress were associated with a lower CD4:CD8 ratio.	
Lee et al[32]	Cross-sectional	595	African American individuals from the Health and Retirement Study (HRS)	Major Experiences of Lifetime Discrimination Scale	2008	Leukocyte telomere length	High discrimination was associated with shorter leukocyte telomere length after controlling for sociodemographic factors.		Sociodemographic characteristics Health behaviors Psychological factors (depressive symptomology, stressful life events, lifetime traumas, daily hassles)
Li et al[36]	Cross-sectional	70	Black and Latino men who have sex with men from the MSM and Substances Cohort at UCLA Linking Infections Noting Effects (mSTUDY)	5 items assessing experiences of homophobic victimization, adapted from the National Health, Aging, and Sexuality/Gender Study	July 2014 to July 2018	CTRA expression	Homophobic victimization experiences were associated with increased CTRA gene expression. CTRA gene expression was significantly higher in those who identified as Black compared with those who identified as Latino.		Sociodemographic characteristics Health behaviors Substance use
Liu and Kawachi[11]	Cross-sectional	3,868	US-born non-Hispanic Black and non-Hispanic White adult participants from the 2008 Health and Retirement Study biomarker sample	Health and Retirement Study Everyday Discrimination Scale	2009	Leukocyte telomere length	Everyday discrimination was associated with shorter leukocyte telomere length among Black people, but not White people. No difference was found in telomere length for Black or White participants reporting major lifetime unfair treatment or everyday discrimination.		Sociodemographic characteristics
Lu et al[31]	Cross-sectional	997	African American women from the Black Women's Health Study (BWHS)	5 items adapted from the Everyday Discrimination Scale 3 items in the form of yes/no experiential questions on institutional racism	1997, 2009: Racism assessment 2013-2018: Telomere length assessment	Leukocyte telomere length Relative telomere length	Everyday racism was significantly associated with shorter telomere length in women who preferred not to discuss their experiences.		Sociodemographic characteristics Health behaviors Depressive symptomology Maternal age at participant's birth
Pacheco et al[39]	Cross-sectional	59	Participants from the Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) and NIA IRP (National Institute on Aging Intramural Research Program)	2 items adapted from the Major Experiences of Discrimination Scale 6 items in the form of yes/no experiential questions on racial discrimination	2004-2009	Peripheral blood mononuclear cell gene expression	High discrimination was associated with 28 differentially expressed genes in African American adults compared to White adults. African American women with high discrimination exposure exhibited significantly differential downregulation		Sociodemographic characteristics

TABLE 2. (*continued*)

References	Study Design	Sample Size	Population Characteristics	Discrimination Measure(s) Used	Sample Timeframe	Immune Health Outcome(s) Measured	Results	Covariates
							of immune response-related genes.	
Santos et al[38]	Longitudinal	147	Healthy Latina mothers living in North Carolina	Everyday Discrimination Scale	May 2016 to March 2017	DNA methylation	Discrimination was negatively associated across timepoints with methylation at CpG sites related to glucocorticoid receptor (NR3C1) and brain-derived neurotrophic factor (BDNF) genes. Discrimination was negatively associated with CpG methylation of a glucocorticoid binding protein CpG (FKBP5) at timepoint 1, but not at timepoint 2.	Sociodemographic characteristics Depressive symptomology
Sluiter et al[44]	Longitudinal	148	Latina women assessed at 24-32 wk gestation and 4-6 wk postpartum	Everyday Discrimination Scale	May 2016 to March 2017	DNA methylation	Discrimination was significantly associated with postpartum depression and anxiety among participants with higher methylation at FOXP3-TSDR and TNFα promoter regions. TNFα promoter methylation mediated the discrimination-distress relationship, but only in those with high FOXP3-TSDR methylation.	Sociodemographic characteristics Acculturation Acculturative stress Pregnancy-related depressive symptomology
Sullivan et al[30]	Cross-sectional	369	White and African American patients with coronary artery disease (CAD) in the Mental Stress Ischemia Mechanisms and Prognosis Study	Everyday Discrimination Scale	June 2011, August 2014	Leukocyte telomere length	Increased everyday discrimination was associated with shortened leukocyte telomere length among both African American and White women.	Sociodemographic characteristics Health behaviors Depressive symptomology Perceived stress
Szanton et al (2012)	Cross-sectional	629	African American and White adults whose red blood cells had been analyzed for heme degradation in the Healthy Aging in Neighborhoods of Diversity across the Life Span (HANDLS) study	1 item on perceived racial discrimination	September 2004 to July 2005	Red blood cell oxidative stress	Racial discrimination was significantly associated with higher red blood cell oxidative stress in African American participants.	Sociodemographic characteristics Health behaviors C-reactive protein levels
Thames et al[18]	Cross-sectional	71	Participants self-identified as African American/Black or European American/White living with HIV	Perceived Ethnic Discrimination Questionnaire	Not given	CTRA expression	Compared with European Americans, African Americans showed greater expression of genes related to proinflammatory and stress-signaling pathways. Over 50% of observed race-	Sociodemographic characteristics Health behaviors HIV-1 viral load

