

EPIGENETIC CONJUGATE
THERAPY PLATFORM:
RETINOIC ACID-BASED
HDAC INHIBITORS

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Innovative bacterial metabolite
mimicries using nano-oral
delivery to target the digestive
tract for disease prevention
and treatment

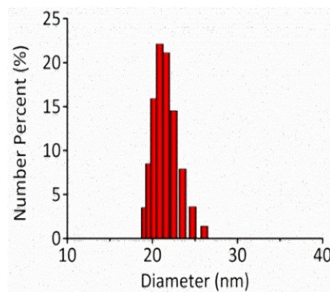
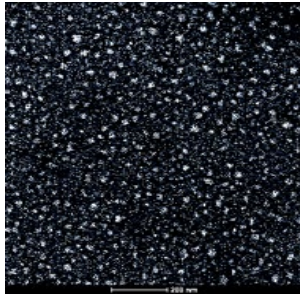
PLATFORM OVERVIEW AND SCIENTIFIC FOUNDATION-

Targeting the Diet-Gut-Liver Axis



EXECUTIVE TECHNOLOGY SUMMARY

Electron microscope photos of
the invented nano-drugs



Innovative Drug Delivery

The platform co-delivers HDAC inhibitors and retinoids to the intestine using a patented polymer-drug conjugate system.

Mechanism of Action

Combines epigenetic remodeling and transcriptional regulation to activate bile acid-regulated metabolism and increase gut immunity.

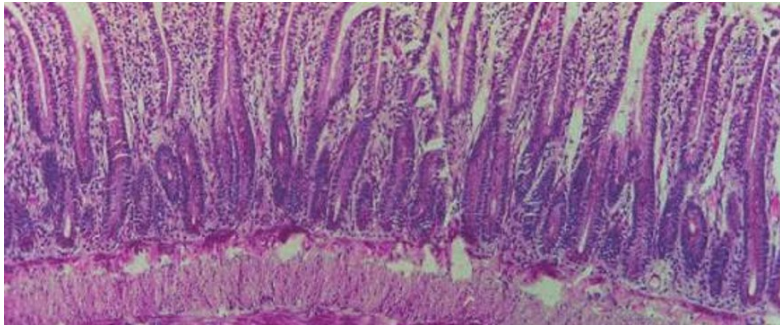
Clinical and Therapeutic Relevance

Improves metabolism and gut immunity, supporting cancer prevention and treatment through validated mechanisms.

Platform Flexibility

Adaptable chemistry supports multiple indications and future pipeline expansion beyond a single asset.

UNMET CLINICAL NEED IN MUCOSAL VULNERABILITY



Poultry: High stocking density, suboptimal feed formulations, and nutritional transitions drive dysbiosis and increase the risk of necrotic enteritis, so robust gut barrier solutions are needed.

Pigs: Diet changes during weaning, anti-nutritional factors in plant-based feeds, and antibiotic withdrawal create critical windows of enteric susceptibility.

Companion Dogs: Highly processed commercial diets and dietary indiscretions exacerbate chronic enteropathies and NSAID/antibiotic-induced mucosal damage, requiring targeted barrier repair.

Human Colitis: Ultra-processed diets and Westernized nutritional patterns trigger gut dysbiosis and mucosal inflammation, driving severe disease recurrence where conventional treatments fail to repair the epithelial barrier.

Antibiotics: Clear pathogens but destroy beneficial microbes and strip protective mucosal layers, leaving the gut vulnerable to reinfection.

Steroids & Immunosuppressants: Suppress downstream inflammation in human colitis without repairing epithelial barriers, leading to high relapse rates and systemic toxicity.

Short-Chain Fatty Acids (SCFAs) & Postbiotics: Rapidly absorbed in the upper GI tract or degraded before reaching target distal tissues at effective therapeutic concentrations.

Fecal Microbiota Transplantation (FMT): Lacks standardization and batch consistency, carries pathogen transmission risks, and fails to directly repair damaged mucosal structures.

UNMET CLINICAL NEED IN METABOLIC DISEASES



T2DM
Hyperlipidemia
Metabolic Dysfunction-Associated Steatohepatitis
(MASH)
Colorectal cancer (CRC)

Obesity, lipid disorders, T2DM, and MASH commonly cluster as metabolic comorbidities that amplify colorectal cancer risk, yet no single approved drug can safely prevent and treat those conditions.

Patients suffering from these chronic metabolic conditions are typically burdened with polypharmacy, requiring them to take a massive daily cocktail of pills to manage their overlapping diseases.

Most prescription medications carry the risk of severe or organ-specific toxic effects when used long-term.

- Statins (Lipid-Lowering): Hepatotoxicity and debilitating, potentially life-threatening myopathy.
- GLP-1 Agonists (Obesity): Induce severe gastrointestinal toxicity (gastroparesis), alongside black-box warnings for pancreatitis and thyroid malignancies.
- THR- β Agonists (MASH): Can cause gastrointestinal distress and carry risks of systemic thyroid hormone imbalances or bone/heart toxicities if selectivity shifts.
- NSAIDs/Aspirin (CRC Prevention): Cause severe gastric mucosal toxicity, resulting in GI bleeding, ulcers, and acute kidney injury.
- Chemotherapies (CRC Treatment): Trigger profound systemic toxicity, including bone marrow suppression and permanent, irreversible peripheral neuropathy.

