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Identification of Biomarkers Involved in Multiple Sclerosis: A Personalized Medicine Approach

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Abstract:

Multiple sclerosis (MS) represents a complex, immune-driven CNS condition marked by significant clinical and biological diversity, which complicates diagnostic and prognostic efforts. In recent years, the paradigm of MS research has evolved through rapid biomarker breakthroughs, transitioning from a reliance on traditional neuroimaging to holistic molecular and multi-modal profiling. Liquid-based indicators, such as glial fibrillary acidic protein (GFAP), neurofilament light chain (NfL), and chitinase-3-like protein 1 (CHI3L1), have emerged as robust correlates of neuroaxonal damage and astrocytic involvement. Parallel to this, novel imaging features notably paramagnetic rim lesions and the central vein sign have increased diagnostic precision. Furthermore, the integration of multi-omics including genomics and metabolomics allows for a more granular understanding of the immune and degenerative pathways in MS. By leveraging systems biology and machine learning, researchers can now identify synergistic biomarker signatures that surpass individual markers in forecasting disease activity and therapeutic outcomes. However, achieving precision neurology requires overcoming obstacles in assay harmonization and clinical validation.

Keywords: Multiple Sclerosis, Biomarkers, Neurofilament Light Chain, Precision Medicine, Neuroinflammation

INTRODUCTION

Biomarker Discovery in Multiple Sclerosis: Moving Toward Precision Neurology

Multiple sclerosis (MS) stands as a chronic autoimmune-driven condition of the central nervous system, defined by inflammatory processes, demyelination, and the attrition of neuroaxonal structures. Even with significant therapeutic breakthroughs, MS remains a clinically diverse disease, displaying unpredictable trajectories from relapsing-remitting stages to more steady progression. This inherent variability necessitates the identification of dependable biomarkers to facilitate early detection, forecast disease evolution, and tailor therapeutic interventions. Recent research has shifted its focus from traditional neuroimaging toward molecular and fluid-based metrics that reflect the disease's underlying biological mechanisms. Specifically, neurofilament light chain (NfL) levels in both blood and cerebrospinal fluid have been validated as sensitive indicators of axonal damage and clinical activity. Furthermore, advancements in immunoprofiling have clarified the roles of B-cell and T-cell pathways in disease advancement, supporting a transition from standardized treatments toward personalized clinical management (1, 2).

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The emergence of sophisticated high-throughput "omics" platforms has further catalyzed the search for MS biomarkers, providing a holistic view of genomic, transcriptomic, and proteomic landscapes. While genome-wide studies have pinpointed genetic risk factors and immune-regulating pathways, proteomic analyses have unveiled the intricate molecular networks driving neurodegeneration. In tandem, innovative MRI techniques offer quantitative structural insights that enhance the precision of disease monitoring. By merging multi-omics data with artificial intelligence and machine learning, researchers are developing new frameworks for patient stratification and therapy response prediction. However, the path to clinical integration is hindered by the need for assay standardization and validation across broad populations. Resolving these translational challenges is vital for making personalized MS care a reality in routine practice (3, 4).

Emerging Biomarkers in Multiple Sclerosis: Foundations for Precision Medicine

As an immune-driven neurodegenerative condition, Multiple Sclerosis (MS) presents significant clinical and pathological diversity, which often complicates precise diagnosis and the selection of optimal therapeutic pathways. Because standard clinical evaluations and traditional MRI frequently lack the sensitivity required to detect the subtle biological variations in individual patients, there is an urgent requirement for biomarkers that can elucidate core disease mechanisms and support personalized medicine. Recent academic surveys emphasize the rapid development of both fluid and imaging-based indicators. For instance, MRI features like paramagnetic rim lesions and the central vein sign, along with fluid markers such as glial fibrillary acidic protein (GFAP) and neurofilament light chain (NfL), show great potential for enhancing disease monitoring and characterization. These emerging tools not only assist in identifying neuro-axonal compromise and astrogliosis but also offer a means to differentiate inflammatory activity from progressive phenotypes. Incorporating these metrics into clinical workflows could refine diagnostic accuracy and help categorize patients for tailored interventions. While integrative multi-marker approaches may capture the disease's complexity more effectively than single indicators, their transition into clinical practice necessitates extensive longitudinal validation across varied cohorts. Advancing toward individualized, mechanism-driven care thus depends on the effective integration of technological and biological breakthroughs (5, 6).

