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Review

Systematic Review of High-Dimensional Omics in Mind-Body Medicine

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Abstract

The multi-dimensional measurement of complex biological systems and sub-systems is made possible by high-dimensional omics technologies. This frontier of research is promising for elucidating disease processes, physiological parameters, and therapeutic action mechanisms. Omics have potential merit for the integrative medicine field that is relatively early in terms of mechanistic research towards understanding the underlining therapeutic processes of mind-body interventions that show to affect multiple systems simultaneously. An inflammatory theory of disease has brought to light molecular and epidemiological evidence proposing that inflammation could be considered a unitary predictor across most disease typologies which may be treated as a central clinical entity. Relatively recent theorizations of disease have built upon epigenetic data showing that complex "interactomes", or disease networks where genetic factors that have downward chain effects on transcriptional, proteomic domains, dynamically modulate in response to environmental, microbial, and immunological domains. Thus, complex conditions underlined by interactive disease networks and dynamics essentially require complex multi-levelled interventions. This is particularly germane for complex patient cases often seen in the integrative medicine clinic. Mind-body

medicine may be part of such care programs that can be made accessible for all. To shed further light on the possibility of building the evidence base in integrative health towards this direction, we reviewed the current use of omics technologies in mind-body medicine within the last 5-years. Use of omics approaches within the field is still developing. Early findings appear to show beneficial impact upon genomic, transcriptional, and proteomic biomarkers across varied chronic inflammatory conditions, including disorders of the cardiovascular, central nervous, endocrine, immune, musculoskeletal, and respiratory, systems.

Keywords
Genomics; integrative medicine; meditation; metabolomics; mindfulness-based intervention; omics technology; proteomics; transcriptomics; yoga medicine

1. Introduction

1.1 Omics Technologies Offer Promising New Tools for Treatment Discovery in Mind-Body Medicine

High-dimensional biology refers to high-throughput techniques used in omics technologies that allow the multi-dimensional measurement of complex biological systems and sub-systems [1]. A basic premise is that biological systems are fundamentally too complex to be comprehensively understood using reductionist approaches [2] which decompose biological systems into the sum of their parts so to examine and test empirical 'silos'. Of course, this empirical paradigm can and has advanced components of biomedical sciences. Although such a reductionist approach aims to analyse biological systems in terms of simplistic models and causal frameworks that do not account for the multi-levelled dynamics of complex biological systems and homoestasis [2]. A more unified understanding of biological systems might best be understood as a whole, achieved via data from holistic approaches where no a-priori knowledge is established, and hypotheses can be generated from the findings. This approach is open ended and flexible to changing conceptual paradigms from actual data, opposed to hypothesis-driven or reductionist scientific approaches that aim to fit (maybe even force) data to pre-established (possibly biased and/or erroneous) casual chains and models. The pinnacle drive of omics methodologies is the holistic systems biology understanding of a given biological question [3]. The expansion of omics technologies is promising for elucidating disease processes, physiological parameters, and therapeutic action mechanisms. This has potential merit for the integrative medicine field that is relatively early in terms of mechanistic research towards understanding complex underlying therapeutic processes of mind-body interventions appearing to affect multiple systems simultaneously. To shed further light on the possibility of building the evidence base in integrative health towards this direction, we reviewed the current state of omics technologies in mind-body medicine.

1.2 Extant Purview of Mind-Body Medicine and Clinical Outcomes

Mind-body interventions are reported as effective for a vast range of clinical conditions [4-10] and are also successfully translating into technology-driven healthcare [11-14]. The

properties/structure of mind-body medicine also imply that they are meaningfully compatible with augmented reality/AR as telehealth develops into the future. Here, we focus on meditation or yoga practices as the main proponents of "mind-body" interventions that constitute evidence-based integrative medicine and whole person holistic care [15]. Disentangling the two modalities - meditation vs. yoga - in conjunction with integrative medicine however, is not a clear-cut process. Medical yoga focuses primarily on physical poses ('asanas'), although also incorporates breathing techniques, yogic diet/nutrition education, and mind components such as mindfulness meditation. Conversely, meditation such as mindfulness-based interventions incorporate some yogic exercises as part of 'mindful movement' practices. Here, we delineate the two with the aim to stratify meditation-based interventions as primarily 'mind' focused, and yoga-based interventions as primarily 'body' focused. This perspective aligns with a developmental-stage model of meditation classification [16], that suggests yoga facilitates neuro-visceral integration to prepare the body for advanced and stable mind practices (aka meditation). This review provides an initial step towards applying such a model when reviewing clinical outcomes of the meditation and yoga intervention evidence base.

1.2.1 Brief Overview of Mind Medicine: Meditation

Clinically, "third-" and "fourth-wave" interventions (that have built upon 1st-wave psychodynamics, and 2nd-wave cognitive-behavioral therapy), utilize focus, awareness, and value/virtue components often found in meditation-based traditions [17]. Mindfulness is the most widely used form of meditation in mind-body treatments programs, first introduced as Mindfulness-Based Stress Reduction (MBSR) in the 1970s [18]. Its prolific use may be due to secular accessibility and emphasis on non-judgmental awareness of present moment internal and external signals, rather than towards attaining specific states of mind. In clinical remits, mindfulness is now an umbrella term, encompassing various structured interventions that have built upon/around the original MBSR program, e.g. Mindfulness-Based Cognitive Therapy (MBCT) for depressive relapse [19], Mindfulness-Based Pain Management (MBPM) [20], Mindfulness-Based Cancer Recovery (MBCR) [21], Cognitively-Based Compassion Training (CBCT) [22], and so on. Mindfulness practices are often conflated with relaxation techniques, in part due to the marketing of copious (possibly superfluous) meditation apps available, albeit it must be clarified that the purpose of practicing mindfulness is not to attain relaxation, although relaxation may sometimes be an outcome. Mindfulness interventions show wide reaching efficacy, from stress reduction, protection from depressive relapse, managing depressogenic rumination, emotion regulation, executive function, and pain perception [10, 23-37]. A meta-analysis of randomized clinical trials for mindfulness-based interventions in 955 cancer patients showed significant improvement in mood, such as depression and anxiety [38]. Meta-analysis including 183 patients with Multiple Sclerosis highlighted significant clinical impact upon psychosocial outcomes, quality of life, anxiety, depression, and select physical symptoms including fatigue, pain, and vestibular symptoms [39]. A further systematic review including 13 studies in fibromyalgia, chronic fatigue, and irritable bowel syndrome demonstrated meaningful effect sizes (in cohen's d), compared with control conditions in reducing pain (d = -0.21), symptom severity (d = -0.40), depression (d = -0.23), and anxiety (d = -0.20) [40]. A review of 257 patients with neurological conditions such as stroke, traumatic-brain injury, and multiple sclerosis, reported moderate effect sizes (mean = 0.37) for mindfulness-based relief of fatigue [41].

Furthermore, mindfulness-based interventions are regarded as safe with no known serious adverse events reported in the literature. Systematic review of 36 randomized controlled trials involving 1231 participants, found that 8.3% of trials mentioned monitoring adverse effects, which is lower than the reported rate of 21% for psychological intervention trials for mental and behavioral disorders [42]. Specifically, reported events pertained to feelings of anger or anxiety during a pain-related trial, and other adverse events pertained to physical "soreness" and "a strained neck" [43].