DIFFERENTIATION FROM EXISTING MEDICATIONS

Our inventions solve these challenges by specifically targeting the digestive tract with high bioavailability and an absolute safety profile.

Retinoids (Retinoic Acid/Tretinoin)

The Failure: Over 95% of orally delivered Tretinoin is absorbed directly into the plasma to treat APL/RAR α abnormalities, leaving metabolites in the plasma and urine.

The Deficit: The digestive tract completely fails to uptake orally delivered retinoids, rendering them useless for localized gut and colorectal therapies.

Synthetic HDAC Inhibitors (Vorinostat/SAHA)

The Failure: Oral SAHA used for cutaneous T-cell lymphoma yields a poor clinical response rate of only 30%.

The Deficit: Severe adverse reactions occur in over 50% of patients, and the compound is completely contraindicated in individuals with hepatic dysfunction.

Short-Chain Fatty Acids (Sodium Butyrate)

The Failure: Clinical trials using Sodium Butyrate to treat acute leukemia were unsuccessful.

The Deficit: The molecule possesses critically low bioavailability, preventing it from reaching therapeutic thresholds in target tissues.

Bile Acid Receptor FXR Agonists (Obeticholic Acid)

The Failure: Approved only for primary biliary cholangitis, this class is severely limited in broad metabolic applications.

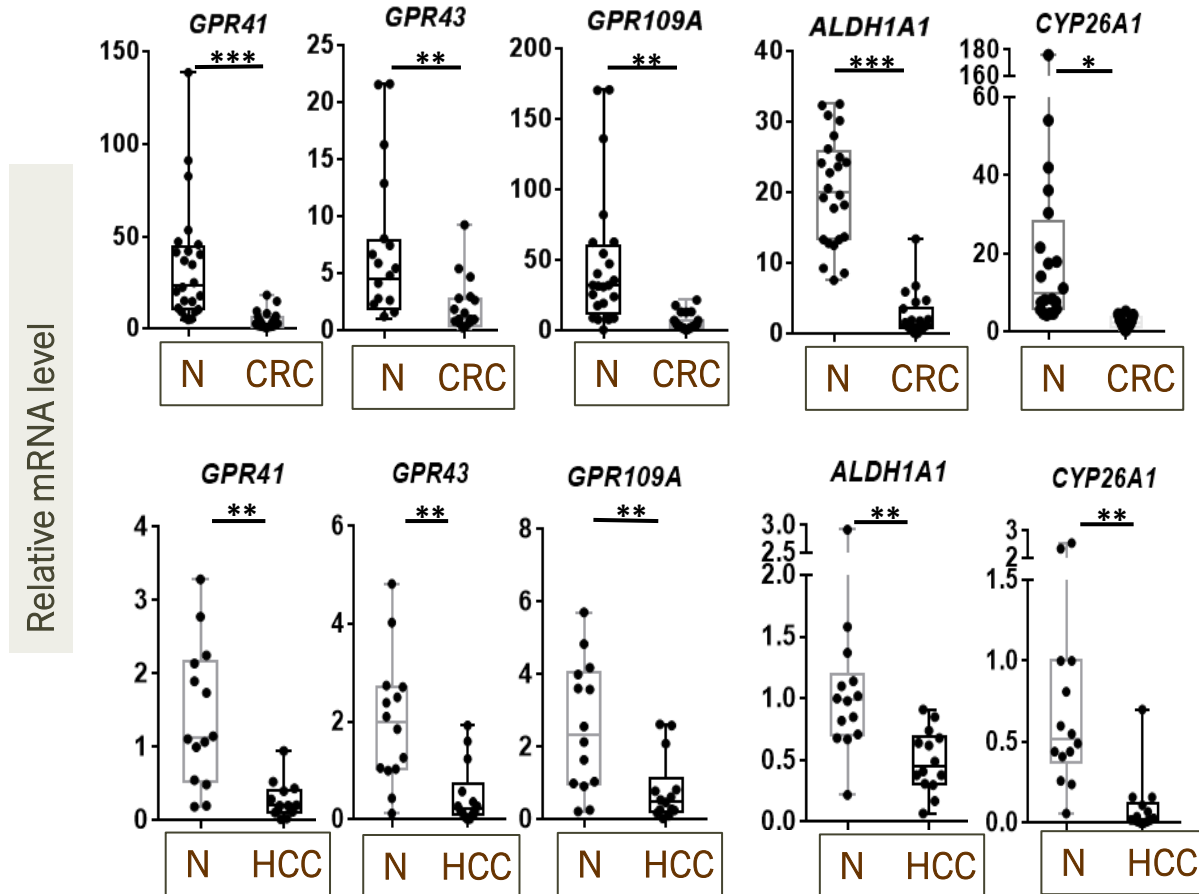
The Deficit: Highly toxic to the liver and systemic pathways.