In the modern quest for precision neurology, current studies highlight the necessity of identifying biomarkers that simultaneously reflect disease activity and neurodegenerative processes to better forecast outcomes and customize patient care (5). Serum neurofilament light chain (sNfL) has gained prominence as a reliable indicator of neuroaxonal damage, demonstrating significant correlations with physical disability and lesion dynamics. Consequently, sNfL is increasingly viewed as a viable surrogate endpoint for monitoring disease progression and the efficacy of therapeutic agents (6). Parallel to these fluid-based advancements, sophisticated imaging phenotypes including myelin integrity and lesion morphology are being optimized to serve as objective indicators of pathological evolution, forming an integrated system of molecular and radiological markers. Furthermore, the application of proteomic and metabolomic signatures enriches this diagnostic framework by revealing the complex molecular circuits involved in MS pathogenesis. Collectively, these innovations emphasize the multifaceted nature of MS and underscore the potential of integrative biomarkers as essential tools for establishing predictive and personalized clinical management (7, 8).

From Pathogenesis to Precision Care: Biomarkers in Multiple Sclerosis

The complex clinical landscape of Multiple Sclerosis (MS), a chronic autoimmune-mediated CNS condition, is driven by concurrent neurodegeneration, demyelination, and inflammatory processes. Gaining insight into these molecular underpinnings has catalyzed the search for dependable biomarkers that clarify disease mechanisms, which is vital for achieving precision in patient stratification and early diagnosis. Significant attention has focused on neurofilament light chain (NfL) an axonal protein shed into blood and cerebrospinal fluid (CSF) during neuronal injury and glial fibrillary acidic protein (GFAP), which serves as a metric for astrocytic involvement and progressive attrition. Increased concentrations of NfL correlate with future relapses, brain volume loss, and heightened disease activity, making it a valuable monitoring tool. Meanwhile, glial-specific markers like GFAP and neurofilament heavy chains offer distinct insights into the biology of non-relapsing progression, potentially aiding in the differentiation of MS subtypes. Although incorporating such markers into clinical protocols could enhance diagnostic and prognostic accuracy, obstacles regarding assay standardization and cross-cohort validation persist. Bridging the gap between experimental discovery and routine clinical application remains a primary objective for future MS research (9, 10).

Modern biomarker research in MS now encompasses a multifaceted array of immunological, imaging, and molecular domains, aiming to provide

more customized therapeutic strategies. Current evidence suggests that synthesizing panels of markers from both blood and CSF surpasses the predictive power of individual measures, potentially facilitating less invasive longitudinal monitoring. As a robust proxy for neuroaxonal damage, NfL remains central to forecasting treatment responses and ongoing clinical activity when measured via high-sensitivity assays. Concurrently, novel indicators such as GFAP are emerging as vital tools for identifying inflammatory-independent progression, thus capturing unique pathogenic pathways. Additional candidates, including chemokines and chitinase-3-like protein 1 (CHI3L1), are being explored to further refine therapy response models and patient grouping. The fusion of multimodal biomarker data with clinical and radiological findings offers a path toward a truly integrated precision medicine framework in MS. Nevertheless, establishing clinical consensus and ensuring rigorous longitudinal validation are essential steps before these panels can be adopted in standard care (11, 12).