Mechanistic research into mindfulness and meditation has received less attention compared with examining efficacy. A seminal longitudinal study reported that mindfulness-based intervention (vs. waitlist control) was associated with increased regional brain gray matter density [44], suggesting its working mechanism involved neuroplastic effects, although these findings have yet to be replicated. Moreover, a review of 20 randomized controlled trials comprising 1602 mixed patients, demonstrated promising effects of mindfulness-based interventions upon biomarkers of immune system activity. Findings included (i) reduction in the cellular transcription of Nuclear Factor kappa B (NF-kB), (ii) reduced circulating levels of blood-based C-reactive protein (CRP) a marker of inflammation, (iii) enhanced T lymphocyte cell counts (CD4+ T), and (iv) increased telomerase activity [45]. Further research has demonstrated that mindfulness meditation (compared to a relaxation condition) increases default mode network resting state functional brain activity with regions involved in top-down executive modulation (i.e. dorsolateral prefrontal cortex) that correlated with decreased circulating cytokinetic IL-6 (blood-based biomarker of systematic inflammation) at 4-month follow-up in a high stress (non-clinical) sample [46]. Collectively, data suggests that aside from the original clinical purpose for treating/managing stress and/or specific psychiatric symptoms (i.e. depression), mindfulness approaches appear to mediate specific neuro-immuno-endocrine biomarkers. Further work in these domains is warranted.

1.2.2 Brief Overview of Body Medicine: Yoga

Yoga is the most used alternative/integrative treatment modality in the United States [47]. There are numerous branches of yoga, each with varying paces, postures, breathing patterns, and/or emphasis on meditation. Here, we focus on studies primarily outlining Hatha yoga because it is the most practiced in the "West", usually comprising 45- to 90-minute sessions including breathwork (pranayama) and many different postures (asanas). Clinical outcomes associated with yoga-based interventions are compelling and wide-reaching. From improving general health, wellbeing, and quality of life; reducing depression, anxiety, chronic pain, cancer-related symptoms, and stress; supporting weight loss and smoking cessation; to managing chronic diseases, such as asthma, coronary artery disease, diabetes, hypertension, and multiple sclerosis [48-56]. However, it must be noted that the general quality of studies into yoga medicine have not always been rigorous. The connection between movement and breathing techniques is proposed to be highly significant since yoga provides the common benefits of traditional exercise with the addition of focused and deep breathing. These dynamics show to activate the parasympathetic branch of the autonomic nervous system and downregulate the sympathetic nervous system [47]. This may explain why yoga tends to promote feelings of relaxation and mitigate stress, the main explanation as to its far-reaching clinical benefits. In terms of safety, a cross-sectional survey including 1702 samples highlighted that one in five adult yoga users reported at least one acute adverse effect, and one in ten at least one chronic adverse effect [57]. These effects were mainly musculoskeletal associated with hand-,

shoulder-, and head-stands (that are advanced yoga techniques and not part of yoga medicine), and/or self-study yoga without supervision (that would not happen in structured yoga medicine). Minor adverse effects, such as faintness, dizziness, muscular pain, joint pain, runny nose and coughing were more likely to be reported by participants with chronic diseases in another survey examining 328 adult practitioners starting yoga for the first time [58]. Overall, yoga is considered safe with little risk of any significant adverse effects, particularly compared with other forms of body-based exercise.

The present mechanistic understanding of yoga medicine remains to be comprehensively researched. Data available does suggest beneficial impact upon inflammatory markers (see systematic review [14]) in 11 out of 15 studies, reported by the authors as "positive effects" although not necessarily statistically significant. Yoga interventions have also shown to modulate other biologic outcomes, such as reduction in basal cortisol and catecholamine secretion, low oxygen consumption as a measure of metabolic rate, and have modulatory effects on neurophysiology and neuromuscular respiratory function [55, 56, 59-61]. Such studies often involve small sample sizes, that may account for reduced statistical power. To note, higher doses of yoga (ascertained as >1000 min) have been associated with greater improvements in the inflammatory markers examined. Most of the studies included were older than 5 years, and the mind-body medicine field has continued to develop in terms of empirical trial designs, methodological rigor, and scientific reporting [62, 63]. Here, part of our aim is to ascertain mechanistic understanding and developments in yoga- and meditation-based interventions within the last ~5 years. In sum, mind-body interventions appear to have beneficial effects on a diverse range of symptoms, and it is not fully clear why this is the case.

1.3 Markers and Targets of Mind-Body Medicine Using Multi-Dimensional Biologics

An inflammatory theory of disease has brought to light molecular and epidemiological evidence showing that not only infectious diseases, but also non-infectious ones include significant inflammatory symptomatology [64]. This would suggest that inflammation could be considered a unitary predictor across many disease types which may be treated as a central entity. It might even be the explanation for the far-reaching clinical effects of mind-body medicine. Improving mechanistic understanding through this inflammatory lens, one has to consider that chronic inflammation does not always cause disease since there are additional genetic (that have downward chain effects on transcriptional, proteomic, metabolic domains) and environmental factors involved [64]. For example, worldwide epidemiological studies show associations between socio-economic status and a range of detrimental inflammatory health outcomes. The evidence even points to inflammatory response as socially patterned and mediated via discrete molecular levels [65], suggesting that those of lower socio-economic status within society require more targeted care/support for reducing inflammatory pathways that may cause increased expression of corresponding disease genes, transcription, and/or proteins, later in life. Such data highlights complex epigenetic processes. Moreover, recent theorizations also suggest that microbial and immunological factors are part of this complex disease matrix, constituting an "interactome" or disease network [66]. Thus, complex conditions underlined by interactive disease networks and dynamics essentially require complex multi-levelled interventions [1, 66]. Mind-body medicine may be part of such care programs made accessible to all. Examining the multi-levelled mechanistic

interplays connected to their wide clinical scope may also require sophisticated multi-dimensional and encompassing approaches to identify/measure the underlying complex therapeutic processes of mind-body interventions that appear to affect multiple systems simultaneously.

An apt approach to examine this line of inquiry is the use of multi-omics, or 'high-dimensional' approaches in systems biology that are underlined by universal, and potentially concurrent, detection of genes (genomics,) mRNA (transcriptomics), proteins (proteomics), and metabolites (metabolomics) [67]. Omics benefit the study and identification of disease genotypes, phenotypes, clinical trajectory, treatment discovery, and clinical efficacy assessment. Figure 1 (below) outlines the concurrent downstream progression of cellular process, omics applications, and the potential intermediary modifications from genotypic to phenotypic expression. We have not included metabolomic approaches/outcome measures in this review of the potential molecular mechanistic impact of mind-body interventions, because such markers represent aggregated biological endpoint/s culminated from various downstream permutations of cellular activity. One advantage is that since metabolomes are the final product of gene transcription, changes in metabolic markers are of greater magnitude compared with the other cellular points (genome, transcriptome, proteome), increasing their quantitative sensitivity. However, this is mitigated by the fact that the metabolome is the smallest domain (~5000 metabolites) [67] within -omes biology, containing a more diverse pool of molecules, and as such, are the most biologically and chemically complex markers in omics approaches. It would be difficult to disentangle at what point in the cellular chain a modification (or several) had ensued so to reflect in the final metabolomic marker. Initially, it seems reasonable to ascertain the mechanistic potential upon inflammatory outcomes and interplay with genetic, transcriptional, proteomic, molecular dynamics. Hence, this review focuses on genomic, transcription, and proteomic levels of investigation conducted thus far within mind-body medicine.