								related differences in proinflammatory transcription factor activity may be related to differing levels of racial discrimination. Proinflammatory and antiviral transcription pathway-related gene expression differed by HIV groups.	
Troxel et al (2023)	Cross-sectional	200	Participants from the THINK PHRESH study with stored blood from a previous assessment	Everyday Discrimination Scale	2017-2018	Leukocyte telomere length	Among those experiencing discrimination, higher air pollution ($PM_{2.5}$) was associated with shorter leukocyte telomere length.	Sociodemographic characteristics Health behaviors
Zhao et al[40]	Cross-sectional	1,151	Participants free of clinical cardiovascular disease from the Multi-Ethnic Study of Atherosclerosis (MESA), Exams I and V	Everyday Discrimination Scale Major Experience of Discrimination Scale	2000-2002: Discrimination assessment 2010-2013: Health assessment	DNA methylation	Perceived discrimination was associated with select CpGs as well as CpGs in specific differentially methylated regions for African American, Hispanic, and Trans-ancestry groups. Identified CpGs are linked with cellular development pathways, transcription factor binding, cancer, and multiple autoimmune and inflammatory diseases.	Sociodemographic characteristics Health behaviors Depressive symptomology

(a ratio of inflammatory gene expression to innate antiviral gene expression) among men who have sex with men who experienced homophobic victimization ($B = 1.63$, 95% CI = 0.26, 3.00; $p = .020$). This association remained significant after adjusting for the relative prevalence of major leukocyte subsets in the analyzed blood samples and sociodemographic factors.

Beyond targeted analyses of inflammatory and antiviral gene expression, a small body of research has begun to explore broader transcriptional and epigenetic alterations associated with discrimination exposure. In 2 studies using data from the Multi-Ethnic Study of Atherosclerosis, Brown and colleagues demonstrated that lifetime discrimination was significantly associated with gene sets involved in inflammation, immune regulation, and stress response.[37] In the other analysis,[23] discrimination was linked to the expression of 196 individual transcripts across a preidentified set of 1,854 genes relevant to disease and stress pathways. Santos et al,[38] for example, reported that perceived discrimination was negatively associated with DNA methylation at CpG sites 1 and 2 within the glucocorticoid receptor gene (*NR3C1*; RR = 0.85, 0.84; $p = .008$ and .004, respectively) and at CpG sites 6 and 7 of the brain-derived neurotrophic factor gene (*BDNF*; RR = 0.86, 0.92, $p = .004$ and .004, respectively) among Latina mothers, with these alterations persisting over time. In the same study, discrimination was also linked to reduced methylation at *FKBP5* (RR = 0.85, $p < .001$), a gene that encodes a glucocorticoid-binding protein, during late pregnancy. However, this association did not persist postpartum, suggesting possible time-dependent effects. In a separate transcriptomic study,[39] African American adults reporting discrimination displayed differential expression of immune-related genes when compared with White adults. Upregulated genes included *IGLV2-11, S100B, IGKV3-20*, and *IGKV4-1*, which are involved in immunoglobulin signaling. The most significantly downregulated genes, including *LUCAT1*, *THBS1*, and *ARPIN*, have been implicated in immune modulation and cancer-related pathways. Additional epigenetic studies have found that discrimination is associated with altered DNA methylation in genes such as *NDUFS5*, *AKIRIN1*, *NCF4*, and *ADSSL1*.[40] These genes play important roles in mitochondrial function, inflammatory signaling, and innate immune responses.[40] Taken together, these findings suggest that discrimination may influence immune cell gene regulation, contributing to long-term risk of immune-related diseases.[40]

Associations Between Discrimination and Immune Cell Composition

Five studies examined how discrimination influences immune cell distribution, with findings indicative of immune aging and senescence. For instance, Klopack et al[27] reported that exposure to chronic stress and lifetime discrimination was associated with greater numbers of terminally differentiated $CD4^+$ and $CD8^+$ T cells in circulating blood ($b = 0.068$, SE = 0.017, $p = .007$ and $b = 0.045$, SE = 0.022, $p = .044$, respectively). While lifestyle factors and cytomegalovirus seropositivity accounted for some of the variance in immune cell composition, the associations between discrimination and these terminally differentiated T cells remained significant after controlling for those effects. Aronoff et al[41] investigated innate immune markers and found that a higher perceived burden of lifetime discrimination, compared with none, was associated with elevated neutrophil counts ($\beta = 0.17$, 95% CI = 0.05, 0.30) and an increased neutrophil-to-lymphocyte ratio (NRL; $\beta = 0.16$, 95% CI = 0.03, 0.29). However, a seemingly paradoxical pattern emerged in which greater perceived burden of discrimination, compared with none, was associated with lower lymphocyte counts ($\beta = -0.28$, 95% CI = −0.52, −0.05), a finding the authors suggest may be driven by reductions in $CD4^+$ T cell levels.

