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[관심분야]

Diabetic complications, mitochondria, immunometabolism

[논문]

1. Comprehensive overview of the role of mitochondrial dysfunction in the pathogenesis of acute kidney ischemia-reperfusion injury: a narrative review. J Yeungnam Med Sci. 2024.
2. Mitochondrial dysfunctions in T cells: focus on inflammatory bowel disease. Front Immunol. 2023 Sep 22;14:1219422.
3. Inhibition of pyruvate dehydrogenase kinase 4 ameliorates kidney ischemia-reperfusion injury by reducing succinate accumulation during ischemia and preserving mitochondrial function during reperfusion. Kidney Int. 2023 Oct;104(4):724-739.
4. Upregulation of the ERRγ-VDAC1 axis underlies the molecular pathogenesis of pancreatitis. Proc Natl Acad Sci U S A. 2023 May 16;120(20):e2219644120.
5. Lee H, Jeon JH, Lee YJ, Kim MJ, Kwon WH, Chanda D, Thoudam T, Pagire HS, Pagire SH, Ahn JH, Harris RA, Kim ES, Lee IK. Inhibition of Pyruvate Dehydrogenase Kinase 4 in CD4+ T Cells Ameliorates Intestinal Inflammation. Cell Mol Gastroenterol Hepatol. 2023;15(2):439-461.

Lessons from clinical trials of Inclisiran: a first-in-class siRNA therapy against PCSK9

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Despite the progress in lipid-lowering treatments, such as statins, a notable number of patients remain unable to reach optimal low-density lipoprotein cholesterol (LDL-C) levels due to reasons like statin intolerance, insufficient response, or severe hypercholesterolemia. This gap in effective management has led to the exploration of new therapeutic avenues, notably targeting the PCSK9 (proprotein convertase subtilisin/kexin type 9) pathway, which plays a vital role in modulating hepatic LDL receptor turnover and cholesterol balance. Inclisiran, a pioneering siRNA (small interfering RNA) therapy, stands out in this new class of drugs by utilizing RNA interference to selectively suppress PCSK9 gene expression in the liver, thus enhancing LDL receptor availability and promoting the removal of LDL-C from the circulation.

The distinct mechanism of action of inclisiran, which allows for prolonged reductions in PCSK9 and LDL-C levels, offers a viable supplement or alternative to conventional lipid-lowering strategies. The efficacy and safety of inclisiran have been thoroughly validated in the ORION clinical trials, which have shown substantial LDL-C reduction with a well-tolerated safety profile and the practicality of bi-annual dosing. These findings emphasize inclisiran's potential to enhance adherence and patient outcomes in managing hypercholesterolemia.

This presentation seeks to detail the biological rationale behind the therapeutic effects of inclisiran, examine the critical data from the ORION trials highlighting its efficacy and safety, and consider its role in the broader context of cardiovascular risk management. Through the introduction of inclisiran, a novel and effective treatment option is now available, marking a significant advance in the effort to alleviate the impact of hypercholesterolemia and, by extension, reduce the global burden of cardiovascular disease. The incorporation of findings from the ORION studies into our understanding of inclisiran's profile underscores its potential as a transformative element in the lipid management landscape.