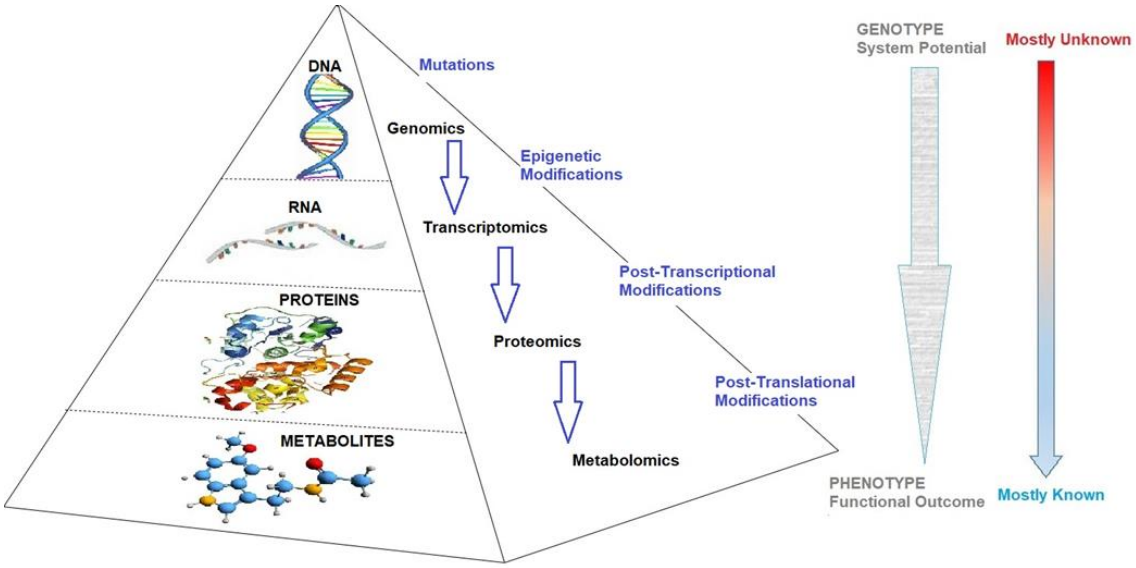


Figure 1 Downward stream of cellular processes and associated omics approaches.

1.4 The Present Review

The aforementioned findings suggest clinical efficacy and safety of mind-body interventions, yet the how/why for their successful clinical impact remains unclear and a highly salient domain of

empirical inquiry. We suggest that mind-body intervention approaches may mediate, adaptively regulate, and/or potentially 'reverse', specific molecular biomarkers associated with neuro-endocrine, immunologic, and neurological factors. A neuroplastic interventional effect may enact on the neuroimmune and neuroinflammatory systems as a whole, opposed to the sum of its parts. To contribute towards this line of investigation in moving the mind-body medicine field in this direction, we set out to systematically examine the following questions when looking at the evidence base: (1) Do mind-body interventions comprising mindfulness or yoga show mechanistic effects upon molecular markers of inflammation? (2) If yes, can these effects be delineated across genomic, transcription, and proteomic levels using high-dimensional biological techniques? and; (3) Can the reported findings be stratified by intervention programs primarily focused on the mind (meditation medicine) compared to the body (yoga medicine), since the two are often conflated? Because omics biology is a rapidly developing field, we examined data reported within the last 5-years.

2. Materials and Methods

2.1 Inclusion/Exclusion Criteria

Included articles were studies reporting original data investigating mind-body interventions in chronic inflammatory diseases and/or disorders shown to be associated within inflammatory pathways, i.e. psychiatric disorders such as depression [68]. Articles were included if published within the past 5 years. Intervention type comprised yoga-based and/or meditation-based intervention programs involving structured and consistent practices, very often incorporated within a psychoeducational format. Primary inclusion criteria were articles in English language, formal primary diagnosis of inflammatory disease, and primary outcome measures including one or more inflammatory markers ascertained from a preliminary code search: Interleukin-6 (IL-6), C-Reactive Protein (CRP), Tumor Necrosis Factor (TNF), telomerase activity, and Nuclear Factor kappa B (NF-kB). Reviews, meta-analyses, and dissertation reports were excluded.

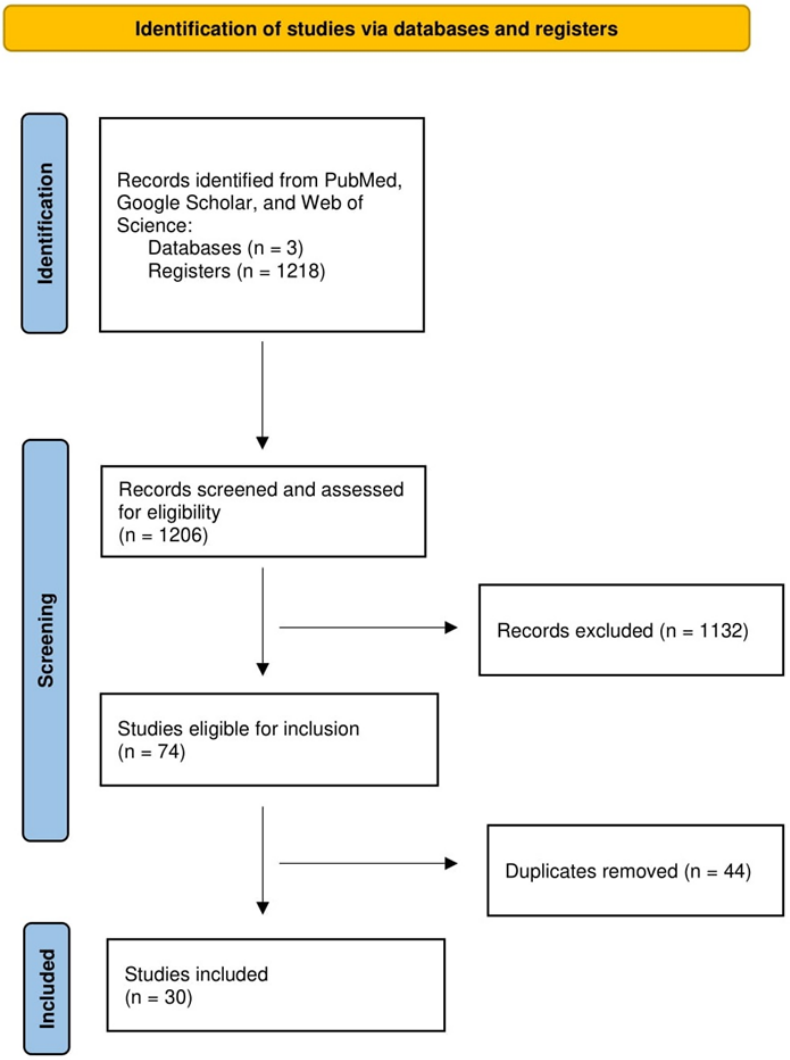
2.2 Quality Assessment

Articles were screened for the above criteria. If inclusion was met, studies were further assessed and deemed of sufficient quality if studies included ethical approval, and comprised a comparison control group, with or without randomization. Both passive control (no-treatment, waitlist) and active control (that were non -yoga or -meditation-based treatment) were included. Studies also needed to report statistical analyses comparing mean change in omics biomarkers (defined above). Either pre-post change, or post comparisons, were included. Studies that did not fulfil these additional quality criteria were excluded.