SCIENTIFIC RATIONALE AND TECHNOLOGICAL DIFFERENTIATION

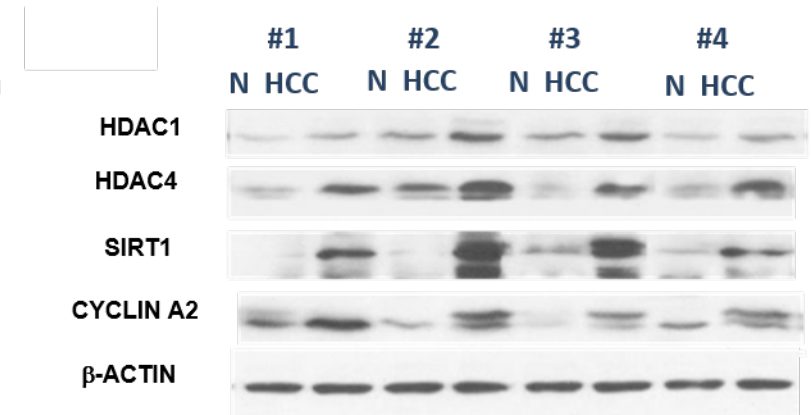
TARGET DISCOVERY BASED ON CLINICAL FINDINGS

The targets are identified based on signaling deficiencies commonly found in CRC and HCC patients, i.e., the gut-liver axis.

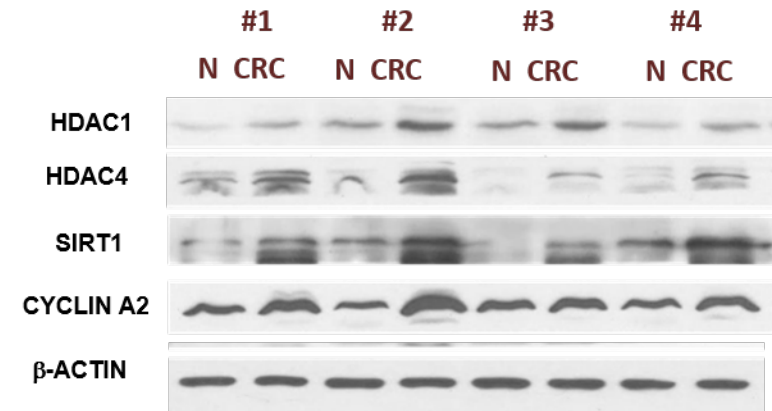
The platform combines HDAC inhibition and retinoid signaling via a polymeric conjugate to treat complex metabolic diseases, improve gut immunity, and prevent and treat colorectal cancer.



Human
HCC

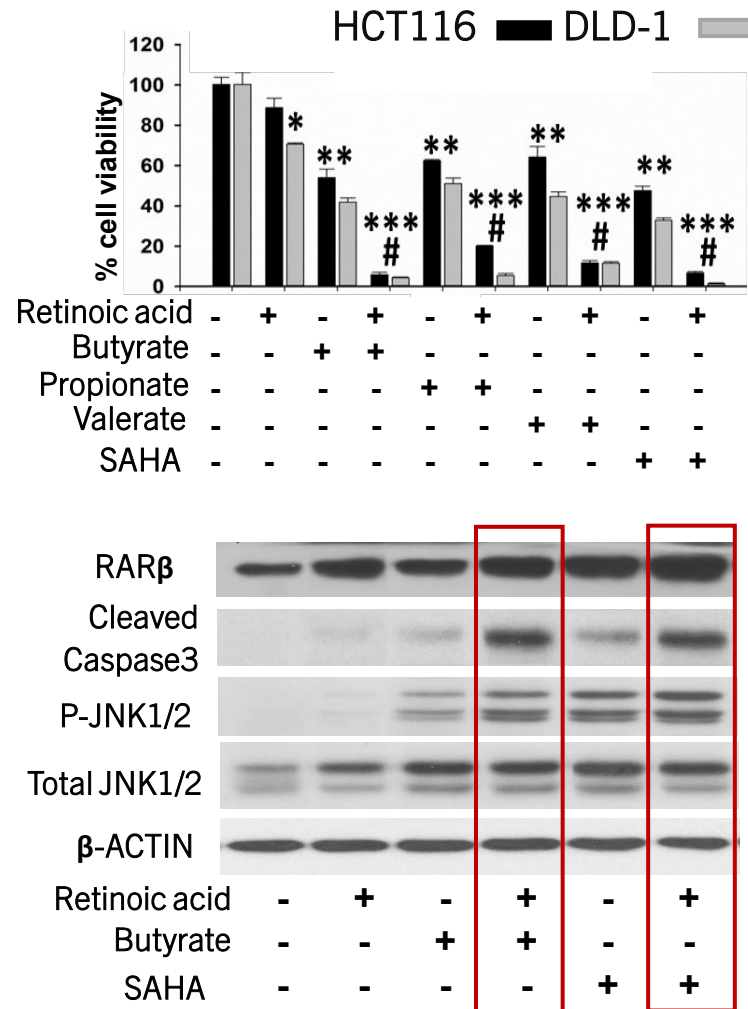


Human
CRC



Short-chain fatty acids, which have HDAC inhibitory property, retinoic acid, and HDAC inhibitory signaling is reduced in human colorectal cancer (CRC) and hepatocellular carcinoma (HCC).

