Interplay of Periodontal Bacterial Metabolites in the Progression of Coronary Artery Disease: A System Biological Approach

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INTRODUCTION

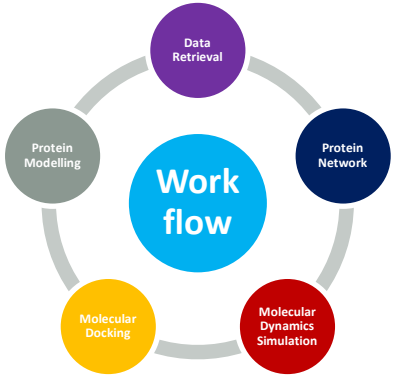
Metalloproteinase inhibitor (TIMP1) plays a pivotal role in cellular signaling, differentiation, cell death, and migration by binding to target metalloproteinases, forming complexes with other molecules (collagenases) to inactivate them. However, the expression of TIMP1 is reduced in both Periodontal disease (PD) and coronary artery disease (CAD), leading to an upregulation of other metalloproteinases. This research explores the hypothesis that metabolites released from (*Porphyromonas gingivalis)*, a prevalent bacterium in atherosclerotic patients, may inhibit TIMP1, thereby influencing CAD progression.

OBJECTIVES

- To retrieve the metabolites of *Porphyromonas gingivalis* from VMH database.
- To identify the TIMP1 regulatory proteins through network analysis
- To explore the effect of metabolites against the target TIMP1 via molecular docking
- To assess the stability of metabolite and TIMP1 with the help of MD simulation

METHODS

- In the initial phase, metabolites from *Porphyromonas gingivalis* were retrieved from the Virtual Metabolic Human (VMH) database.
- The proteins associated with the TIMP1 were identified through the construction of a protein interaction network in Cytoscape.
- Subsequently, the TIMP1 underwent modeling using the Swiss-Model web server and was docked with bacterial metabolites.
- Furthermore, the structural stability of both the protein and metabolite was evaluated over a 100 ns simulation period.

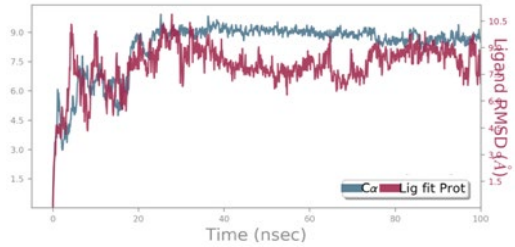


CONCLUSION

The computational analysis suggests that these metabolites may disrupt the function of TIMP1, thereby contributing to the elevated levels of metalloproteinases observed in CAD patients.

RESULTS

- In total, 370 metabolites from *Porphyromonas gingivalis* were obtained from the database.
- Notably, the network analysis revealed that MMP1, MMP9, and MMP14 were closely associated with TIMP1.
- Molecular docking outcomes demonstrated that Malonyl CoA displayed a binding affinity of -8.82 kcal/mol at the active sites of TIMP1.
- Additionally, a stable complex between TIMP1 and Malonyl CoA was observed throughout the simulation period.



Reference

Sanz M, Marco Del Castillo A, Jepsen S, et al. Periodontitis and cardiovascular diseases: Consensus report. *J Clin Periodontol*. 2020;47(3):268-288. doi:10.1111/jcpe.13189

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