2.3 Search Strategy

Relevant studies were identified by searching PubMED, Web of Science (WoS), and google scholar; see Figure 2 for the review process. Only studies within the last 5-years were included. The key words "yoga", "mindfulness", "meditation", were searched with the following terms using the AND, function; "inflammation", "NF Kappa B", OR "nuclear factor kappa B", OR "transcript", OR "transcript s", OR "transcripted", OR "transcription, genetic", OR "genetic transcription", OR

"genome", OR "genomes", OR "genomically", OR "genomic", OR "genomics", OR "telomere", OR "telomeres", OR "telomeric". A supplementary google scholar search was conducted using the following terms "yoga intervention", OR "mindfulness intervention", with the AND function for the following terms; "inflammatory markers", OR "control trial" OR "controlled trial", OR "nuclear factor kappa b" OR "NF Kappa B".



Adapted From: Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ 2021;372:n71. doi: 10.1136/bmj.n71

Figure 2 PRISMA diagram: Study search and screening process [69].

3. Results

3.1 Overview of Included Studies

A total of 392 studies were identified with PubMED and Web of Science (WoS) using the above defined strategy. Of these, 51 met primary inclusion criteria and the quality assessment. A total of 826 studies were identified using Google Scholar, 23 of which met inclusion and quality assessment.

After duplicate removal, a total of 30 clinical studies were included in the final review. Tables 1-5 provide an overview of included studies.

Table 1 Genomics Yoga Intervention.

Authors	**Sample** **a) Participants** **b) N (sex)** **c) Age range (years)**	**Biomarkers**	**Design** **(a) Conditions** **(b) Randomized (Y/N)** **(c) Blind (single/double/not blinded)** **(d) Duration of yoga/MF intervention** **(e) Frequency of yoga/MF sessions** **(f) Duration of yoga/MF sessions (min)** **(g) Follow-up**	**Results**	**Biomarker Change?** **Key:** **o = no within-group change** **↓ = sig. within-group decrease (p < 0.05)** **↑ sig. within-group increase (p <0.05)** **• = no between-group change** **⇑ = sig. between-group increase (p < 0.05)** **⇓ = sig. between-group decrease (p < 0.05)**
Tolahunase et. al (2020) *, [70]	(a) **MDD** (b) 58 (31 F, 27 M) (c) 19-50	TA, TL, IL-6	(a) Yoga Based Lifestyle Intervention (n = 29) versus CG (n = 29) (b) Y (c) single (d) 12 weeks (e) 5×/week (f) 120 (g) No	sig. ↑ in TA within YBLI only and compared to CG no sig. change in TL within and between groups sig. ↓ in IL-6 within YBLI only and compared to CG	↑ TA ⇑ TA o TL • TL ↓ IL-6 ⇓ IL-6
Gautam et. al (2019) *, [71]	(a) **RA** (b) 72 (56 F, 16 M) (c) 18-60	TA, TL, IL-6, CRP, TNF-α	(a) YG with DMARDs (n = 36) versus UC (DMARDs only) CG (n = 36) (b) Y (c) single (d) 8 weeks (e) 5x/week (f) 120 (g) No	sig. ↓ in IL-6 within YG and compared to CG sig. ↓ in TNF-α within YG and compared to CG sig. ↑ in TA in within YG and compared to CG no sig. change in TL within or between groups sig. ↓ in CRP within YG and compared to CG	↓ IL-6 ⇓ IL-6 ↓ TNF-α ⇓ TNF-α ↑ TA ⇑ TA o TL • TL ↓ CRP ⇓ CRP

*study includes proteomic data

Two studies included genomic data from yoga interventions for participants with inflammatory disorders. 100% (n = 2) tested TA, TL, and IL-6. 50% (n = 1) tested CRP and TNF-α. The average sample size was n = 65. Inflammatory disorders included were MDD (n = 1) and RA (n = 1). 100% of the

studies showed positive improvements in TA (n = 2), TNF-α (n = 1), and CRP (n = 1), while 0% (n = 0) showed positive improvements in TL. 100% (n = 2) of the studies showed positive improvements in IL-6.

Table 2 Genomics Meditation Intervention.

Authors	**Sample** **a) Participants** **b) N (sex)** **c) Age range (years)**	**Biomarkers**	**Design** **(a) Conditions** **(b) Randomized (Y/N)** **(c) Blind (single/double/ not blinded)** **(d) Duration of yoga/MF intervention** **(e) Frequency of yoga/MF sessions** **(f) Duration of yoga/MF sessions (min)** **(g) Follow-up**	**Results**	**Biomarker Change?** **Key:** **o = no within-group change** **↓ = sig. within-group decrease (p <0.05)** **↑ sig. within-group increase (p <0.05)** **• = no between-group change** **⇑ = sig. between-group increase (p <0.05)** **⇓ = sig. between-group decrease (p <0.05)**
Mason et. al (2018) [72]	(a) **Obesity** (b) 162 (128 F, 34 M) (c) mean = 48.2	TL	(a) Weight loss program + MF (n = 87) versus weight loss program only CG (n = 74) (b) Y (c) double (d) 5.5 months (e) 1x/week for 12 weeks, 3 biweekly sessions, and 1 session 4 weeks later + at home practice (f) 120-150 (g) Yes; 6 and 12 months	no sig. change in TL between groups	• TL
Wang et. al (2017) [73]	(a) **Anxiety or stress, depression, and adjustment disorders** (b) 181 (159 F, 22 M) (c) 20-64	TL	(a) MBI (n = 88) versus UC (n = 89) (b) Y (c) single[74] (d) 8 weeks (e) 1x/week + at home practice (f) 120 (g) No	no sig. change in TL within or between groups	o TL • TL
Innes et. al (2019) [75]	(a) **Subjective cognitive decline** (b) 53 (46 F, 7 M) (c) 50-87	TL, TA	(a) Kirtan Kriya meditation (n = 25) or Music Listening group (n = 28) (b) Y (c) single (d) 12 weeks (e) daily (f) 12 (g) No	no sig. change in TA or TL within or between groups	o TL o TA • TL • TA

Of the included studies, three investigated genomic data from meditation interventions for participants with inflammatory disorders. 100% (n = 3) of the studies examined TL and 33.3% (n = 1)

of the studies included TA data. Inflammatory disorder included obesity (n = 1), anxiety or stress, depression and adjustment disorders (n = 1), and subject cognitive decline (n = 1). The average sample size was n = 132. 0% (n = 0) of the studies showed positive improvements in TL or TA.

Table 3 Transcription Meditation Intervention.

Authors	**Sample** **a) Participants** **b) N (sex)** **c) Age range (years)**	**Biomarkers**	**Design** **(a) Conditions** **(b) Randomized (Y/N)** **(c) Blind (single/double/not blinded)** **(d) Duration of yoga/MF intervention**	**(e) Frequency of yoga/MF sessions** **(f) Duration of yoga/MF sessions (min)** **(g) Follow-up**	**Results**	**Biomarker Change?** **Key:** **o = no within-group change** **↓ = sig. within-group decrease (p <0.05)** **↑ sig. within-group increase (p <0.05)** **• = no between-group change** **⇑ = sig. between-group increase (p <0.05)** **⇓ = sig. between-group decrease (p <0.05)**
Lee et. al (2019) * [76]	(a) **Type 2 diabetes and/or hypertension** (b) 18 (8 F, 10 M) (c) 57-87	NFKB2 RELA RELB (IL-1B included in this study although not part of our initial search criteria)	(a) Brain education-based meditation (n = 9) and health education (n = 9) (b) Y (c) not blinded (d) 8 weeks	(e) 2x/week (f) no data (g) No	sig. ↓ in NFKB2, RELA, IL-1B no sig. change in RELB	↓ NFKB2 ↓IL-1B • RELB
Mahendra et. al (2017) [77]	(a) **Chronic periodontitis** (b) 60 (c) 30-65	NF-κB	(a) Treatment + pranayama (n = 30) versus treatment only CG (n = 30) (b) Y (c) no data (d) 3 months	(e) daily (f) 20 (g) No	sig. ↓ in NF-kB within pranayama group only and between groups	↓ NF-kB ⇓ NF-kB

*study includes proteomic data

Two studies investigated transcription data from meditation interventions for participants with inflammatory disorders, including Type 2 diabetes and/or hypertension (n = 1), and chronic periodontitis (n = 1). The average sample size was n = 39. Of the studies, 50% (n = 1) investigated NF-κb, and 50% (n = 1) tested gene expression levels of NFKB2, RELA, and RELB. 100% (n = 1) of studies showed positive improvements in levels of NF-κB, RELA, and NFKB2.