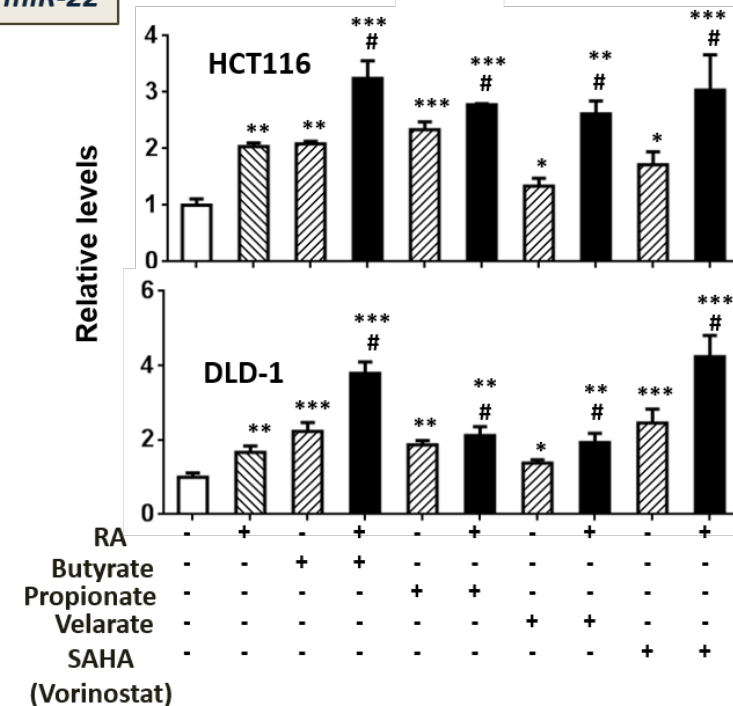
TARGET VALIDATION



Synergistic Gene Reprogramming

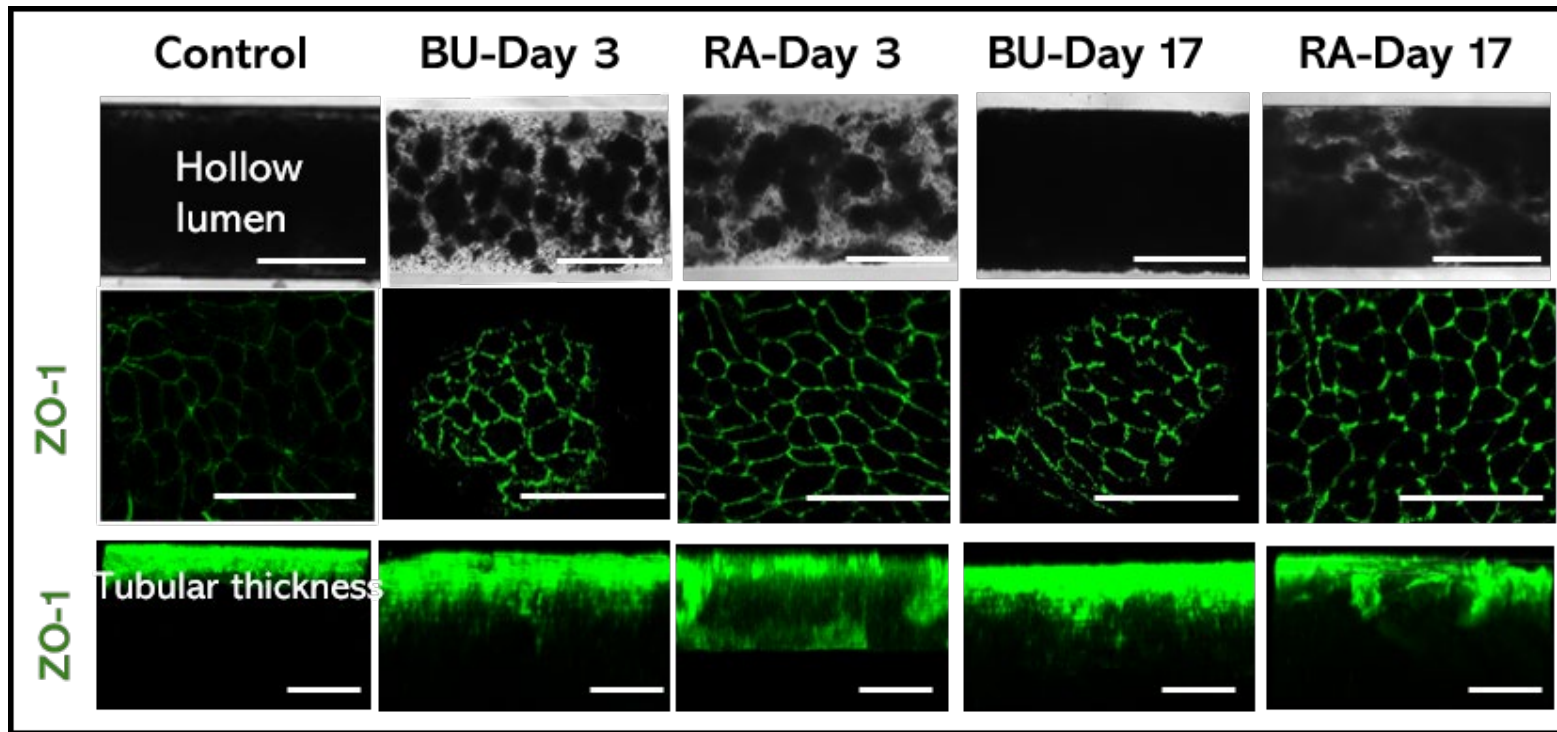
Combining HDAC inhibition and retinoids enhances chromatin accessibility, enabling synergistic cellular reprogramming by inducing colorectal cancer cell death and the expression of the tumor suppressor retinoic acid receptor (RAR β) and miR-22.

