"The AGE-RAGE Axis and its Crucial Role in Coronary Artery Disease- A New Era of Personalised Medicine"

Pradeep Kumar Dabla*

Professor, Department of Biochemistry, G. B. Pant Institute of Postgraduate Medical Education & Research (GIPMER), Associated Maulana Azad Medical College, GNCTD, Delhi-110002, India.

*Corresponding Author(s): Pradeep Kumar Dabla

Professor, Department of Biochemistry, G. B. Pant Institute of Postgraduate Medical Education & Research (GIP-MER), Associated Maulana Azad Medical College, GNCTD, Delhi-110002, India.

Email: pradeep_dabla@yahoo.com

Editorial

Coronary Artery Disease (CAD) is a leading cause of morbidity and mortality worldwide, posing significant challenges to healthcare systems and societies at large. The disease manifests as a result of atherosclerosis, a condition characterized by the formation of atherosclerotic plaques within the coronary arteries, impeding blood flow to the heart muscle which can lead to angina, myocardial infarction, and potentially life-threatening arrhythmias.

Coronary Artery Disease (CAD) stands as a formidable health challenge, accounting for millions of deaths globally each year. As medical science delves deeper into the intricacies of this con- dition, emerging evidence points towards the pivotal role of the AGE-RAGE axis in its pathophysiology. Understanding this mo-lecular mechanism not only offers fresh perspectives on disease management but also opens avenues for targeted therapeutic interventions.

AGEs and RAGE: An overview

Advanced Glycation End products (AGEs) are a diverse group of compounds that form through non-enzymatic reactions be-tween reducing sugars and free amino groups of proteins, lipids, and nucleic acids. These compounds accumulate in various tis-sues with age, hence the name. Once formed, AGEs can interact with a cell surface receptor known as RAGE (Receptor for AGEs),

initiating a cascade of inflammatory and oxidative processes.

The Molecular interplay in CAD

In recent years, the landscape of CAD research has been enriched by the discovery of intricate molecular pathways underlying the disease process. Among these, the Advanced Glycation End products (AGEs) and their receptor, RAGE (Receptor for AGEs), have garnered significant attention. AGEs are compounds that accumulate in various tissues over time, particularly in the setting of conditions like diabetes and aging. Their interaction with RAGE sets off a cascade of cellular responses that have profound implications for vascular health.The interaction between AGEs and RAGE sets off a series of events detrimental to vascular health. Activation of RAGE leads to the upregulation of pro-inflammatory cytokines, adhesion molecules, and growth factors, fostering a pro-atherogenic environment within the arterial walls. This chronic inflammatory state promotes the recruitment of immune cells, primarily monocytes, which transform into macrophages. These macrophages engulf oxidized LDL cholesterol, giving rise to foam cells—the hallmark of early atherosclerotic lesions.

Moreover, the AGE-RAGE axis induces oxidative stress by stimulating the production of Reactive Oxygen Species (ROS) within vascular cells. ROS further exacerbate endothelial dysfunction, a critical precursor to atherosclerosis. In addition to these direct effects, AGEs can also modulate intracellular signalling pathways involved in vascular remodelling and thrombosis, further complicating the disease process.

Therapeutic implications

Given the central role of the AGE-RAGE axis in CAD progression, targeting this molecular pathway emerges as a promising therapeutic strategy. Several approaches are under investigation:

1.   RAGE blockade: Inhibiting the interaction between AGEs and RAGE using specific antagonists or antibodies can mitigate downstream inflammatory responses. Preliminary studies indicate that RAGE blockade can reduce atherosclerotic plaque formation and improve vascular function in animal models.

2.   AGE inhibition: Therapies aimed at reducing the formation or accumulation of AGEs, such as dietary modifications or pharmacological agents, hold potential in attenuating vascular complications associated with CAD.

3.   Antioxidant therapy: Given the prominent role of oxidative stress in CAD pathogenesis, antioxidant agents capable of neutralizing ROS may offer protective benefits. Natural antioxidants, including vitamins C and E, as well as synthetic compounds, are being explored for their potential in combating oxidative damage.

4.   Lifestyle interventions: Modifying lifestyle factors known to accelerate AGE formation, such as high sugar consumption and smoking, can complement pharmacological interventions. Adopting a healthy diet, engaging in regular physical activity, and avoiding tobacco use are cornerstone strategies in CAD prevention and management.

Conclusion

The intricate relationship between the AGE-RAGE axis and coronary artery disease underscores the multifaceted nature of vascular pathologies. The exploration of the AGE-RAGE axis in the context of CAD represents a convergence of molecular biology, clinical medicine, and translational research. As our understanding of this molecular mechanism deepens, the prospects for innovative therapeutic interventions brighten. However, translating these insights into clinical practice necessitates rigorous research, collaborative efforts, and a patient-centric approach.

While the journey towards unravelling the complexities of CAD continues, the AGE-RAGE axis stands out as a beacon of hope in the quest for effective treatments. By targeting this molecular pathway, we may usher in a new era of personalized medicine, where interventions are tailored to the unique molecular profiles of individual patients, paving the way for improved outcomes and enhanced quality of life.

References

1.   Khalid M, Petroianu G, Adem A. Advanced Glycation End Products and Diabetes Mellitus: Mechanisms and Perspectives. Biomolecules. 2022; 12: 542.

2.   Cepas V, Collino M, Mayo JC, Sainz RM. Redox Signaling and Advanced Glycation Endproducts (AGEs) in Diet-Related Diseases. Antioxidants (Basel). 2020; 9: 142.

3.   Dariya B, Nagaraju GP. Advanced Glycation End Products in Diabetes, Cancer and Phytochemical Therapy. Drug Discov. Today. 2020; 25: 1614–1623.

4.   Qiu HY, Hou NN, Shi JF, Liu YP, Kan CX, et al. Comprehensive Overview of Human Serum Albumin Glycation in Diabetes Mellitus. World J. Diabetes. 2021; 12: 1057–1069.

5.   Helsley RN, Moreau F, Gupta MK, Radulescu A, DeBosch B, et al. Tissue-Specific Fructose Metabolism in Obesity and Diabetes. Curr. Diab. Rep. 2020; 20: 64.