Table 4 Proteomics Yoga Intervention.

Authors	**Sample** **a) Participants** **b) N (sex)** **c) Age range (years)**	**Biomarkers**	**Design** **(a) Conditions** **(b) Randomized (Y/N)** **(c) Blind (single/double/not blinded)** **(d) Duration of yoga/MF intervention** **(e) Frequency of yoga/MF sessions** **(f) Duration of yoga/MF sessions (min)** **(g) Follow-up**	**Results**	**Biomarker Change?** **Key:** **o = no within-group change** **↓ = sig. within-group decrease (p <0.05)** **↑ sig. within-group increase (p <0.05)** **• = no between-group change** **⇑ = sig. between-group increase (p <0.05)** **⇓ = sig. between-group decrease (p <0.05)**
Chanta et. al (2022) [78]	(a) **Allergic rhinitis** (b) 27 (21 F, 6 M) (c) 18-45	IL-6	(a) Hatha YG (n = 14) versus sedentary CG (n = 13) (b) Y (c) double (d) 8 weeks (e) 3x/week (f) 60 (g) No	no sig. change in IL-6 levels within or between groups	o IL-6 • IL-6
Awasthi et. al (2017) [79]	(a) **OA knee** (b) 120 (78 F, 42 M) (c) 40-60	IL-6	(a) Conventional treatment + YG (n = 60) versus conventional treatment only CG (n = 60) (b) Y (c) no data (d) 6 months (e) 5x/week (f) 45 (g) No	sig. ↓ in IL-6 within YG only	↓ IL-6
Kaminsky et. al (2017) [80]	(a) **COPD** (b) 46 (26 F, 20 M) (c) mean = 68	IL-6, CRP	(a) Yogic breathing + education (n = 21) versus education only CG (n = 22) (b) Y (c) double (d) 12 weeks (e) 2x/week for 1st 2 weeks + daily at home practice after 2 weeks (f) 60 (g) No	no sig. change in IL-6 or CRP within or between groups	o IL-6 • IL-6 o CRP • CRP
Fathollahi et. al (2020) [81]	(a) **Post-CABG surgery** (b) 19 M (c) 40-75	IL-6, hs-CRP	(a) Yoga-cardiac rehabilitation group (n = 10) versus cardiac rehabilitation group only (n = 9) (b) Y (c) no data (d) 8 weeks (e) 3x/week (f) 60 (g) No	no sig. change in IL-6 or hs-CRP between groups	• IL-6 • hs-CRP
Madhusmita et. al (2019) [82]	(a) Paraplegia (b) 54 (38 F, 16 M)	CRP	(a) Integrated yoga + physiotherapy (n (e) 75 (f) 6x/week (g) No	sig. ↓ in CRP within YG and	↓ CRP ⇓ CRP

	(c) 17-31 +		= 62) versus physiotherapy only CG (n = 62) (b) Y (c) single (d) 1 month		physiotherapy groups sig. ↓ in YG compared to physiotherapy	
Yadav et. al (2019) [83]	(a) **Met S** (b) 260 (177 F, 83 M) (c) 20-45	IL-6, TNF-α	(a) Yoga-based lifestyle intervention (n = 130) versus dietary intervention CG (n = 130) (b) Y (c) not blinded (d) 12 weeks	(e) daily (f) 120 (g) No	sig. ↓ in IL-6 within YG no sig. change in TNF-α within YG no sig. change in IL-6 or TNF-α between group	↓ IL-6 • IL-6 o TNF-α • TNF-α
Nugent et. al (2019) [84]	(a) **MDD** (b) 87 (73 F, 14 M) (c) mean = 45.20	IL-6, TNF-α, hs-CRP	(a) Hatha yoga (n = 48) versus health education (n = 39) (b) Y (c) single (d) 10 weeks	(e) 1x/week min, 2x/week + at home max (f) 80 (g) No	sig. ↓ in IL-6 for YG compared to HE no sig. change in TNF- α or hs-CRP between groups	⇓ IL-6 • hs-CRP • TNF-α
Harkess et. al (2016) *, [85]	(a) **Chronic stress** (b) 26 F (c) mean = 41.12	IL-6, CRP, TNF-α and DNA methylation of IL-6, CRP, TNF-α	(a) Yoga intervention (n = 11) versus wait-list CG (n = 15) (b) Y (c) no data (d) 8 weeks	(e) 2x/week (f) 60 (g) Yes; 1 month	no sig. change in IL-6, hs-CRP, or TNF-α between groups sig. ↓ in DNA methylation of *TNF-α* for YG compared to CG no sig. change in DNA methylation of *IL-6* or *hs-CRP* between groups	• IL-6 • TNF-α • hs-CRP
Gautam et. al (2020) *, [86]	(a) **RA** (b) 66 (53 F, 13 M) (c) 18-60	IL-6, TNF-α and mRNA expression levels of IL-6, TNF-α, and NFKB1	(a) Yoga-Based Lifestyle Intervention (n = 33) versus UC CG (n = 33) (b) Y (c) single (d) 8 weeks	(e) 5x/week (f) 120 (g) No	-sig. ↓ in IL-6 and TNF-α in YBLI vs. UC -sig. ↓ in regulation of mRNA expression levels of *IL-6* and *TNF-α* YBLI vs. UC -no sig. change in mRNA expression of *NFKB1*	⇓ IL-6 ⇓ TNF-α

Ganesan et. al (2020) [87]	(a) **RA** (b) 143 (131 F, 12 M) (c) 30-60	IL-6, TNF-α	(a) YG (n = 68) and CG (n = 75) (b) Y (c) no data (d) 12 weeks	(e) 3x/week (f) 30 (g) No	no sig. change in IL-6 or TNF-α between groups sig. ↓ in IL-6 and TNF-α within both YG and CG	↓ IL-6 • IL-6 ↓ TNF-α • TNF-α

*study includes transcription data

Of the included articles, 10 produced proteomic data for yoga interventions, with 50.0% (n = 5) of the studies including transcription data. The average sample size was n = 84.8, and the disorders investigated included allergic rhinitis (n = 1), OA knee (n = 1), COPD (n = 1), post-CABG surgery (n = 1), RA (n = 2), Met S (n = 1), MDD (n = 1), paraplegia (n = 1), and chronic stress (n = 1). 90.0% (n = 9) of the studies tested IL-6 and 50.0% (n = 5) tested CRP. 50.0% (n = 5) tested TNF-α and 10.0% (n = 1) investigated DNA methylation of IL-6 and TNF-α. Of the studies that investigated respective markers; 55.6% (n = 5) of the studies found positive effects in levels of IL-6, 20.0% (n = 1) in levels of CRP, and 60.0% (n = 3) in levels of TNF-α. Positive effects for DNA methylation of only TNF-α were found.