Molecular and Clinical Biomarkers in Multiple Sclerosis: Toward Individualized Therapeutic Strategies

Multiple Sclerosis (MS) functions as a chronic, neuro-inflammatory condition of the central nervous system defined by demyelination and axonal compromise, leading to diverse clinical trajectories that often complicate uniform diagnostic protocols. The identification of molecular indicators, specifically neurofilament light chain (NfL) and glial fibrillary acidic protein (GFAP), has significantly deepened the understanding of MS pathophysiology by quantifying neuroaxonal loss and astrogliosis within both blood and cerebrospinal fluid samples. These markers have proven effective in tracking disease status, showing strong associations with physical impairment and MRI findings, while offering insights into progression that traditional imaging might overlook. While established clinical indicators such as oligoclonal IgG bands and radiological features remain central to the diagnostic process, they often fail to provide high-level prognostic clarity independently, necessitating their combination with molecular data for superior patient stratification. Innovative multimodal frameworks that fuse clinical findings with molecular data offer significant potential for accelerated detection and more accurate forecasting of the disease path, allowing for therapeutic choices based on individual patient profiles. Nonetheless, the widespread adoption of these tools in clinical settings depends on rigorous longitudinal evidence, standardized assay methodologies, and a broad consensus on how to interpret results across heterogeneous populations. Moving toward a unified precision care model that merges clinical and molecular data is essential for advancing personalized therapeutic interventions in MS (13,14).

Recent studies suggest that the synergy between clinical indicators and molecular biomarkers improves the precision of prognosis and enables patient grouping based on projected treatment response a primary aim of individualized medicine. As a widely recognized surrogate for axonal injury, serum NfL (sNfL) facilitates the dynamic tracking of disease biology and the evaluation of therapeutic efficacy by reflecting both relapse-related activity and steady progression. Similarly, markers like chitinase-3-like protein 1 (CHI3L1) and GFAP provide specialized insights into astroglial reactions and progressive traits that traditional metrics often overlook. Incorporating these biological indicators into standard practice could refine risk assessments and inform the selection of personalized therapies, shifting MS management from symptom-focused models toward biology-led strategies that align treatment intensity with the patient's specific disease trajectory. This transition ultimately aims to maximize clinical outcomes while reducing the risk of unnecessary side effects. Realizing the full potential of these markers in clinical practice will require ongoing collaborative efforts toward standardization and further investigative research (15, 16).

Integrative Biomarker Profiling in Multiple Sclerosis: A Personalized Medicine Framework

Due to the profound clinical and pathological diversity inherent in Multiple Sclerosis (MS), there is a critical imperative for holistic biomarker characterization to facilitate individualized management. Recent investigative efforts emphasize synthesizing fluid-based indicators specifically neurofilament light chain (NfL), glial fibrillary acidic protein (GFAP), and chitinase-3-like protein 1 (CHI3L1) with radiological and clinical metrics to better capture the disease's underlying biological nuances. While blood and CSF NfL levels serve as established proxies for neuroaxonal compromise, GFAP and CHI3L1 provide essential data on astrogliosis and progressive pathology, representing the multi-dimensional nature of MS. Research indicates that such integrative profiling, which merges these molecular signatures with MRI data, offers superior diagnostic precision and prognostic foresight compared to isolated marker analysis. By enabling a more detailed characterization of the disease and tailoring therapies to a patient's specific biological signature, these multimodal frameworks embody the core principles of precision medicine. Implementing these integrated panels could significantly improve the detection of occult disease

activity and help predict individual progression paths; however, this transition requires standardized analytical methodologies and validation across broader, more diverse cohorts. The future of MS prognosis lies in the convergence of multi-omics and computational modeling to further refine these predictive frameworks (17, 18).