miR-22

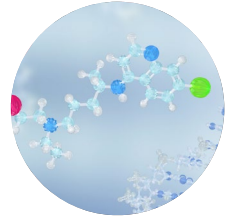


TARGET VALIDATION

Butyric acid (BU) and retinoic acid (RA) each increased intestinal lumen thickness, ZO-1 expression, and ZO-1-positive tubular structure in intestinal organoid culture. ZO-1 (Zonula Occludens-1) is a key tight junction scaffolding protein that maintains epithelial barrier integrity. The culture lasted 25 days, and treatments began on day 3 or day 17.



CORE INNOVATION: POLYMER EPIGENETIC CONJUGATION



Advancing precision nutrition

Compensate for the lack of specific signaling in HCC and CRC patients, rather than relying on a single genetic or oncogenic driver.

Challenges in Traditional Therapy

Traditional therapies use separate drugs, causing mismatched exposure and increased toxicity risks.

Polymeric Backbone Linkage

A polymeric backbone covalently links HDAC inhibitors and retinoids into a single conjugate for coordinated co-delivery with controlled drug release to optimize therapy.

Modular Design Flexibility

Linker chemistry, substitution density, and molar ratio allow tuning of solubility, stability, and biological activity.

Strategic Platform for Optimization

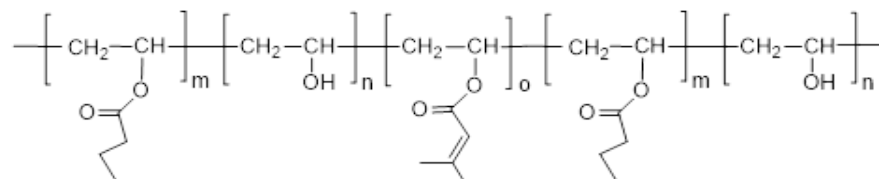
The platform design supports future optimization and customization for different therapeutic indications.

**SYNTHESIS, IN VIVO EFFICACY
VALIDATION, MECHANISM, AND
COMPETITIVE POSITIONING**

SYNTHESIS OF RETINOIC ACID-BASED HDAC INHIBITORS: SHORT-CHAIN FATTY ACID-RA: **THE FARA PLATFORM**

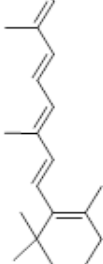


BURA

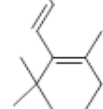


Polyvinyl alcohol (PVA)

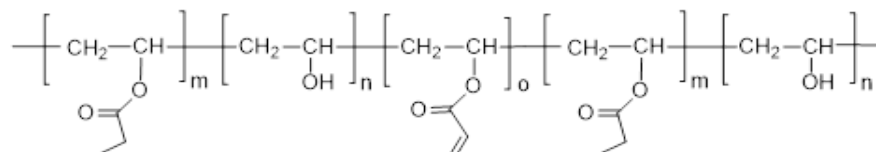
Butyric acid (BU)



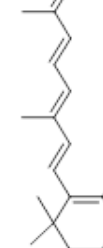
All trans-retinoic acid (RA)



RRORA



Propionic acid (PRO)