Table 5 Proteomics Meditation Intervention.

Authors	**Sample** **a) Participants** **b) N (sex)** **c) Age range (years)**	**Biomarkers**	**Design** **(a) Conditions** **(b) Randomized (Y/N)** **(c) Blind (single/double/ not blinded)** **(d) Duration of yoga/MF intervention**	**(e) Frequency of yoga/MF sessions** **(f) Duration of yoga/MF sessions (min)** **(g) Follow-up**	**Results**	**Biomarker Change?** **Key:** **o = no within-group change** **↓ = sig. within-group decrease (p <0.05)** **↑ sig. within-group increase (p <0.05)** **• = no between-group change** **⇑ = sig. between-group increase (p <0.05)** **⇓ = sig. between-group decrease (p <0.05)**
Grazzi et. al (2017) [88]	(a) **Chronic migraine with medication overuse** (b) 39 (c) 18-65	IL-6	a) MF (n = 20) versus medication CG (n = 19) b) N (c) not blinded (d) 6 weeks	(e) 1x/week + at home (f) 45 (g) Yes: 12 months	sig. ↓ in IL-6 for MF group compared to MA group at 12-month follow-up	⇓ IL-6
McClintock et. al (2019) [89]	(a) **Alcohol dependency** (b) 72 (26 F, 46 M) (c) mean = 43.4	IL-6	(a) MF-Based Relapse Prevention for Alcohol Dependence (n = 46) versus WL CG (n = 26)	(e) 1x/week + at home practice (f) 120 (g) Yes; 26 and 34 weeks	no sig. change in IL-6 within MF group	o IL-6

			(b) Y (c) not blinded (d) 8 weeks			
Memon et. al (2017) [90]	(a) **Mild to moderate depression and anxiety** (b) 166 (c) 20-64	hs-CRP	(a) MBI (n = 81) versus CBT (n = 85) (b) Y (c) single (d) 8 weeks	(e) 1x/week (f) 120 (g) No	no sig. change in hs-CRP within MF or CBT	o hs-CRP
Buijze et. al (2019) [91]	(a) **axSpA** (b) 24 (9 F, 15 M) (c) 18-55	ASDAS-CRP	(a) Meditation-based intervention (n = 13) versus late intervention CG (n = 11) (b) Y (c) not blinded (d) 8 weeks	(e) 2x/week for 1st 4 weeks, and 1x/week for 2nd 4 weeks (f) unclear (g) Yes: 16 weeks post-intervention	sig. ↓ in ASDAS-CRP within MBI only	↓ ASDAS-CRP
Ng et. al (2020) [92]	(a) **Mild cognitive impairment** (b) 55 (c) 60-86	IL-6, hs-CRP	(a) MF awareness practice (n = 28), versus health education program (n = 27) (b) Y (c) single (d) 9 months	(e) 1x/week for first 3 months, then 1x/month + at home practice (f) 60 (g) No	no sig. change in IL-6 in MF group compared to HE group sig. ↓ in hs-CRP in MF group compared to HE group	• IL-6 ⇓ hs-CRP
Smith et. al (2017) [93]	(a) **Post-menopausal with obesity** (b) 36 F (c) 50-70	IL-6, CRP	(a) MF lifestyle (n = 18) versus active CG (n = 18) (b) Y (c) not blinded (d) 6 weeks	(e) 1x/week (f) 120 (g) Yes; 4 months, 9 months, and 1 year	sig. ↓ in IL-6 and CRP for MFG compared to UC	⇓ IL-6 ⇓ CRP
Walsh et. al (2016) [94]	(a) **Depression** (b) 64 F (c) 18-25	IL-6, TNF-α	(a) MBI (n = 31) versus contact CG (n = 33) (b) N (c) single (d) 4 weeks	(e) 1x/week (f) 50 (g) Yes; 3 months	sig. ↓ in IL-6 and TNF-α within MBI only and for MBI compared to CG	↓ IL-6 ⇓ IL-6 o TNF-α ⇓ TNF-α
Reich et. al (2017) [95]	(a) **Breast cancer survivors** (b) 322 F (c) mean = 57	IL-6, TNF-α	(a) MSBR (n = 152) versus UC (n = 147) (b) Y (c) no data (d) 6 weeks	(e) 1x/week + at home practice (f) 120 (g) Yes; 12 weeks	sig. ↑ TNF- α and IL-6 in the MSBR group compared to UC from baseline to 12-week follow-up	⇑ IL-6 ⇑ TNF-a
Dada et. al (2018) [96]	(a) **POAG** (b) 90 (40 F, 50 M)	IL-6, TNF-α	(a) MM intervention (n	(e) daily (f) 60 (g) No	sig. ↓ IL-6 and TNF-α	⇓ IL-6 ⇓ TNF-α

	(c) MM mean = 57.88 CG mean = 56.63		= 45) versus WL CG (n = 45) (b) Y (c) single (d) 3 weeks		in MF group compared to CG	
Hoge et. al (2018) [97]	(a) **GAD** (b) 70 (32 F, 38 M) (c) MSBR mean = 40 SME mean = 38	IL-6, TNF-α	(a) MSBR (n = 42) versus Stress Management Education (n = 28) (b) Y (c) single[95] (d) 8 weeks	(e) 1x/week + at home practice (f) 120 (g) No	sig. ↓ in TNF-α and IL-6 in MSBR compared to SME from baseline after TSST to post-intervention TSST	⇓ IL-6 ⇓ TNF-α
Morin-Alain (2020) [74]	(a) **AD** (b) 23 (11 F, 12 M) (c) MBI mean = 72 PBI mean = 69	IL-6, TNF-α	(a) MBI (n = 11) versus psycho-education intervention (n = 12) (b) Y (c) no data (d) 8 weeks	(e) 1x/week + at home practice (f) 150 (g) No	no sig. change in TNF-α within MBI or PBI sig. ↑ in IL-6 within MBI only	↑ IL-6 o TNF-α
Chacko et. al (2016) [98]	(a) **1-5 years post-bariatric surgery** (b) 18 (c) 18-65	IL-6, TNF-α, hs-CRP	(a) MBI (n = 9) versus standard intervention (n = 9) (b) Y (c) single (d) 10 weeks	(e) 1x/week +at home (f) 90 (g) Yes; 12 weeks and 6 months	no sig. change in IL-6, TNF-α, or hs-CRP between groups at 12 weeks or 6 months	• IL-6 • hs-CRP • TNF-α
Ewais et. Al (2021) [99]	(a) **IBD** (b) 64 (c) 16-24	IL-6, CRP	(a) MBCT (n = 33) versus treatment-as-usual (n = 31) (b) Y (c) single (d) 8 weeks	(e) 1x/week (f) 120 (g) Yes; 20 weeks	no sig. change in IL-6 or CRP between groups at 8 weeks or follow-up	• IL-6 • CRP

Of the included studies, 13 investigated proteomic data for meditation interventions, with 46.2% (n = 6) including transcription data. The average sample size was n = 80.2. Inflammatory disorders included chronic migraine with medication overuse (n = 1), alcohol dependency (n = 1), mild to moderate depression and anxiety (n = 1), axSpA (n = 1), mild cognitive impairment (n = 1), obesity (n = 1), depressive symptomology (n = 1), breast cancer survivors (n = 1), POAG (n = 1), GAD (n = 1), AD (n = 1), IBD (n = 1) and post-bariatric surgery (n = 1). 84.6% (n = 11) of the studies tested IL-6, 46.2% (n = 6) tested CRP, and 46.2% (n = 6) tested TNF-α. 36.4% (n = 4) showed positive improvements in levels of IL-6, 50% (n = 3) in levels of CRP, and 50% (n = 3) in levels of TNF-α.