DISCUSSION

This systematic review finds evidence that experiences of discrimination are associated with multiple alterations in immune cell biology, including leukocyte telomere erosion, systematic alterations in leukocyte gene regulation, and immune cell composition. Collectively, these effects are consistent with accelerated immune aging, heightened inflammatory biology, and alterations in immune cell homeostasis that provide biologically plausible pathways through which experiences of discrimination might potentially elevate the risk of immune-mediated disease.

Shorter leukocyte telomeres are consistently associated with higher levels of discrimination exposure, particularly among Black individuals and women across racial and ethnic groups. These associations suggest that discrimination may contribute to accelerated cellular aging. While longitudinal analyses further show that cumulative exposure or domain-specific forms of discrimination predict telomere shortening over time, some studies report null findings after adjusting for covariates. As previous reviews have pointed out,[21,42] the inconsistency in longitudinal studies may reflect differences in study design, sample size, and the timing or measurement of both exposure and outcome.

Converging evidence from gene expression studies suggests that discrimination is also associated with alterations in immune cell gene regulation and transcriptional profiles.[19,39,43] Multiple studies reported elevated expression of proinflammatory genes and reduced expression of antiviral genes in association with discrimination exposure, aligning with the CTRA framework. Recent studies employing epigenome-wide analyses have also revealing altered methylation patterns at several immune- and stress-related loci, including *NR3C1, FKBP5, FOXP3,* and *BDNF*.[38,44] Such findings underscore the possibility that discrimination influences a broad array of genes and may produce diverse patterns of transcriptional alteration. Future analyses in large samples capable of supporting well-powered exploratory/discovery analyses at the genome-wide level will be a key step

in providing a more comprehensive understanding of how discrimination affects leukocyte function and cellular immune regulation.

In addition to these molecular changes at the genetic, epigenetic, and transcriptomic level, discrimination exposure may also change immune cell populations in ways that either modify immune function (eg, as a result of stress biology) or reflect differences in microbial exposures (eg, driving differences in immune cell maturation and aging/senescence). For example, Klopack et al[27] found that lifetime discrimination was associated with increased percentages of terminally differentiated T cells, which may reflect accelerated immunosenescence. This terminal differentiation may arise from telomere shortening, as T cells with critically short telomeres stop dividing and become senescent.[45] Aronoff et al[41] reported associations between high perceived burden from lifetime discrimination and increased neutrophil counts and neutrophil-to-lymphocyte ratios, suggesting heightened inflammatory activation. Furthermore, Chen et al[46] observed elevated counts of classical monocytes among adolescents reporting high levels of everyday discrimination, suggesting increased myelopoiesis and inflammatory mobilization. Together, these studies point to the possibility that discrimination may simultaneously alter gene expression profiles and reshape the circulating leukocyte population structure, contributing to long-term immune dysregulation.

Overall, this body of evidence supports the hypothesis that discrimination may initiate and sustain chronic immune dysregulation through cellular mechanisms. However, advancing this area of research requires addressing several key challenges, including the need for more longitudinal study designs, broader and more systematic examination of immune cell types, improved sample diversity, and more rigorous assessment of both biological and behavioral pathways. Also critical will be studies that document the functional impacts of these observed cellular and molecular changes (eg, quantifying impacts on immune effector functions such as cytotoxic activity, antibody production, etc.) as well as their implications for health (eg, are the observed cellular and molecular alterations associated with differential disease vulnerability in ways that might account for the association between discrimination exposure and health?).

Experimental and Longitudinal Designs Are Critically Needed

Perhaps one of the most pressing limitations across studies is the predominance of cross-sectional designs. Experimental approaches can help more strongly establish the relationship between discrimination and immune function. For instance, Lucas et al[47] found that participants reporting high perceived discrimination exhibited elevated C-reactive protein levels during recovery (60 minutes after participants were exposed to acute psychosocial stress). Similar experimental assessments could be applied to cellular immune outcomes, although markers of interest, such as changes in gene expression, may take longer to be detected. In these cases, longitudinal designs are particularly valuable, as they allow researchers to observe associations between discrimination and markers of immunological aging over time and at the population level. Without such data, it is difficult to determine whether discrimination precedes biological changes, whether biological changes might potentially affect experiences of discrimination (either by changing health outcomes or potentially impacting social perception through cytokine effects on the brain) or whether both coevolve over time. In addition, longitudinal assessments may help resolve inconsistent findings by accounting for baseline biological profiles and controlling for time-varying confounders. Within these designs, it is important to carefully consider the inclusion of other psychosocial stressors, such as financial strain or relationship difficulties, which often co-occur with discrimination.[48] It is thus imperative to include other stressors in the model to better characterize the independent effects of discrimination on the outcomes. While adjusting for these factors can clarify the independent effects of discrimination, overadjustment may also occur if some stressors lie on the causal pathway linking discrimination to immunological aging outcomes. Klopack et al,[27] for instance, tested 5 well-established, health-relevant measures of social stress simultaneously: stressful life events, chronic stress, everyday discrimination, lifetime discrimination, and life trauma. Among these stressors, lifetime discrimination and chronic stress were associated with CD4 and CD8 T cells, but everyday discrimination was not. It is plausible, however, that everyday discrimination may operate indirectly through some of these other stressors. Prospective multi-wave studies that assess cumulative effects and carefully model these pathways are particularly valuable, as they permit evaluation of theoretical frameworks that conceptualize chronic or repeated discrimination as a driver of biological wear and tear.

