ISSN(O): 3107-7889

Jana Nexus: Journal of Health and Medicine

Publisher's Name: Jana Publication and Research LLP

https://www.jananexushm.com

REVIEWER'S REPORT

Manuscript No.: JNHM- 160

Title: Biochemical features, pathophysiology and medicalsignificance of Matrix Metalloproteinase-9 (MMP-9): a review article,

Recommendation:

Accept after minor revision

Rating	Excel.	Good	Fair	Poor
Originality			✔	
Techn. Quality			✔	
Clarity		✔		
Significance	✔			

Reviewer's ID: JPR-Bilqees Hamza

Detailed Reviewer's Report

Overview

The manuscript presents a comprehensive literature review focusing on Matrix Metalloproteinase-9 (MMP-9/gelatinase B), detailing its structural domain organization, physiological homeostatic roles, involvement in pathological tissue remodeling, cancer biology, cardiovascular and inflammatory diseases, and its emerging utility as a clinical biomarker and therapeutic target. The authors trace MMP-9 from its domain structure—comprising the N-terminal propeptide, zinc-binding catalytic domain, fibronectin type II repeats, and hemopexin-like C-terminal domain—to its functional cleavage of both extracellular matrix (ECM) components (such as type IV collagen, gelatin, and elastin) and non-ECM substrates (including cytokines, chemokines, and surface receptors).

The manuscript effectively synthesizes current understanding across several clinical domains. In oncology, the role of MMP-9 in basement membrane degradation, vascular endothelial growth factor (VEGF) mobilization, pre-metastatic niche formation, and immune evasion (via cleavage of CXCL9/10/11 and CD25) is thoroughly outlined. In cardiovascular, respiratory, and musculoskeletal conditions, the diagnostic and prognostic relevance of circulating MMP-9 levels and MMP-9/TIMP-1 ratios is well developed, particularly concerning acute myocardial infarction, aortic aneurysms, chronic obstructive pulmonary disease (COPD), rheumatoid arthritis, and Duchenne muscular dystrophy (DMD). Finally, the manuscript highlights recent advances in targeted biotherapeutics, such as the monoclonal antibody andecaliximab, designed to overcome the historical musculoskeletal toxicity of broad-spectrum zinc-chelating inhibitors.

ISSN(O): 3107-7889
Jana Nexus: Journal of Health and Medicine
Publisher's Name: Jana Publication and Research LLP
https://www.jananexushm.com

REVIEWER'S REPORT

While the review addresses a highly relevant topic with significant clinical depth, several formatting errors, citation inconsistencies, typographical oversights, and structural redundancies require substantial revision prior to publication.

Detailed Recommendations for Improvement

1. Citation Inconsistencies and Bibliographic Formatting

- **Duplicate Citation Entries:** References 12 and 26 are completely identical (*Sharma et al., 2018 / Huang, 2018* referencing the exact same paper in *Sensors*, 18(10), p. 3249). The reference list must be systematically scrubbed to eliminate duplicates, and corresponding inline text callouts adjusted accordingly.
- **Inconsistent Reference Styling:** The bibliography exhibits mixed formatting styles. For example, several entries utilize standard abbreviation styles while others retain full titles with varying capitalization rules. Additionally, standard journal volume/issue parentheses and DOI formatting should be standardized across all entries in full accordance with the journal guidelines.
- **Mismatched Text Callouts:** In the third paragraph of "MMP-9 in Tissue Homeostasis and Pathological Remodeling", the text reads "...in chronic obstructive pulmonary disease (COPD) patients [9] (Dimic-Janjic et al., 2023)". A numeric brackets artifact ([9]) is left directly adjacent to the author-year parenthetical callout. The authors should adopt a single, uniform citation system throughout the draft.

2. Typographical, Grammatical, and Structural Refinements

- **Textual Artifacts & Header Noise:** The manuscript contains visible layout and conversion artifacts, including stray running strings like "INHM" under the Introduction header and "NHM" above the reference list. These editorial artifacts must be removed.
- **Grammatical Integrity in Scientific Prose:** Several key sentences suffer from fragmented syntax or awkward phrasing that hinders readability.
    - In the Introduction: "Serum MMP-9 levels are a poor outcome predictor in acute inflammatory syndromes (examples: COVID-19); with ranges (most extreme vs non-extreme patients give large difference (Ding et al., 2023)". This should be rephrased for academic clarity (e.g., "Elevated serum MMP-9 levels serve as a predictor of adverse outcomes in acute inflammatory syndromes, including COVID-19, with significant concentration variances observed between severe and non-severe patient cohorts").
    - In the Pathological Remodeling section: "These data are being that MMP-9 is a marker of matrix turnover not only during but also plays an active role on disease progression". This sentence is grammatically incomplete and requires re-writing.

ISSN(O): 3107-7889
Jana Nexus: Journal of Health and Medicine
Publisher's Name: Jana Publication and Research LLP
https://www.jananexushm.com

REVIEWER'S REPORT

- **Inconsistent Chemical and Biological Nomenclature:** Ensure consistent notation for ionic species and molecular pathways (e.g., standardizing Zn^{2+} vs Zn^{+2}, and italicizing gene/protein nomenclature appropriately according to standard biochemical conventions).

3. Conceptual & Content Enhancement

- **Tabular Summary of Clinical Indications:** To enhance the visual scaffolding and reader engagement, the authors are strongly encouraged to add a comprehensive summary table comparing the clinical relevance of MMP-9 across major disease categories. This table should contrast the pathophysiological role, biofluid measured (e.g., serum, plasma, synovial fluid, CSF), clinical utility (diagnostic, prognostic, therapeutic monitoring), and current targeted therapeutic strategies for each disease state.
- **Critical Evaluation of Preclinical Limitations:** While the manuscript mentions obstacles regarding inhibitor specificity, a more detailed discussion on why historical broad-spectrum matrix metalloproteinase inhibitors (MMPIs) failed in clinical trials (e.g., musculoskeletal syndrome/MSS, lack of domain specificity, target overlap with protective MMPs like MMP-8) would add significant analytical depth to the section on novel targeted therapies.

Final Recommendation

Decision: Minor Revisions

Note to the Editor

The review article titled *"Biochemical features, pathophysiology and medical significance of Matrix Metalloproteinase-9 (MMP-9): a review article"* provides a thorough and timely consolidation of the literature surrounding MMP-9 in tissue homeostasis, oncology, and inflammatory disorders. The author team has successfully captured the dual nature of MMP-9 as both a functional pathological effector and a clinically accessible diagnostic/prognostic biomarker.

However, the manuscript in its present form requires revisions to rectify duplicate citations, repair broken/fragmented sentence structures, clear structural layout artifacts, and consolidate the citation framework. Incorporating a structured summary table of MMP-9 disease associations and therapeutic modalities will significantly elevate the utility and impact of this review for the journal's readership.

.