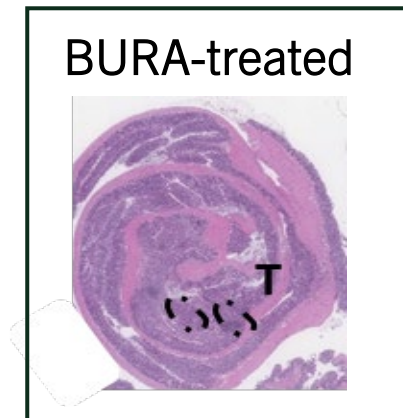
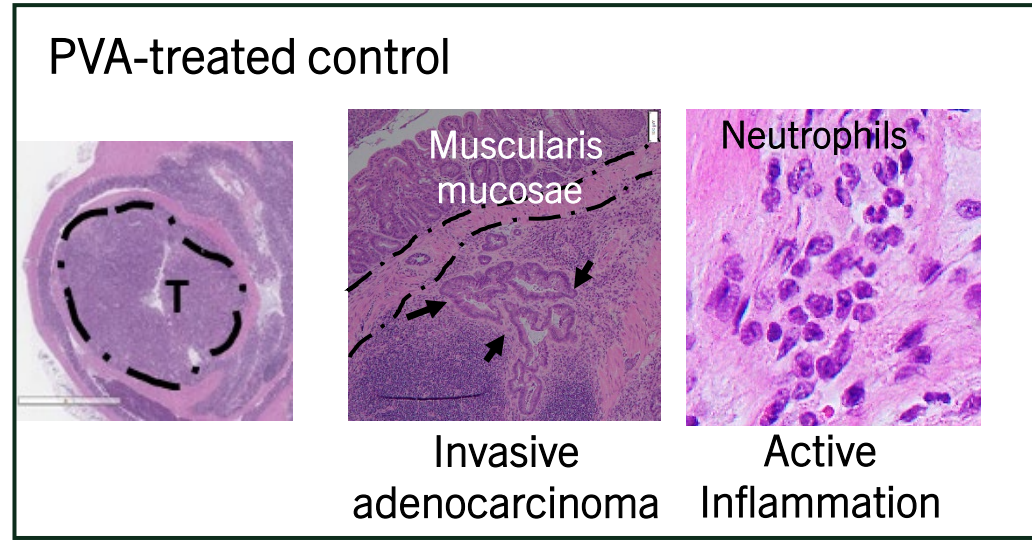
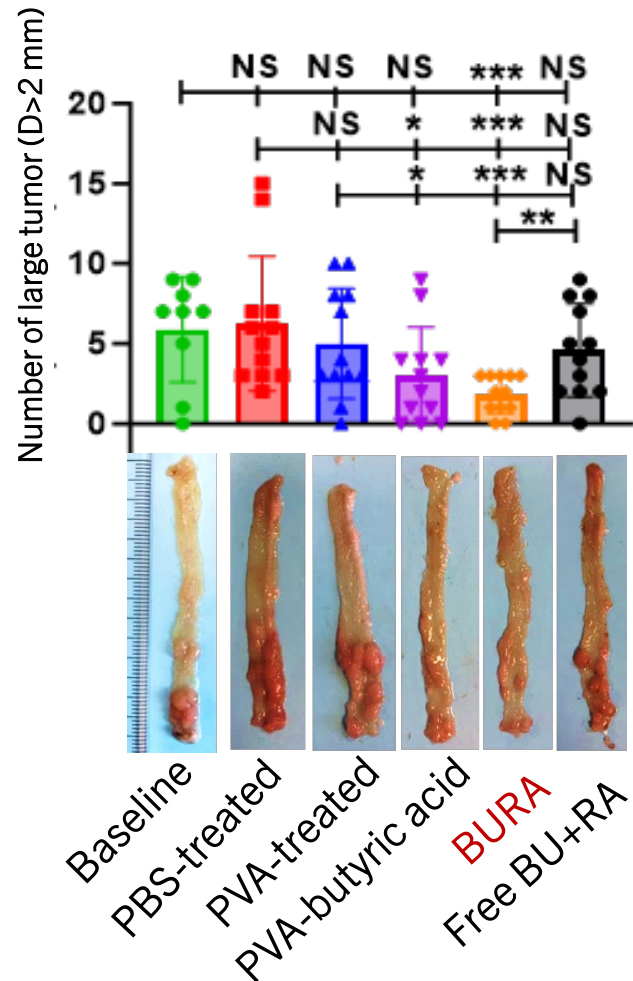


All trans-retinoic acid (RA)



IN VIVO EFFICACY

BURA treats CRC in preclinical mouse models (colitis-associated)
(Treatment started after the tumors developed – baseline tumor load shown)



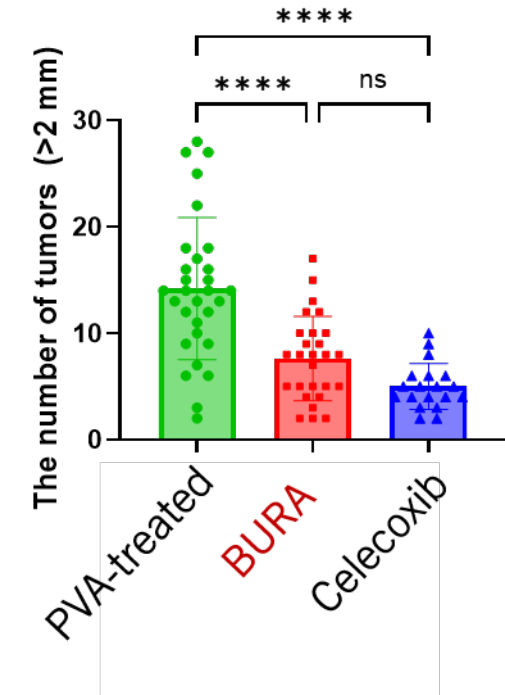
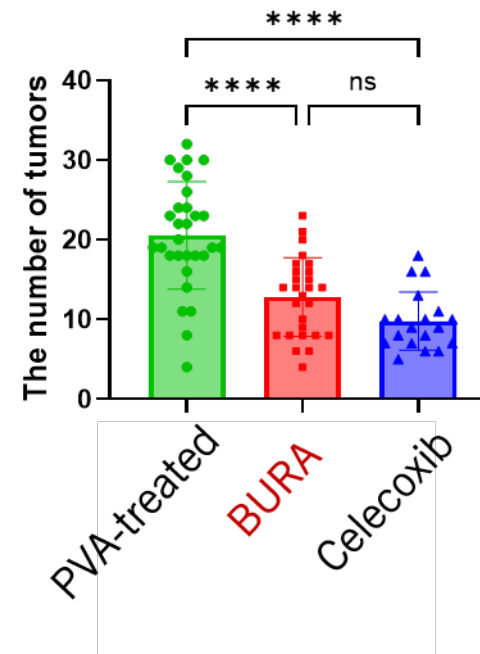
BU stands for butyric acid
RA stands for retinoic acid