Accounting for Biological and Health Behaviors

Accurately characterizing the relationship between discrimination and immune outcomes requires attention to potential mediating and moderating pathways. The interplay between immune cells, gene regulation, protein-level inflammatory markers, and stress hormones is both complex and bidirectional, reflecting dynamic feedback mechanisms across biological systems involved in stress and immune regulation.[49] For instance, while alterations in gene expression and shifts in immune cell composition can precede and drive elevated production of pro-inflammatory proteins such as cytokines, it is equally well-established that circulating inflammatory proteins and stress hormones can directly influence gene transcription and immune cell differentiation through various signaling mechanisms.[50–54] Inflammation and stress hormones can also influence behavior and mood in ways that further affect immune functioning. For example, sustained elevations in pro-inflammatory cytokines, such as TNF alpha, IL-1 beta, and IL-6, not only drive systemic inflammation but also impact neurobiological processes,

contributing to changes in moods, behaviors, social perception, and risk for psychiatric and neurodegenerative conditions.[55–57] These psychobiological changes may function as mediators, shaped by discrimination and, in turn, influencing immune and cellular health. Alternatively, they may act as moderators or confounders, simultaneously affecting both the experience of discrimination and the physiological response to it.[3,58,59] For instance, high sugar and unhealthy fats can promote a pro-inflammatory gut microbiome, leading to systemic inflammation.[60,61] In turn, inflammation has been shown to affect neural circuits involved in threat processing, potentially heightening perceptions of discrimination.[62–65] Without careful theoretical and statistical attention to these factors, research may obscure or misrepresent the relationship between discrimination and cellular health. To move the field forward, future studies should clearly articulate the role of physiological markers and health behaviors, whether as confounders, mediators, or effect modifiers, and structure analytic models accordingly.

Broadening Cellular Scope

The CTRA framework has provided one foundational hypothesis for analyzing how discrimination and other social experiences "get under the skin" to influence immune function and health outcomes. However, there are likely a wide variety of other biological pathways and neuro-immune interactions through which discrimination may affect immune function, and mapping these pathways remains an important topic for future research. As Pacheco et al[39] note, the CTRA represents a relatively general transcriptional response to multiple forms of social stress, including low socioeconomic status and social isolation, and it is possible that transcriptome-wide analytic approaches may yield novel insights into gene pathways that are more uniquely implicated in the biology of discrimination (ie, relatively specific responses to discrimination as opposed to other forms of social stress). Broader strategies, such as unbiased differential gene expression analyses, pathway enrichment methods, and network-based modeling may enable the identification of novel molecular targets and clarify which transcriptional processes most directly reflect stress responses linked to discrimination. Such genome-wide exploratory/discovery analyses require much larger sample sizes than have been available so far to yield statistically reliable findings (due to the need to correct for multiple hypothesis testing across $>20{,}000$ gene transcripts), underscoring the need for much larger and more representative study samples. Relative to analyses of immune cell gene expression, research linking discrimination to immune cell composition remains comparatively limited. Existing studies have primarily focused on monocytes and lymphocytes and their subsets.[25,27,41] However, expanding this focus to include a wider range of immune cells is essential for capturing the full scope of biological responses to psychosocial stress. For instance, dendritic cells and natural killer cells are key players in antigen presentation and innate immune defense, and may be particularly responsive to chronic social stressors.[19,66–68] Future studies should adopt more inclusive immune phenotyping strategies, such as expanded flow cytometry panels, to capture a comprehensive picture of how discrimination shapes immune cell abundance and composition. Such work would also clarify whether observed shifts reflect immunosenescence or other dysregulatory processes.

