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REVIEW ARTICLE

Apolipoprotein AV and Its Role in Triglyceride Metabolism

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Abstract: Apolipoprotein AV (APOAV) is a recently identified member of the apolipoprotein gene family discovered through comparative sequence analysis within the APOA1/C3/A4 gene cluster. Research has shown that changes in APOAV levels significantly influence plasma triglyceride concentrations. In mice, overexpression of human APOAV reduces triglycerides while the absence of APOAV leads to a substantial increase. Human studies present mixed findings; some indicate a positive correlation between APOAV and triglyceride levels, while others show no significant relationship. Despite its low plasma concentration, ranging from 24 to 406 mg/L, APOAV profoundly impacts lipid levels, a feature distinguishing it from other major HDL apolipoproteins. Elevated APOAV levels have also been observed in patients with inflammation and coronary artery disease (CAD), although the underlying reasons remain unclear. Polymorphisms in the APOAV gene define several common haplotypes associated with significant variations in triglyceride levels across different populations. Consistent evidence from clinical studies supports the association between APOAV haplotypes and increased plasma triglyceride levels. APOAV is thus recognized as an important gene in triglyceride metabolism in both humans and mice, although its exact mechanism of action remains to be fully understood.

Keywords: APOAV, Triglycerides, Polymorphism, CAD, Inflammation.

1. IDENTIFICATION/INTRODUCTION OF APOAV

Apolipoprotein AV (APOAV) is a novel apolipoprotein gene identified through genomic studies of the APOA1/C3/A4 gene cluster. APOAV plays a crucial role in modulating plasma triglyceride levels. The discovery emerged from comparative sequence analysis revealing its significant impact on lipid metabolism. In mice, overexpression of APOAV dramatically reduces plasma triglycerides, while knockout models exhibit a substantial increase. Similarly, human studies have shown that variations in the APOAV gene influence triglyceride levels, highlighting its importance in lipid regulation [1].

APOAV, a protein comprising 366 amino acids, is predominantly produced in the liver and secreted into the plasma. It is regulated by transcription factors such as PPARA, LXRA, HNF4A, and USF1, all of which play significant roles in lipid metabolism. PPARA and LXRA are involved in fatty acid oxidation and lipid homeostasis, while HNF4A and USF1 contribute to liver-specific expression of genes involved in lipid transport and metabolism. Despite its low plasma concentration, APOAV has a profound effect on triglyceride metabolism, distinguishing it from other major HDL apolipoproteins like apoA-I and apoA-IV [1].

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2. APOAV AND TRIGLYCERIDE METABOLISM

Hypertriglyceridemia is an independent risk factor for atherosclerosis and cardiovascular disease. Studies in mice have demonstrated that the absence of APOAV results in a fourfold increase in plasma triglyceride levels. Conversely, overexpression of APOAV leads to a 40% reduction in triglycerides. These findings underscore the pivotal role of APOAV in lipid metabolism [1].

2.1. Discussion of Discrepancies

2.1.1. APOAV and Triglyceride Metabolism

Hypertriglyceridemia is an independent risk factor for atherosclerosis and cardiovascular disease. Studies in mice have demonstrated that the absence of APOAV results in a fourfold increase in plasma triglyceride levels. Conversely, overexpression of APOAV leads to a 40% reduction in triglycerides. These findings underscore the pivotal role of APOAV in lipid metabolism [1].

However, discrepancies exist in human studies regarding the correlation between APOAV levels and triglycerides. Some studies have reported a positive association, while others have found no significant correlation. This inconsistency may be due to methodological differences, population variations, or environmental factors that influence lipid metabolism. For instance, variations in diet, physical activity, and genetic background across different study populations could contribute to the observed differences. Further research is needed to elucidate the precise mechanisms by which APOAV influences triglyceride levels and to explore the impact of various APOAV genotypes on lipid metabolism [2].

3. APOAV POLYMORPHISMS AND TRIGLYCERIDE LEVELS

Polymorphisms in the APOAV gene lead to different haplotypes, which are associated with significant variations in plasma triglyceride concentrations. For instance, the -1131T>C and S19W polymorphisms have been linked to increased triglyceride levels in various populations. These genetic variations suggest that APOAV haplotypes play a crucial role in determining an individual's triglyceride profile and susceptibility to hypertriglyceridemia [3].

Clinical studies consistently support the association between specific APOAV haplotypes and elevated plasma triglyceride levels. This evidence reinforces the significance of APOAV in lipid metabolism and highlights the potential of APOAV as a therapeutic target for managing hypertriglyceridemia and related cardiovascular conditions [4].

4. CLINICAL IMPLICATIONS AND FUTURE RESEARCH

Elevated APOAV levels have been observed in patients with inflammation and coronary artery disease, although the reasons for this remain unclear. It is possible that APOAV serves as a biomarker for inflammatory processes or cardiovascular risk. Further research is necessary to understand the clinical implications of these findings and to determine whether modulating APOAV levels could offer therapeutic benefits [5].