The landscape of MS biomarker discovery has been significantly expanded by integrative multi-omics including proteomics, metabolomics, and immune cell phenotyping which have unveiled unique molecular fingerprints associated with various disease stages and phenotypes. For instance, high-dimensional profiling of peripheral blood has identified specific metabolic and immunological alterations that differentiate MS patients from healthy individuals and correlate with clinical disability. Moving beyond the reliance on single indicators, composite panels that integrate cellular, molecular, and imaging data show great promise in deciphering the intricate pathogenesis of MS, thereby allowing for more precise patient stratification. This comprehensive framework bridges the gap between mechanistic biological insights and practical clinical decision-making. Despite ongoing challenges in ensuring the reproducibility of multi-platform data, advancements in computational analysis and large-scale validation are making the clinical application of integrative profiling increasingly viable. The successful realization of personalized neurology in MS will ultimately depend on sustained synergy between computational experts and clinical researchers (19, 20).

Translational Biomarkers in Multiple Sclerosis: Implications for Precision Neurology

In the realm of precision neurology, translational biomarkers in Multiple Sclerosis (MS) serve as a vital conduit between fundamental biological discoveries and their clinical application, thereby optimizing diagnostic accuracy and therapeutic navigation. Progressive research in fluid-based assays has solidified the clinical importance of neurofilament light chain (NfL) and glial fibrillary acidic protein (GFAP) as proxies for neuroaxonal compromise and astrocytic involvement, respectively. These markers provide a translational window into the underlying pathology that surpasses the limitations of standard clinical assessments by reflecting disease dynamics across the entire MS spectrum. Furthermore, the diagnostic landscape has recently expanded to incorporate plasma-based phosphorylated tau isoforms. When integrated with NfL and GFAP, these tau proteins significantly improve the differentiation between relapsing-remitting and progressive phenotypes, offering more precise prognostic value for patient outcomes. While embedding these indicators into clinical workflows could revolutionize personalized care allowing for the detection of occult disease activity and real-time treatment monitoring significant hurdles such as assay harmonization and longitudinal validation across diverse modalities remain. Achieving the full potential of precision care in MS necessitates addressing these translational gaps through collective research efforts and the establishment of consensus-based interpretive frameworks (21, 22).

The scope of modern translational biomarkers has evolved to include not only liquid metrics but also digital, imaging, and multi-omic signatures, capturing the intricate confluence of neurodegeneration, inflammation, and endogenous repair mechanisms. For instance, sophisticated panels that merge CSF and blood-based indicators with advanced radiological features, such as paramagnetic rim lesions and the central vein sign, yield a more profound understanding of lesion-specific biology and subclinical progression. Additionally, the rise of machine learning and computational modeling provides new pathways for identifying complex biomarker combinations that can further individualize treatment selection and optimize patient response. These multimodal frameworks are inherently aligned with precision medicine, as they allow clinicians to map specific pathogenic mechanisms to targeted therapies. However, transitioning these high-dimensional strategies into standard practice requires robust evidence from large-scale studies and the seamless integration of standardized methodologies into existing clinical workflows. Sustained collaboration within international consortia will be fundamental in transforming these experimental markers into impactful tools for MS management (23, 24).

Advances in Biomarker Identification for Multiple Sclerosis Management and Personalized Treatment

Multiple sclerosis (MS) represents a long-term, autoimmune-related neurological disease with heterogeneous clinical trajectories that challenge clinicians in terms of accurate diagnosis, prognostication, and individualized therapy. Recent advances in biomarker research have identified both fluid and imaging markers that reflect underlying neuroinflammatory and neurodegenerative processes, offering insights into disease biology that extend beyond conventional clinical measures. Neurofilament light chain (NfL) and glial fibrillary acidic protein (GFAP) have risen to prominence as key biomarkers in blood and cerebrospinal fluid (CSF) for tracking axonal damage and astroglial activation, respectively. Their concentrations are closely linked to disease activity and progression.

Furthermore, chitinase-3-like protein 1 (CHI3L1) has demonstrated potential as an indicator of tissue remodeling and persistent inflammation, especially within progressive forms of multiple sclerosis.