4. Discussion

Our review of the evidence base within the last 5 years shows promising results with regards to trends in the application of multi-dimensional biologics (omics) to examine the effects of mind-body interventions (with a focus on meditation and yoga in this review) upon genomic, transcription, and proteomic markers across a diverse sample of chronic diseases/conditions associated with significant inflammation. The findings of this review highlight that 60.0% of the included studies

enacted positive effects upon inflammation, reflected by adaptive change in the studied omics biomarkers to statistically significant levels. The remaining 40.0% produced no observable clinical change or impact upon omic biomarkers across a range of medical conditions. Importantly, no studies reported genomic/transcription/proteomic findings that were the associated with adverse effects for participants exposed to the meditation- and/or yoga-based mind-body interventions studied. Stratifying by high-dimensional biologics, or omics, 40% of those examining genomics yielded significant results, 60.9% measuring proteomics, and 100% of the transcription technologies showed significant positive effects on the markers when solely investigating this domain (although this included only two studies). When accounting for all studies that included transcription markers in their study designs, 100% yielded positive effects. Due to the heterogeneity of findings, it was not possible to quantify the magnitude of mind-body interventions upon inflammatory markers using meta-analysis, for example. Although during the time our report was in peer-review, a meta-analysis into immunity-related biomarkers associated with mindfulness-based practices was also published [100], examining a mix of clinical conditions and healthy populations. The authors conceded small sample sizes and reduced statistical power limited their meta-analyses, although proposed that mindfulness practices may facilitate salutogenesis through improved immune function [100]. Back to our review, only studies that included a control group and reported statistical analyses comparing mean change pre-to-post intervention were included, that may have eliminated the inclusion of all possible studies. However, we were interested to include studies with stronger empirical designs and methodological strategies.

4.1 Genomics

Overall, 16.7% of included studies assessing mind-body interventions comprising yoga and/or meditation examined genomics. Telomere markers, specifically telomere length (TL) and telomerase activity (TA), constituted the genomic measures studied. Telomeres encapsulate chromosomes in turn serving to protect the integrity of DNA across the cell cycle. During successive cellular division, telomeres prevent base pair loss of chromosomal DNA, and as telomere attrition increases with age, telomeres ultimately shorten such that the cell can no longer divide, resulting in “cell senescence”. As such, telomere length is associated with longevity, and rate of telomere shortening is an indication of biological aging. For example, humans start with significantly shorter telomere lengths compared to mice (~5-15 kb vs. 40 kb), yet human telomere length degrades at a much slower rate in comparison (~70bp p/yr vs. ~7000 bp p/yr), possibly explaining the longer human life span [101]. Telomerase activity is associated with an enzyme (protein reverse transcriptase) that acts as a catalytic unit to hinder cell senescence by reversing the effects of telomere degradation and lengthening telomeres [102]. Interestingly, the meditation focused studies showed no differences/changes in either telomerase activity or telomere length compared with controls. However, mind-body approaches comprising yoga showed significant increases in telomerase activity (not telomere length), suggesting the potential to ‘reverse biological aging’, and protect telomere length and cell quality. Furthermore, these differences in telomerase activity in the yoga groups were also accompanied by reduction in proteins associated with oxidative stress and inflammation, including interleukin-6 (IL-6), C-Reactive Protein (CRP), and Tumor Necrosis Factor (TNF-α), discussed further below in ‘proteomics’.

4.2 Transcription

Only 6.7% of the reviewed clinical studies solely examined this omic approach (see Table 3). Transcriptomics measure messenger ribonucleic acid (mRNA) within a cell, tissue, or organism, corresponding to gene expression [1]. Transcription also provides the template for protein synthesis via the process of 'translation' that in turn forms the proteome (protein expression of the cell) [103]. A gene may remain dormant until expressed within the mRNA, thus, examining transcription markers is reasonably more salient for disease and treatment trajectory. NF-kB consists of a coalition of transcription factors that are critical in inflammation, immunity, cell proliferation, differentiation, and survival [104]. Specifically, the Nuclear Factor kappa B (NF-kB) transcription factor group in mammals consists of five proteins; RELA (or the p65 subunit), RELB, RELC, NF-kB1 (or the p105/p50 subunit), and NF-kB2 (or the p100/p52 subunit) [104]. These transcription factors control expression of various gene targets to changes in micro- and macro-environments, in turn facilitating germane molecular cell/mediator production. Our review found that while no yoga intervention studies examined transcriptomics, two meditation studies found promising early results. Both focused on gene expression levels of Nuclear Factor kappa B (NF-kB) that regulates the transcription of DNA, cytokine production, and cell longevity [105]. NF-kB is central to immune response, where the dysregulation of NF-kB is associated with the development of autoimmune disease, cancers, and other non-adaptive inflammatory responses [106]. Specifically, one study allocated patients with Type 2 diabetes and/or hypertension to an 8-week brain education-based meditation program versus a health education control group [75]. Levels of expression of the NF-kB2 were significantly reduced within the brain education-based meditation program group, following meditation exposure. Such findings suggest that meditation may reduce low-grade inflammation by decreasing Nuclear Factor kappa B (NF-kB) expression levels. Additionally, one study found a significant decrease in the DNA methylation of TNF-α in the yoga group, although there was no significant difference in levels of protein TNF-α [85]. Another study found a significant downregulation in mRNA expression levels of IL-6 and TNF-α in the yoga intervention group when compared to the control group [86]. Further research is warranted using transcriptomics to assess mind-body medicine mechanism/s and clinical impact.

4.3 Proteomics

The predominant omics technology used for mind-body interventions reviewed here involved proteomics, included in 86.7% of studies. The dynamic interaction between nature (genes) and nurture (environment) culminates in the proteome, i.e. all expressed proteins in the cell, tissue and/or organism encoded by the genome [107]. The study of proteins is particularly pertinent for identifying biomarkers of mind-body interventions and ensuing clinical action since protein changes associated with disease and treatment response are universal and pervasive. However, this is confounded by the known value of proteins in the region of >100,000 [1, 108], making for a particularly complex domain of study. Albeit, some protein markers of inflammation have been replicated across clinical populations, and thus reflect non-specific proteins associated with low-grade inflammation. An example are interleukins (ILs), a group of immunomodulatory proteins that are a subclass of larger cellular messenger molecules, cytokines. Cytokines/interleukins are secreted as proteins and signal molecules with a central role in immune response and inflammation [109]. The human genome encodes ~50 known interleukins and related proteins [110]. Interleukins

modulate growth, differentiation, and activation during immune response, granting them both inflammatory and anti-inflammatory properties. This distinguishes interleukins from other cytokines, such as chemokines whose main role is to direct immune cells to inflammation sites via chemotaxis, or interferons which primarily direct cells in response to viral infection [111]. Interleukins are key in the physiological response to immune response triggers and have a significant role in the pathophysiology of many medical conditions (from physical to mental disorders), making them putative candidate targets for therapeutic intervention. Our review highlighted that specifically Interleukin-6 (IL-6) was the most investigated protein in mind-body medicine studies included within the last 5-years (see Tables 1, 4 and 5). Interleukin-6 serves both anti- and pro-inflammatory functions associated with inflammation, immunity, and disease [112]. It acts upon a variety of cells and tissues, promoting differentiation of B-cells, promotion of cell growth in some cells, and inhibiting growth in others, and as such elevated levels may be present during inflammation, autoimmune disorders, cardiovascular diseases, and some cancers [113, 114]. Another important protein marker highlighted during our review was C-Reactive Protein (CRP), since C-Reactive Protein levels increase following the secretion of interleukin-6 by macrophages and lymphocyte cells [115]. C-Reactive Protein is thus considered a marker of systemic inflammation related to pro-inflammatory cytokines from immune-related cells and the chronic activation of the innate immune system. A third proteomic marker relevant to our review of mind-body intervention studies is Tumor Necrosis Factor alpha (TNF-α), a multi-functional cytokine secreted primarily by macrophages, lymphocytes, and natural killer cells [116].