Improving Sample Representativeness and Inclusion

The generalizability and representativeness of most studies linking discrimination to immune cell biology remain limited due to small sample sizes. These methodological issues raise concerns about whether findings can be generalizable to the population. Compounding this limitation are differences in sample composition, particularly clinical status and recruitment methods, likely shape who participates in studies and thus the patterns that are observed. For example, people living with HIV often experience high levels of stigma-related discrimination, which may amplify or operate differently from other forms of discrimination, and at the same time HIV infection directly alters immune cell profiles and accelerates immune aging. These overlapping social and biological processes make it difficult to disentangle whether associations reflect the unique effects of discrimination, the consequences of the disease, or their interaction. Similarly, convenience samples drawn from specific institutions or geographic areas may overrepresent individuals with particular life histories, stress exposures, or health conditions, thereby limiting the generalizability of results. To address these limitations, future studies should adopt sampling frameworks that support nationally representative conclusions. This approach would enable more rigorous hypothesis testing in large-scale studies that already collect genomic and biomarker data, such as Midlife in the United States, the Health and Retirement Study, the National Longitudinal Study of Adolescent to Adult Health (Add Health), and the Jackson Heart Study. Another persistent limitation is the lack of diversity in study populations. Most research has focused on Black and White Americans, which is a result of both the centrality of anti-Black discrimination in the literature and the frequent use of White participants as a comparison group. However, other racialized groups, including Hispanic and Latino, Asian American, Native American, and multiracial populations, also report frequent experiences of discrimination and remain underexamined in this area of research.[69] Discrimination can also accrue to a wide variety of other social dimensions beyond racial or ethnic identity, including sexual, cultural, economic, and educational status. To better understand the biological consequences of discrimination across the full spectrum of U.S. populations, future studies should prioritize the inclusion of underrepresented and historically marginalized populations and conduct analyses that consider how exposure to discrimination is patterned across social identities.

Measuring Discrimination in Immunological Aging Studies

The vast majority of studies used the Everyday Discrimination Scale, which captures recurrent day-to-day indignities, and most of these studies focused on general discrimination or discrimination attributed to race. Although race-based and general attributions of discrimination tend to demonstrate similar associations with health outcomes, it remains unclear whether these patterns extend to markers of immunological aging. Relatively little is known about the effects of other forms of discrimination, such as sexism or classism. For instance, one study found that experiences of homophobia were associated with pro-inflammatory gene expression, yet the extent to which different forms of discrimination influence immunological aging, vary across social groups, or accumulate over time remains poorly understood. The Everyday Discrimination Scale is the most commonly used measure in the broader discrimination literature and is likewise dominant in research on immunological aging. This reliance is partly grounded in the idea that everyday discrimination exerts stronger health effects than acute, major experiences of discrimination. However, it remains uncertain whether this distinction applies to immunological aging. Greater use of diverse and theoretically grounded measures will be essential for comprehensively evaluating the immunological effects of discrimination.

CONCLUSIONS

As research on discrimination and biological health continues to grow, there is increasing interest in understanding how discrimination shapes cellular processes. The evidence reviewed here in the context of the immune system points to telomere shortening, altered gene expression, and changes in immune cell composition as key ways discrimination may potentially influence immune cell function and thus potentially contribute to differences in disease risk and social epidemiology. It is important to note, however, that potential publication bias may affect these conclusions, as studies reporting null results could be underrepresented in the literature. These findings thus far underscore the relevance of discrimination as a social stressor with consequences for cellular immune regulation and aging. At the same time, major limitations remain. Much of the existing research relies on cross-sectional data, focuses narrowly on select genes or immune cells, and draws from samples that lack racial/ethnic diversity. Implications for immunological aging remain poorly understood (eg, are the observed cellular and molecular alterations sufficient to impact disease incidence or antimicrobial resistance?) and much remains to be understood about the neural or endocrine pathways that may mediate the effects of discrimination experience on immune cell biology (eg, at the level of the brain's threat response systems or peripheral distribution pathways such as SNS and HPA axis). Most existing research in this area is correlational and highly vulnerable to confounding, raising the importance of intervention research for not only addressing scientific questions regarding causal pathways but also delivering clinically impactful solutions for protecting people against the detrimental health effects of discrimination. Addressing these methodological and conceptual gaps through longitudinal designs, controlled experiments, clearer modeling of behavioral and physiological pathways, expansion of cellular markers and immunologic measures, and more representative sampling will be essential for generating a more complete understanding of how discrimination affects cellular aspects of immunological aging and their role in overall biological health.

