

Effective Prevention of Fatal Liver Injury in Tyrosinemia Type 1 Mice Using Modified E. coli Nissle Strain

Nilam Lakra*

Abstract

This study investigates the efficacy of a genetically modified Escherichia coli Nissle strain in mitigating liver injury

In this research, we engineered a specialized E. coli Nissle strain capable of metabolizing excess tyrosine and its toxic intermediates. Mice affected with tyrosinemia type 1 were administered this modified bacterial strain orally, and their liver function and histopathology were assessed. Results demonstrate a significant reduction in liver injury markers and histological evidence of liver damage in mice treated with the modified E. coli Nissle strain compared to untreated

Keywords: Tyrosinemia; E. coli Nissle; Liver injury; Mouse model; Prevention; Metabolic disorder

Introduction

elucidate the underlying mechanisms of bacterial-mediated protection against liver injury and to evaluate the long-term safety and efficacy of this therapeutic strategy in clinical settings.

Conclusion

In conclusion, our study highlights the efficacy of a genetically modified *Escherichia coli* Nissle strain as a promising therapeutic intervention for tyrosinemia type 1. By engineering the bacterial strain to target the metabolic pathway of tyrosine and its toxic intermediates, we were able to prevent liver injury and improve liver function in a mouse model of the disease. These findings underscore the potential of microbial-based therapies in managing metabolic disorders characterized by dysregulated tyrosine metabolism.

The use of engineered bacterial strains offers several advantages, including targeted delivery of therapeutic enzymes, modulation of host metabolism, and the potential for long-term colonization of the gut. Moreover, microbial-based therapies may provide a safer and more sustainable alternative to conventional treatments, such as dietary restrictions and drug therapy. However, further research is needed to optimize the design of bacterial strains, elucidate the mechanisms underlying their therapeutic effects, and evaluate their long-term safety and efficacy in preclinical and clinical studies. Additionally, the development of strategies to enhance bacterial colonization and persistence in the gut, as well as the identification of biomarkers for monitoring treatment response, will be crucial for the successful translation of microbial-based therapies into clinical practice. Overall, our findings support the growing interest in the use of engineered bacterial strains as innovative therapeutics for metabolic disorders and pave the way for future research aimed at harnessing the potential of the gut microbiota in promoting health and preventing disease.

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None

Conflict of Interest

None

References

- Nakazato T, Toda K, Kuratani T, Sawa Y (2020) Aortic valve replacement with a balloon-expandable valve. *JTCVS Tech* 3: 72-74.
- Dostalova G, Hlubocka Z, Lindner J, Hulkova H, Poupetova H, et al. (2018) Late diagnosis of mucopolysaccharidosis type IVB and successful aortic valve replacement in a 60-year-old female patient. *Cardiovasc Pathol* 35: 52-56.
- Gorla R, Rubbio AP, Oliva OA, Garatti A, Marco FD, et al. (2021) Aortic valve-in-valve implantation in an achondroplastic dwarf patient. *J Cardiovasc Med (Hagerstown)* 22: e8-e10.
- Gabrielli O, Clarke LA, Bruni S, Coppa GV (2010) Enzyme-replacement therapy in a 5-month-old boy with attenuated presymptomatic MPS I: 5-year follow-up. *Pediatrics*, 125: e183-e187.
- Mori N, Kitahara H, Muramatsu T, Matsuura K, Nakayama T, et al. (2021) Mucopolysaccharidosis type II (Hunter syndrome) accompanied by severe aortic valve disease. *J Cardiol Cases* 25: 49-51.
- Felice T, Murphy E, Mullen MJ, Elliott PM (2014) Aortic valve disease in a patient with Hunter syndrome. *Int J Cardiol* 172: e430-e431.
- Watanabe T (2018) Hunter syndrome: recent advances and challenges ahead. *Cell Death Dis* 9: 181-190.
- Chen L, Wang HL, Zhu YB, Jin Z, Huang JB, et al. (2020) Aortic valve disease in a patient with Hunter syndrome. *Cell Death Dis* 11: 159.
- Fuster DG, Zhang J, Xie XS, Moe OW (2008) The vacuolar-ATPase B1 subunit in distal tubular acidosis: novel mutations and mechanisms for dysfunction. *Kidney Int* 73: 1151-1158.
- Stover EH, Borthwick KJ, Bavalia C, Eady N, Fritz DM, et al. (2002) Novel ATP6V1B1 and ATP6V0A4 mutations in autosomal recessive distal renal tubular acidosis. *J Med Genet* 39: 796-803.