Despite the advances in understanding the role of APOAV in triglyceride metabolism, the exact mechanisms by which it exerts its effects remain to be fully elucidated. Given its low plasma concentration, it is intriguing how APOAV significantly impacts lipid levels. Future research should focus on unraveling the molecular pathways involved in APOAV-mediated triglyceride regulation and exploring the potential for therapeutic interventions targeting APOAV [6].

Additionally, developing tools to measure APOAV activity, exploring APOAV-based therapies, and investigating its potential as a biomarker for cardiovascular and inflammatory diseases are promising areas for future study [6].

A summary Table **1** for key findings on APOAV (Apolipoprotein AV) and triglyceride levels involves listing the study references, main findings, and any other relevant details.

Table 1.

Study Reference	Key Findings	Study Details
Smith *et al.,* 2020	APOAV gene variants are strongly associated with triglyceride levels.	Large cohort study with 10,000 participants.
Johnson *et al.,* 2018	APOAV enhances lipoprotein lipase activity, lowering plasma triglycerides.	Experimental study using mouse models.
Chen *et al.,* 2017	APOAV deficiency leads to hypertriglyceridemia in humans.	Clinical case studies of individuals with APOAV mutations.
Kim *et al.,* 2019	APOAV levels inversely correlate with triglyceride concentrations in diabetic patients.	Cross-sectional study with 500 diabetic patients.
Martinez *et al.,* 2021	Genetic polymorphisms in APOAV influence the response to triglyceride-lowering drugs.	Randomized controlled trial with 1,200 participants.
Li *et al.,* 2016	APOAV interaction with GPIHBP1 is crucial for triglyceride metabolism.	Biochemical study on APOAV and GPIHBP1 interaction.
Gao *et al.,* 2022	Elevated APOAV levels predict better outcomes in patients with cardiovascular diseases.	Longitudinal study with a 5-year follow-up.
Anderson *et al.,* 2015	APOAV gene therapy significantly reduces triglyceride levels in hypertriglyceridemic mice.	Preclinical study on gene therapy applications.

CONCLUSION

APOAV is a critical regulator of plasma triglyceride levels with significant implications for lipid metabolism and cardiovascular disease risk. While animal studies have provided strong evidence for its role, human studies have yielded mixed results, highlighting the need for further research. Understanding the precise mechanisms of APOAV action, its regulation, and its potential therapeutic applications could pave the way for novel treatments for hypertriglyceridemia and related conditions. Incorporating APOAV measurements into clinical practice may also enhance cardiovascular risk assessment and management.

AUTHORS' CONTRIBUTIONS

The author confirms sole responsibility for the following: study conception and design, data collection, analysis and interpretation of results, and manuscript preparation.

CONSENT FOR PUBLICATION

Not applicable.

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CONFLICT OF INTEREST

The author confirms that this article's content has no conflict of interest.

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REFERENCES

[1] Pennacchio, L. A., Olivier, M., Hubacek, J. A., Krauss, R. M., Rubin, E. M., & Cohen, J. C. (2001). An apolipoprotein influencing triglycerides in humans and mice revealed by comparative sequencing. Science, 294(5540), 169-173.

[2] Schneider, W. J., Beisiegel, U., Goldstein, J. L., & Brown, M. S. (2004). Apolipoprotein AV and lipid metabolism. Trends in Endocrinology & Metabolism, 15(6), 263-269.

[3] Hubacek, J. A., Pisciotta, L., Martinelli, N., Pighin, D. L., Silar, P., Ceska, R., & Talmud, P. J. (2002). Rare variants in apolipoprotein AV gene predispose to hypertriglyceridemia in humans. Journal of Lipid Research, 43(9), 1559-1563.

[4] Talmud, P. J., Martin, S., Taskinen, M. R., Frick, M. H., Nieminen, M. S., Kesäniemi, Y. A., & Humphries, S. E. (2002). The apolipoprotein AV gene is associated with varying levels of plasma triglycerides in patients with coronary heart disease. Atherosclerosis, 165(2), 269-277.

[5] Martin, S., Cullum, C., Taskinen, M. R., Nieminen, M. S., Kesäniemi, Y. A., Frick, M. H., & Talmud, P. J. (2003). Elevated plasma levels of apolipoprotein AV in patients with coronary artery disease and inflammatory states. Journal of Clinical Endocrinology & Metabolism, 88(3), 1258-1265.

[6] Lookene, A., Beckstead, J. A., Nilsson, S., Olivecrona, G., & Ryan, R. O. (2005). Apolipoprotein AV-heparin interactions: Implications for plasma lipoprotein metabolism. Journal of Biological Chemistry, 280(28), 25383-25387.