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REFERENCES

1. Ellis JL, Woehrle L, Millon-Underwood S, Davidson D, Mkandawire-Valhmu L, Shah P, et al. The effect of racism and discrimination on the health of Milwaukee's African American Population. *WMJ*. 2022;121:132–144.
2. Bailey ZD, Krieger N, Agénor M, Graves J, Linos N, Bassett MT. Structural racism and health inequities in the USA: evidence and interventions. *Lancet*. 2017;389:1453–1463.
3. Williams DR, Lawrence JA, Davis BA, Vu C. Understanding how discrimination can affect health. *Health Serv Res*. 2019;54(suppl 2): 1374–1388.
4. Lewis TT, Cogburn CD, Williams DR. Self-reported experiences of discrimination and health: scientific advances, ongoing controversies, and emerging issues. *Annu Rev Clin Psychol*. 2015;11:407–440.
5. Pascoe EA, Smart Richman L. Perceived discrimination and health: a meta-analytic review. *Psychol Bull*. 2009;135:531.
6. Williams DR, Yu null Y, Jackson JS, Anderson NB. Racial differences in physical and mental health: socio-economic status, stress and discrimination. *J Health Psychol*. 1997;2:335–351.
7. Geronimus AT, Hicken M, Keene D, Bound J. "Weathering" and age patterns of allostatic load scores among Blacks and Whites in the United States. *Am J Public Health*. 2006;96:826–833.
8. Rodriquez EJ, Kim EN, Sumner AE, Nápoles AM, Pérez-Stable EJ. Allostatic load: importance, markers, and score determination in minority and disparity populations. *J Urban Health*. 2019;96(suppl 1):3–11.
9. Miller HN, LaFave S, Marineau L, Stephens J, Thorpe RJ. The impact of discrimination on allostatic load in adults: an integrative review of literature. *J Psychosom Res*. 2021;146:110434.
10. Chae DH, Epel ES, Nuru-Jeter AM, Lincoln KD, Taylor RJ, Lin J, et al. Discrimination, mental health, and leukocyte telomere length among African American men. *Psychoneuroendocrinology*. 2016;63: 10–16.
11. Liu SY, Kawachi I. Discrimination and telomere length among older adults in the United States: does the association vary by race and type of discrimination? *Public Health Rep*. 2017;132:220–230.
12. Rej PH, HEAT Steering Committee, Gravlee CC, Mulligan CJ. Shortened telomere length is associated with unfair treatment attributed to race in African Americans living in Tallahassee, Florida. *Am J Hum Biol*. 2020;32:e23375.
13. López-Otín C, Blasco MA, Partridge L, Serrano M, Kroemer G. The hallmarks of aging. *Cell*. 2013;153:1194–1217.
14. Blackburn EH. Telomere states and cell fates. *Nature*. 2000;408: 53–56.
15. Geronimus AT, Pearson JA, Linnenbringer E, Schulz AJ, Reyes AG, Epel ES, et al. Race/ethnicity, poverty, urban stressors and telomere length in a Detroit community-based sample. *J Health Soc Behav*. 2015;56:199–224.
16. Epel ES, Blackburn EH, Lin J, Dhabhar FS, Adler NE, Morrow

