Gut Microbiota-Derived Nicotinamide Compounds Regulate Fatty Acid β-Oxidation and Inflammation in MASLD

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AIM

Metabolic dysfunction–associated steatotic liver disease is a major metabolic disorder associated with gut microbiota-derived metabolites involved in metabolism and inflammation. This study investigated the therapeutic effects of NAM, NA, and NR on lipid metabolism, inflammation, and intestinal barrier function in MASLD.

METHODS

Gut microbiota-derived metabolites were analyzed, and the effects of NAM, NA, and NR were tested in cell, animal, and computational studies using a Western diet-induced MASLD model. Their mechanisms were investigated through gene/protein expression, network pharmacology, and molecular docking analyses.

RESULTS

NAM, NA, and NR improved MASLD by promoting fatty acid β-oxidation, reducing inflammation, and strengthening intestinal barrier function. They regulated lipid metabolism, decreased pro-inflammatory cytokines, and increased tight junction proteins, supporting their therapeutic potential in MASLD.

CONCLUSION

Our findings suggest that nicotinamide-related microbial metabolites improve MASLD by enhancing fatty acid β-oxidation, reducing inflammation, and strengthening intestinal barrier function. These results highlight the therapeutic potential of NAM, NA, and NR and suggest that targeting gut microbiota–host metabolic interactions could be an effective strategy for MASLD treatment.