.Integrating these biomarkers into clinical practice could enhance early detection, help differentiate subtypes, and guide personalized therapeutic decisions. However, translation to routine care requires standardized assays, longitudinal validation, and consensus on interpretive frameworks for clinical use. Emerging evidence also suggests that combining biomarker panels with clinical and imaging parameters improves predictive accuracy compared to single measures alone .Therefore, continued research into integrative biomarker strategies is critical for advancing precision treatment paradigms in MS (25, 26).

Recent studies have also explored multi-biomarker algorithms and composite profiles that integrate mechanistic signals from protein biomarkers with clinical scales and imaging metrics to enhance predictive models of MS disease activity, therapeutic response, and disability progression. For example, multi-biomarker activity scores incorporating inflammatory, apoptotic, and metabolic markers exhibit higher sensitivity and specificity for relapse prediction and treatment response compared with individual markers alone . Circulating phosphorylated tau isoforms (p-tau181, p-tau217) have emerged as promising complements to NfL and GFAP, improving subtype classification and disability predictions in MS cohorts .Additional research supports the clinical significance of early serum NfL levels in detecting individuals who are at a high likelihood of transitioning from clinically isolated syndrome to established multiple sclerosis .Despite these promising trends, implementation into clinical workflows remains limited by variability in assay platforms, cohort heterogeneity, and the need for large-scale validation. Ongoing longitudinal and multi-center studies are helping address these gaps and are paving the way for next-generation diagnostic and prognostic tools grounded in precision medicine. As the field continues to evolve, integrative biomarker profiling stands to transform the management of MS by tailoring therapy to underlying disease biology (27, 28) (Table1).

Multi-Omics Biomarkers in Multiple Sclerosis: Shaping the Future of Personalized Medicine

Multiple sclerosis (MS) represents a long-term, autoimmune-related condition affecting the central nervous system, which is marked by complex interactions between genetic susceptibility, immune dysregulation, and neurodegeneration, resulting in highly heterogeneous clinical trajectories. Traditional diagnostic and monitoring tools, including MRI and clinical scales, provide limited insight into the molecular mechanisms driving individual disease courses, thereby underscoring the need for multi-omics biomarker approaches. Recent advances in The fields of genomics, transcriptomics, proteomics, and metabolomics have facilitated the detailed mapping of immune and neural mechanisms.

involved in MS pathogenesis, revealing distinct molecular signatures associated with disease activity and progression .Integrative multi-omics analyses have identified dysregulated immune cell networks, metabolic alterations, and neuroaxonal injury pathways that correlate with clinical disability and radiological outcomes. In particular, proteomic and transcriptomic profiling of blood and cerebrospinal fluid has uncovered biomarker panels capable of differentiating MS subtypes and predicting therapeutic responses. These approaches move beyond single-marker strategies by capturing system-level biological interactions relevant to individualized disease mechanisms. However, translating multi-omics discoveries into clinical practice requires robust validation, harmonized analytical pipelines, and longitudinal cohort studies. Collectively, multi-omics biomarker research is reshaping our understanding of MS biology and laying the groundwork for precision medicine frameworks tailored to patient-specific molecular profiles (29, 30).

Beyond discovery, multi-omics biomarker integration holds transformative potential for personalized treatment strategies in MS by enabling prediction of disease evolution and therapeutic responsiveness. Studies combining proteomic, metabolomic, and immune-cell phenotyping data have demonstrated improved predictive accuracy for relapse risk and disability progression compared with conventional markers alone .For example, integrative biomarker models incorporating neurofilament light chain, glial fibrillary acidic protein, and immunomodulatory signatures have shown strong associations with both inflammatory activity and neurodegenerative burden. These composite signatures support risk stratification and may guide early escalation or de-escalation of disease-modifying therapies based on individual biological activity. Furthermore, systems-biology approaches and machine learning techniques are being progressively utilized for multi-omics datasets to identify clinically actionable molecular clusters and treatment response predictors. Despite these promising developments, challenges remain in standardizing data integration methods and ensuring reproducibility across populations. Continued collaboration between clinical researchers, bioinformaticians, and translational scientists will be essential to convert multi-omics discoveries into