JD, et al. Accelerated telomere shortening in response to life stress. *Proc Natl Acad Sci*. 2004;101:17312–17315.
17. Geronimus AT, Hicken MT, Pearson JA, Seashols SJ, Brown KL, Cruz TD. Do US black women experience stress-related accelerated biological aging? *Hum Nat*. 2010;21:19–38.
18. Thames AD, Irwin MR, Breen EC, Cole SW. Experienced discrimination and racial differences in leukocyte gene expression. *Psychoneuroendocrinology*. 2019;106:277–283.
19. Cole SW. The conserved transcriptional response to adversity. *Curr Opin Behav Sci*. 2019;28:31–37.
20. Rentscher KE, Carroll JE, Mitchell C. Psychosocial stressors and telomere length: a current review of the science. *Annu Rev Public Health*. 2020;41:223–245.
21. Coimbra BM, Carvalho CM, Ota VK, Vieira-Fonseca T, Bugiga A, Mello AF, et al. A systematic review on the effects of social discrimination on telomere length. *Psychoneuroendocrinology*. 2020; 120:104766.
22. Cole SW. Human social genomics. *PLoS Genet*. 2014;10:e1004601.
23. Brown KM, Diez-Roux AV, Smith JA, Needham BL, Mukherjee B, Ware EB, et al. Expression of socially sensitive genes: the multi-ethnic study of atherosclerosis. *PLoS ONE*. 2019;14:e0214061.
24. Cuevas AG, Freilich CD, Mann FD, Cole SW, Krueger RF. Intersectional vulnerability in the relationship between discrimination and inflammatory gene expression. *Brain Behav Immun Health*. 2023;27:100580.
25. Chen E, Yu T, Brody GH, Lam PH, Goosby BJ, Miller GE. Discrimination and inflammation in adolescents of color. *Biol Psychiatry Glob Open Sci*. 2022;3:204–212.
26. Miller GE, Cohen S, Ritchey AK. Chronic psychological stress and the regulation of pro-inflammatory cytokines: a glucocorticoid-resistance model. *Health Psychol*. 2002;21:531–541.
27. Klopack ET, Crimmins EM, Cole SW, Seeman TE, Carroll JE. Social stressors associated with age-related T lymphocyte percentages in older US adults: evidence from the US Health and Retirement Study. *Proc Natl Acad Sci*. 2022;119:e2202780119.
28. Krieger N. Racial and gender discrimination: risk factors for high blood pressure? *Soc Sci Med*. 1990;30:1273–1281.
29. Chae DH, Wang Y, Martz CD, Slopen N, Yip T, Adler NE, et al. Racial discrimination and telomere shortening among African Americans: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Health Psychol*. 2020;39:209.
30. Sullivan S, Hammadah M, Al Mheid I, Shah A, Sun YV, Kutner M, et al. An investigation of racial/ethnic and sex differences in the association between experiences of everyday discrimination and leukocyte telomere length among patients with coronary artery disease. *Psychoneuroendocrinology*. 2019;106:122–128.
31. Lu D, Palmer JR, Rosenberg L, Shields AE, Orr EH, DeVivo I, et al. Perceived racism in relation to telomere length among African American women in the Black Women's Health Study. *Ann Epidemiol*. 2019;36:33–39.
32. Lee DB, Kim ES, Neblett EW Jr. The link between discrimination and telomere length in African American adults. *Health Psychol*. 2017;36:458.
33. Hailu EM, Lewis TT, Needham BL, Lin J, Seeman TE, Mujahid MS. Longitudinal associations between discrimination, neighborhood social cohesion, and telomere length: the multi-ethnic study of atherosclerosis. *J Gerontol A*. 2022;77:365–374.
34. Hailu EM, Needham BL, Lewis TT, Lin J, Seeman TE, Roux AD, et al. Discrimination, social support, and telomere length: the Multi-Ethnic Study of Atherosclerosis (MESA). *Ann Epidemiol*. 2020;42:58–63.
35. Kimani RW, Tobin JN, Cole SW, Campbell A, Jarvis ED. Biomarkers of racism-based stress injury: a feasibility and correlation study. *J Clin Transl Sci*. 2024;9:e23.
36. Li MJ, Takada S, Okafor CN, Gorbach PM, Shoptaw SJ, Cole SW. Experienced homophobia and gene expression alterations in Black and Latino men who have sex with men in Los Angeles County. *Brain Behav Immun*. 2020;83:120–125.
37. Brown KM, Diez-Roux AV, Smith JA, Needham BL, Mukherjee B, Ware EB, et al. Social regulation of inflammation related gene expression in the multi-ethnic study of atherosclerosis. *Psychoneuroendocrinology*. 2020;117:104654.
38. Santos HP, Nephew BC, Bhattacharya A, Tan X, Smith L, Alyamani RAS, et al. Discrimination exposure and DNA methylation of stress-related genes in Latina mothers. *Psychoneuroendocrinology*. 2018;98:131–138.
39. Pacheco NL, Noren Hooten N, Wu SF, Mensah-Bonsu M, Zhang Y, Chitrala KN, et al. Genome-wide transcriptome differences associated with perceived discrimination in an urban, community-dwelling middle-aged cohort. *FASEB J*. 2025;39:e70366.
40. Zhao W, Lin L, Kelly KM, Opsasnick LA, Needham BL, Liu Y, et al. Epigenome-wide association study of perceived discrimination in the Multi-Ethnic Study of Atherosclerosis (MESA). *Epigenetics*. 2025;20:2445447.
41. Aronoff JE, Quinn EB, Forde AT, Glover LM, Reiner A, McDade TW, et al. Associations between perceived discrimination and immune cell composition in the Jackson Heart Study. *Brain Behav Immun*. 2022;103:28–36.
42. Lawrence JA, Kawachi I, White K, Bassett MT, Priest N, Masunga JG, et al. A systematic review and meta-analysis of the Everyday Discrimination Scale and biomarker outcomes. *Psychoneuroendocrinology*. 2022;142:105772.
43. Bird CM, Kate Webb E, Cole SW, Tomas CW, Knight JM, Timmer-Murillo SC, et al. Experiences of racial discrimination and adverse gene expression among black individuals in a level 1 trauma center sample. *Brain Behav Immun*. 2024;116:229–236.
44. Sluiter F, Incollingo Rodriguez AC, Nephew BC, Cali R, Murgatroyd C, Santos HP. Pregnancy associated epigenetic markers of inflammation predict depression and anxiety symptoms in response to discrimination. *Neurobiol Stress*. 2020;13:100273.
45. Shay JW, Wright WE. Hayflick, his limit, and cellular ageing. *Nat Rev Mol Cell Biol*. 2000;1:72–76.
46. Chen E, Yu T, Brody GH, Lam PH, Goosby BJ, Miller GE. Discrimination and inflammation in adolescents of color. *Biol Psychiatry Glob Open Sci*. 2023;3:204–212.
47. Lucas T, Wegner R, Pierce J, Lumley MA, Laurent HK, Granger DA. Perceived discrimination, racial identity, and multisystem stress response to social evaluative threat among African American men and women. *Psychosom Med*. 2017;79:293–305.
48. Sternthal MJ, Slopen N, Williams DR. Racial disparities in health: how much does stress really matter? *Du Bois Rev*. 2011;8:95–113.
49. Goosby BJ, Cheadle JE. The immune system is a complex system: inflammatory morbidity and systemic racism. *Köln Z Soziol*. 2024; 76:713–744.
50. Franchimont D. Overview of the actions of glucocorticoids on the immune response: a good model to characterize new pathways of immunosuppression for new treatment strategies. *Ann N Y Acad Sci*. 2004;1024:124–137.
51. Yurtsever T, Streit F, Foo JC, Trifonova S, Kumsta R, Muller CP, et al. Temporal dynamics of cortisol-associated changes in mRNA expression of glucocorticoid responsive genes *FKBP5*, *GILZ*, *SDPR, PER1, PER2* and *PER3* in healthy humans. *Psychoneuroendocrinology*. 2019;102:63–67.
52. Sproston NR, Ashworth JJ. Role of C-reactive protein at sites of inflammation and infection. *Front Immunol*. 2018;9:754. doi:10.3389/fimmu.2018.00754
53. Lepik K, Annilo T, Kukuškina V, Kisand K, Kutalik Z, Peterson P, et al. C-reactive protein upregulates the whole blood expression of CD59–an integrative analysis. *PLoS Comput Biol*. 2017;13:e1005766.
54. Wang Q, Zhu X, Xu Q, Ding X, Chen YE, Song Q. Effect of C-reactive protein on gene expression in vascular endothelial cells. *Am J Physiol Heart Circ Physiol*. 2005;288:H1539–H1545.
55. Kipnis J, Filiano AJ. The central nervous system: privileged by immune connections. *Nat Rev Immunol*. 2018;18:83–84.
56. Dantzer R, O'Connor JC, Freund GG, Johnson RW, Kelley KW. From inflammation to sickness and depression: when the immune system subjugates the brain. *Nat Rev Neurosci*. 2008;9:46–56.
57. Miller AH, Maletic V, Raison CL. Inflammation and its discontents: the role of cytokines in the pathophysiology of major depression. *Biol Psychiatry*. 2009;65:732–741.
58. Majeno A, Molina KM, Frisard CF, Lemon SC, Rosal MC. Discrimination and sleep: differential effects by type and coping strategy. *Ann Behav Med*. 2022;57:442–452.