IN VIVO EFFICACY

BURA prevents CRC without toxicity
(Intervention initiated before tumors formed)

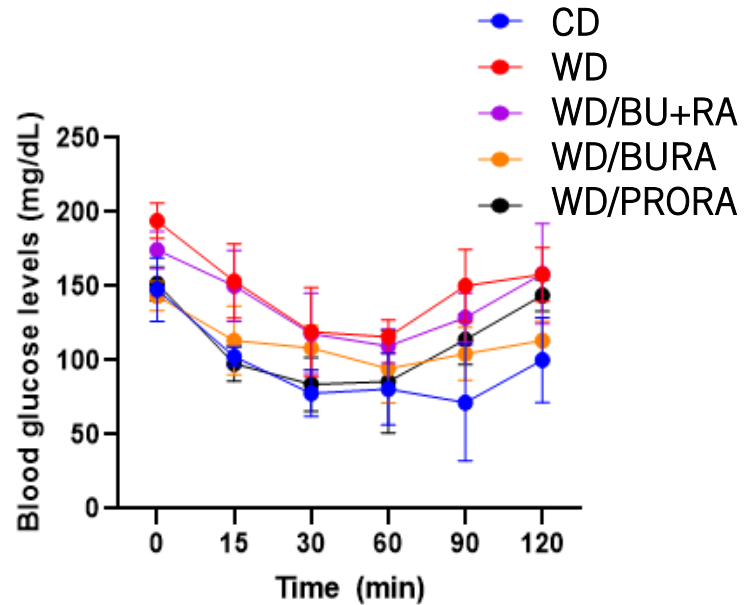
Treatments	The number of surviving mice reached the experimental endpoint
PVA	31/40
BURA	28/40
Celecoxib	19/40

Celecoxib can be toxic in mice and humans.

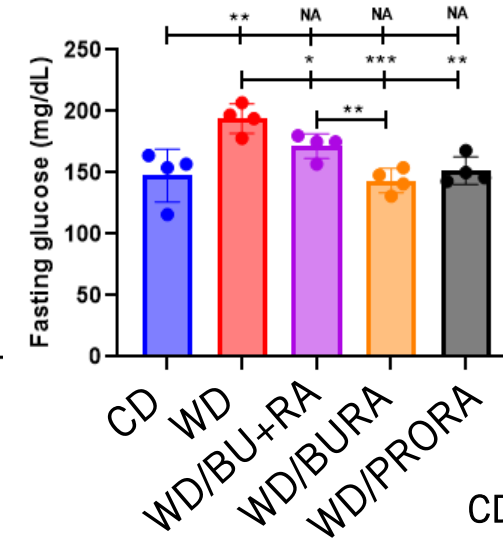
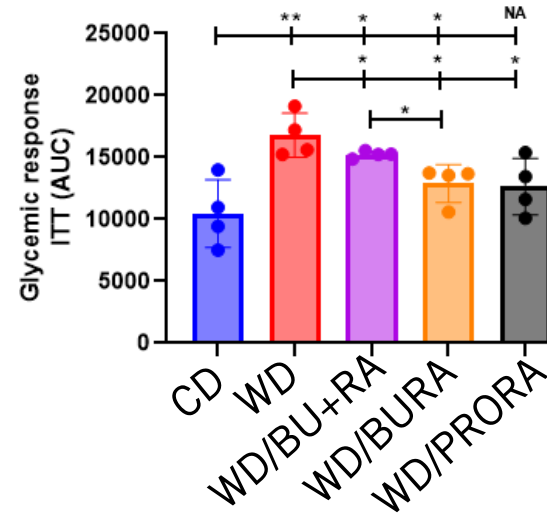


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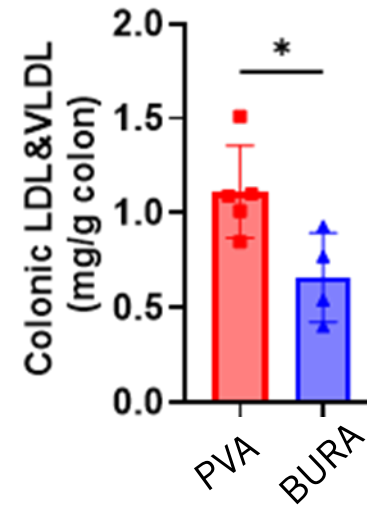
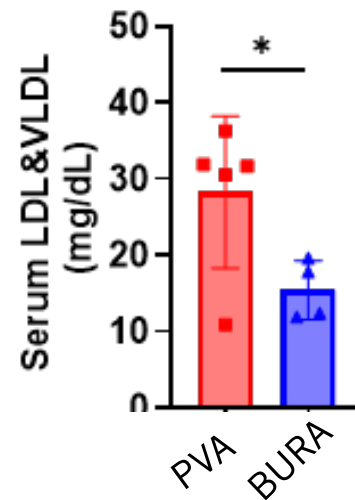
BURA and PRORA have metabolic benefits by reducing fasting glucose levels and insulin resistance in Western diet (WD)-induced obese mice