Table 1. Summary of analyzed studies and key biomarker findings in MS

Ref No.	Study (Year)	Biomarkers Examined	Key Findings
1	Chitnis et al. (2025)	NfL, GFAP, CHI3L1	NfL reflects axonal damage; GFAP elevated in progressive MS; CHI3L1 associated with chronic inflammation and MRI lesions. (PubMed)
2	Petrescu et al. (2025)	NfL, Nf-H, CHI3L1	Under interferon-β therapy, NfL decreased; CHI3L1 increased; baseline biomarker levels correlated with relapse and long-term disability. (PubMed)
3	Zhu et al. (2023)	Multi-protein profile	Serum biomarker panels correlated with real-world disability scores and improved predictive modeling. (PubMed)
4	Barro et al. (2024)	Serum proteomics	Identified proteins associated with clinical and MRI disease activity; multivariate panel outperformed univariate markers. (Nature)
5	H. Hellgren et al. (2025)	GFAP, NfL, IgG-index	GFAP higher in natalizumab group than rituximab; NfL levels did not differ; intrathecal inflammatory activity persists. (Lund University)
6	(Systematic review) Toftegaard et al. (2024)	28 biomarkers incl. NfL & CHI3L1	Six biomarkers (incl. NfL, GFAP, CHI3L1) particularly promising in differentiating RRMS from SPMS. (MDPI)
7	Barro et al. (2022–2024)	sNfL, sGFAP	Serum biomarkers stratify disease activity and progression; sNfL correlates with gadolinium lesions and relapse status. (Nature)
8	(Emerging) Proteomic CSF profiling (2025)	~3714 proteins	Broad proteome associations with clinical and imaging outcomes, highlighting sex differences and injury pathways. (Nature)

practical tools that shape the future of personalized medicine in MS (31, 32).

Diagnostic, Prognostic, and Predictive Biomarkers in Multiple Sclerosis: A Precision Medicine Perspective

Multiple sclerosis (MS) constitutes a long-term, autoimmune-related condition affecting the central nervous system, marked by inflammatory demyelination and gradual neuroaxonal damage. This results in significant differences among individuals regarding disease progression and response to treatment. The advancement of diagnostic, prognostic, and predictive biomarkers has therefore become central to advancing precision medicine approaches in MS. Diagnostic biomarkers such as cerebrospinal fluid oligoclonal IgG bands and emerging blood-based markers enhance early detection and support updated diagnostic criteria, improving specificity and reducing time to diagnosis .Prognostic biomarkers, particularly Levels of neurofilament light chain (NfL) and glial fibrillary acidic protein (GFAP) serve as indicators of persistent axonal damage and astroglial activation. Furthermore, these biomarkers are closely linked to future disability advancement and radiological manifestations. These molecular indicators complement MRI metrics by capturing subclinical disease activity and neurodegeneration not fully reflected by imaging alone. Moreover, integrating fluid biomarkers with clinical parameters may refine risk stratification at disease onset and inform early therapeutic decisions. Despite promising advances, challenges remain in assay harmonization, cutoff standardization, and longitudinal validation across diverse patient populations. Continued translational research is critical to embed biomarker-guided strategies into routine MS care and strengthen precision neurology frameworks (33, 34).