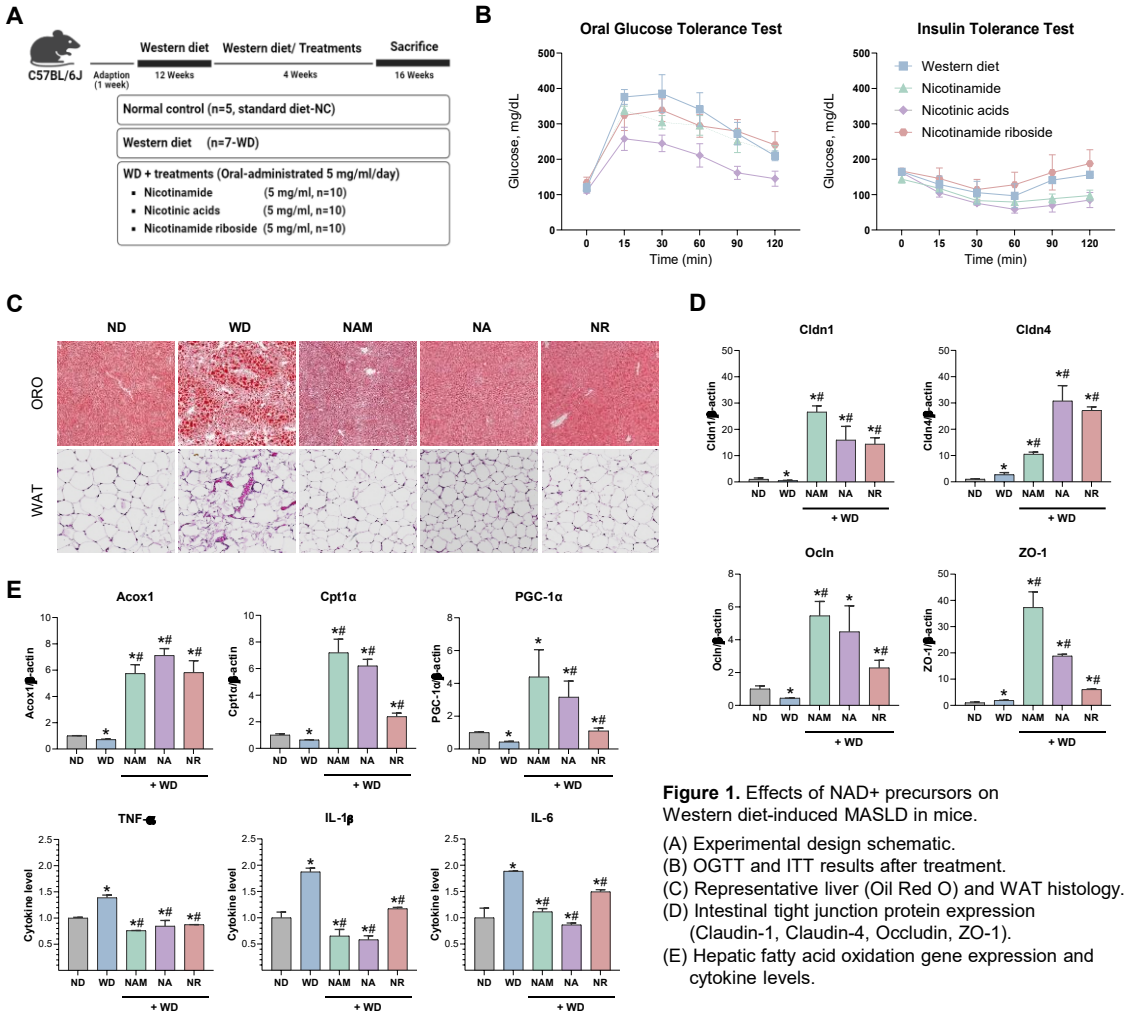

Figure 1. Effects of NAD+ precursors on Western diet-induced MASLD in mice.

(A) Experimental design schematic.
(B) OGTT and ITT results after treatment.
(C) Representative liver (Oil Red O) and WAT histology.
(D) Intestinal tight junction protein expression (Claudin-1, Claudin-4, Occludin, ZO-1).
(E) Hepatic fatty acid oxidation gene expression and cytokine levels.

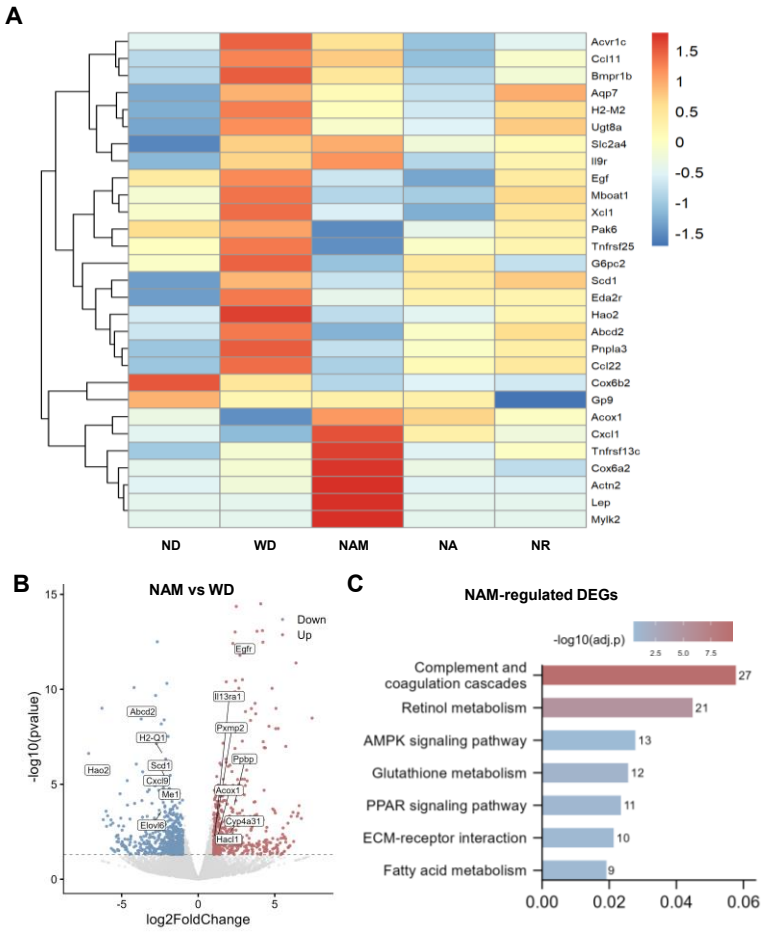

Figure 2. Transcriptomic analysis of NAD⁺ precursor-regulated gene expression.
(A) Heatmap of DEGs across all groups.
(B) Volcano plot of NAM vs. WD comparison.
(C) KEGG pathway enrichment analysis of NAM-regulated DEGs.