Overall, 30.8% of the included studies reported no change in any of the proteomic markers that were examined following mind-body interventions. Although 53.8% of studies reported no change in at least one proteomic biomarker included in the assays. Of the 18 studies reporting change, the majority (16) found decreases in proteomic measures, suggesting reduction in inflammation. The remaining two studies that reported *increased* inflammatory markers were exclusive to meditation-based intervention, and specifically included interleukin-6 and Tumor Necrosis Factor alpha/TNF-α. In the first case, Mindfulness-Based Stress Reduction/MBSR was compared with usual care in normalizing blood levels of pro-inflammatory cytokines among breast cancer survivors [95]. Firstly, interleukin-6 and Tumor Necrosis Factor alpha/TNF-α cytokine levels did not significantly differ between the breast cancer survivors compared with a healthy control baseline group. Increased interleukin-6 and Tumor Necrosis Factor alpha/TNF-α were apparent when assessing these markers across patients only, revealing cytokine expression subgroups, i.e. treatment with mastectomy associated with higher Tumor Necrosis Factor alpha/TNF-α levels post-recovery. Interestingly, cytokine levels were lower in those patients who had received radiation treatment only. Furthermore, increased cytokine levels were apparent when comparing Mindfulness-Based Stress Reduction/MBSR vs. usual care during the 6-12 week follow up period, compared with during treatment. Interleukin-6 and Tumor Necrosis Factor alpha/TNF-α showed a more rapid increase post-MBSR intervention compared to usual care, although this was not the case during the MBSR treatment itself [95]. These multi-faceted results were interpreted by the study authors within a framework that posited B-cell modulation as part of immune recovery during breast cancer management, and that the increased Interleukin-6 and Tumor Necrosis Factor alpha/TNF-α levels may have reflected an MBSR-related immune restoration process post-breast cancer treatment [95]. The second study that reported contradictory results (i.e. increased proteomic levels), in inflammatory markers associated with mind-body interventions (vs. psychoeducation-based

intervention), was a pilot study in individuals with amnestic mild cognitive impairment [74]. The authors reported decreased Tumor Necrosis Factor alpha/TNF-α in patients with higher baseline levels of this cytokine, and increased interleukin-6 levels for all patients, post meditation intervention based on a Mindfulness-Based Stress Reduction/MBSR program. No changes were evident pre-to-post the psychoeducation-based intervention group. Despite the two diverging findings, that were more complex when disentangling multiple levels of analyses, 88.9% of the mind-body intervention studies that reported significant change yielded decreased levels following mind-body medicine exposure compared with control groups that correlated with enhanced health and wellbeing. Overall, these reports show promising adaptive and beneficial effects on proteomic biomarkers associated with mind-body interventions.

5. Synthesis

Integrative medicine is garnering popularity among patients and doctors/providers due to its humanistic, patient-centred, pragmatic, and pluralistic approach. Integrative medicine focuses on the whole person and the patient-practitioner relationship, advocating the holistic treatment of disease, prevention, and health. One distinction between conventional versus integrative medicine is the use of mind-body interventions, such as meditation and yoga-based interventions. The extant evidence-base largely pertains to efficacy studies, with less attention to mechanistic understanding. Greater elucidation of mechanism has clinical intrinsic value of its own, may inform personalized optimized interventions, and further provide predictive trajectories for response. These factors are particularly germane for complex patient cases, often seen in the integrative medicine clinic, where lengthy 'trial-and-error' can potentially be stressful for patients (and their doctors/providers), erode the patient-doctor relationship, and trust in the medical system overall from the patient perspective. For integrative medicine to gain full mainstream traction, evidence-based mechanistic applications are key. This review supports that (1) omics technologies provide optimized methods to investigate mechanistic effects of mind-body interventions on molecular genomic, transcription, and/or proteomic pathways, opposed to solely focusing on uni-dimensional outcomes, (2) inflammatory conditions and disorders that have more recently been associated with significant inflammation (i.e. mood disorders) are beneficially regulated from mind-body interventions that may be pertinent mechanistically given the ubiquitous presentation of inflammation across many disease/disorder typologies, (3) for unified understanding of treatment mechanism in mind-body medicine, multi-levelled omics that also consider environmental, microbial, and immunological factors might be most enlightening moving forward. We suggest that mind-body interventions, based in yoga and meditation, may not necessarily specifically target inflammatory biomarkers, rather modulate the centralized and connective pathways associated with disease networks and interactomes. Finally, it is important to note that our review does not take into account the metabolic branch of the omics. Currently, limited data is available and appears to be in a process of development. Further research is needed to elucidate how metabolomics may be impacted by mind-body interventions and how they interplay with the genomic, transcriptomic, and proteomic biomarkers identified.

Acronym List

AD	Alzheimer's disease
axSpA	Axial spondyloarthritis

ASDAS-CRP	Ankylosing Spondylitis Disease Activity Score-C Reactive Protein
BEM	Brain education-based meditation
CABG	Coronary artery bypass graft
CG	Control group
COPD	Chronic obstructive pulmonary disease
CRP	C Reactive Protein
DMARDs	Disease-modifying antirheumatic drugs
GAD	Generalized anxiety disorder
HE	Health education
hs-CRP	High sensitivity-C Reactive Protein
IBD	Inflammatory bowel disease
IL-1B	Interleukin-1β/beta
IL-6	Interleukin-6
LTL	Leukocyte telomere length
MBCT	Mindfulness-Based Cognitive Therapy
MBI	Mindfulness-Based Intervention
MDD	Major depressive disorder
Met S	Metabolic syndrome
MF	Mindfulness
MM	Mindfulness-meditation
MSBR	Mindfulness-Based Stress Reduction
NF-κb	Nuclear Factor kappa B
NF-kB1	Nuclear Factor kappa B p105/p50 subunit
NF-kB2	Nuclear Factor kappa B p100/p52 subunit
OA	Osteoarthritis
POAG	Primary open angle glaucoma
RA	Rheumatoid arthritis
RELA	Nuclear Factor kappa B RelA/p65 subunit
RELB	Nuclear Factor kappa B RelB subunit
RELC	Nuclear Factor kappa B cRel subunit
TA	Telomerase activity
TL	Telomere length
TNF	Tumor Necrosis Factor
UC	Usual Care
YBLI	Yoga-based lifestyle intervention
YG	Yoga group

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Conceptualization: PLAS. Methodology: PLAS, KMG. Review: KMG. Supervision: PLAS. Analysis: PLAS, KMG. Visualization: PLAS, KMG. Writing: PLAS.

Competing Interests

The authors have declared that no competing interests exist.

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