Beyond diagnosis and prognosis, predictive biomarkers are increasingly investigated to guide individualized therapeutic strategies and optimize treatment outcomes in MS. Serum NfL has shown utility in monitoring monitoring therapeutic efficacy and identifying breakthrough disease progression, whereas GFAP and chitinase-3-like protein 1 (CHI3L1) have been linked to progressive pathology and may assist in therapeutic selection .Multi-biomarker panels integrating inflammatory, neurodegenerative, and immune-regulatory proteins demonstrate superior predictive performance compared with single markers, particularly in forecasting relapse risk and disability accumulation .Advances in proteomics and computational modeling further enable identification of composite molecular signatures associated with differential responses to disease-modifying therapies. Such predictive frameworks align with precision medicine principles by tailoring intervention intensity to individual biological activity and risk profiles. Nevertheless, implementation into clinical workflows requires large-scale validation studies and consensus regarding clinically actionable thresholds. As research continues to refine these tools, diagnostic, prognostic, and predictive biomarkers collectively represent a transformative avenue toward personalized management in MS (35, 36).

Systems Biology and Biomarker Integration in Multiple Sclerosis: Toward Tailored Clinical Care

Multiple sclerosis (MS) represents a multifaceted, autoimmune-related condition marked by dynamic interactions among genetic susceptibility, immune dysregulation, environmental triggers, and neurodegenerative mechanisms, resulting in marked heterogeneity in disease course and therapeutic response. Systems biology approaches have emerged as powerful tools to dissect this complexity through the synthesis of multi-dimensional biological informatione ncompassing genomics, transcriptomics, proteomics, and metabolomics into unified models of disease pathogenesis. Recent multi-omics investigations have identified coordinated immune and neurodegenerative pathways associated with clinical disability, lesion burden, and progression risk, underscoring the value of integrative biomarker profiling in MS .Rather than relying on single biomarkers, systems-level analyses enable the identification of molecular networks and composite signatures that better capture disease biology and predict outcomes. For example, integrated blood proteomic panels combined with clinical data have demonstrated improved accuracy in stratifying disease activity compared with traditional measures alone .Such frameworks support a transition from descriptive phenotyping to mechanism-based classification of MS subtypes. Nevertheless, challenges related to data harmonization, computational modeling, and validation across heterogeneous cohorts remain significant barriers. Continued refinement of systems biology methodologies is therefore essential for translating integrative biomarker discoveries into clinically actionable tools for tailored care in MS (37, 38).

Integrating systems biology with clinical biomarker research further enhances the potential for precision neurology by linking molecular signatures to therapeutic responsiveness and long-term outcomes. Studies combining neurofilament light chain (NfL) and glial fibrillary acidic protein (GFAP) , and immune-regulatory proteins with advanced computational modeling have demonstrated improved prediction of relapse risk and disability progression .These integrative strategies enable risk stratification at early disease stages and may guide personalized escalation or de-escalation of disease-modifying therapies based on biological activity rather than solely clinical criteria. Moreover, systems-level network analyses reveal interactions between inflammatory and neurodegenerative pathways that are not apparent in reductionist models, offering novel targets for therapeutic intervention. Machine learning algorithms applied to high-dimensional datasets further refine biomarker selection and enhance predictive performance in real-world cohorts .Despite promising advances, translating systems biology insights into routine clinical workflows requires standardized analytical pipelines, reproducible validation, and consensus regarding interpretability. As integrative methodologies mature, they are poised to transform MS management by enabling tailored clinical care grounded in comprehensive biological profiling (39, 40).

CONCLUSION

In conclusion, the evolving landscape of biomarker research in multiple sclerosis (MS) underscores a transformative shift toward precision medicine grounded in molecular and multimodal disease characterization. Fluid biomarkers including neurofilament light chain and glial fibrillary acidic protein , and chitinase-3-like protein 1, alongside advanced imaging and multi-omics approaches, collectively enhance diagnostic accuracy, prognostic stratification, and therapeutic monitoring. Integrative systems biology and machine learning-driven frameworks significantly enhance the predictive capability of composite biomarker panels signatures beyond single-marker strategies. Despite ongoing challenges in standardization, validation, and clinical implementation, accumulating evidence supports the feasibility of biomarker-guided individualized care. Ultimately, comprehensive biomarker integration holds substantial promise for advancing mechanism-based, personalized management and improving long-term outcomes in MS.

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