59. Hisler GC, Brenner RE. Does sleep partially mediate the effect of everyday discrimination on future mental and physical health? *Soc Sci Med*. 2019;221:115–123.
60. Satokari R. High intake of sugar and the balance between pro- and anti-inflammatory gut bacteria. *Nutrients*. 2020;12:1348.
61. Mamun MAA, Rakib A, Mandal M, Singh UP. Impact of a high-fat diet on the gut microbiome: a comprehensive study of microbial and metabolite shifts during obesity. *Cells*. 2025;14:463.
62. Fani N, Carter SE, Harnett NG, Ressler KJ, Bradley B. Association of racial discrimination with neural response to threat in Black women in the US exposed to trauma. *JAMA Psychiatry*. 2021;78:1005–1012.
63. Webb EK, Bird CM, deRoon-Cassini TA, Weis CN, Huggins AA, Fitzgerald JM, et al. Racial discrimination and resting-state functional connectivity of salience network nodes in trauma-exposed black adults in the United States. *JAMA Netw Open*. 2022;5:e2144759.
64. McEwen BS. Physiology and neurobiology of stress and adaptation: central role of the brain. *Physiol Rev*. 2007;87:873–904.
65. Lockwood KG, Marsland AL, Matthews KA, Gianaros PJ. Perceived discrimination and cardiovascular health disparities: a multisystem review and health neuroscience perspective. Annals of the New York Academy of Sciences. 2018;1428; 170–207.
66. Capellino S, Claus M, Watzl C. Regulation of natural killer cell activity by glucocorticoids, serotonin, dopamine, and epinephrine. *Cell Mol Immunol*. 2020;17:705–711.
67. Wohleb ES, McKim DB, Sheridan JF, Godbout JP. Monocyte trafficking to the brain with stress and inflammation: a novel axis of immune-to-brain communication that influences mood and behavior. *Front Neurosci*. 2015;8:447.
68. Weber MD, Godbout JP, Sheridan JF. Repeated social defeat, neuroinflammation, and behavior: monocytes carry the signal. *Neuropsychopharmacol*. 2017;42:46–61.
69. National Public Radio (NPR). The Robert Wood Johnson Foundation, Harvard TH Chan School of Public Health. Discrimination in America: Final Summary. Published online 2018. https://content.sph.harvard.edu/wwwhsph/sites/94/2018/01/NPR-RWJF-HSPH-Discrimination-Final-Summary.pdf