BURA reduced serum and colon LDL/VLDL



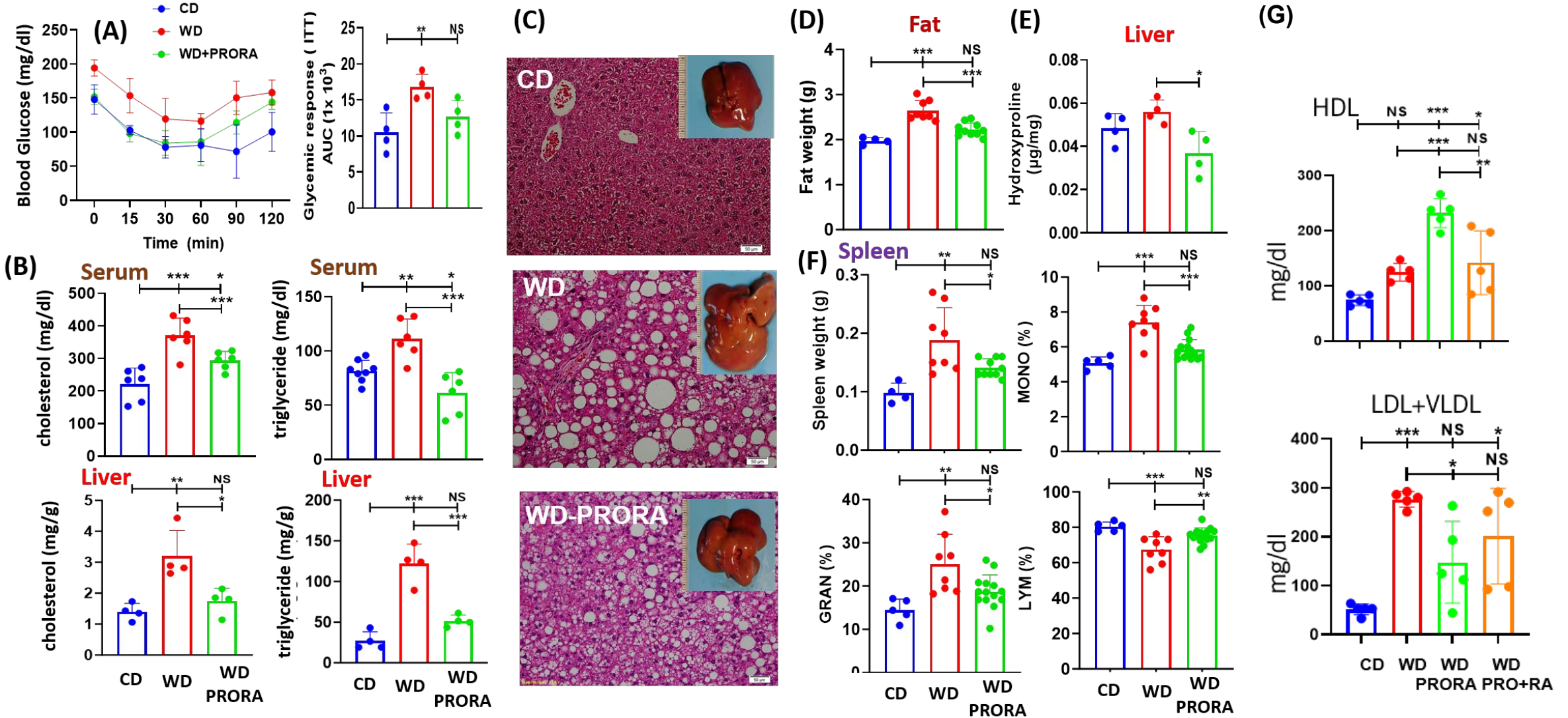
CD = control diet (healthy diet)
WD = Western diet



IN VIVO EFFICACY

The metabolic benefits of PRORA in Western diet (WD)-induced obese mice.

PRORA increases insulin sensitivity (A), lowers serum and hepatic lipids (B, C), reduces body white fat (D) and liver fibrotic tissue (E), reduces splenomegaly, monocytes, and granulocytes and increases lymphocytes (F), increases HDL and reduces LDL+VLDL (G).



MECHANISMS OF ACTION:

BOOST INTESTINAL IMMUNITY AND METABOLISM

- Boost adaptive immunity by recruiting immune cells in the intestine
- Activate hepatic and intestinal bile acid receptor FXR
- Increase the production of chenodeoxycholic acid, the primary bile acid.
- Increase the secretion of GLP-1 in the intestine.
- Enhance short-chain fatty acid and retinoic acid signaling, as well as HDAC inhibitory effects in the digestive tract.

IP, MARKET OPPORTUNITY, AND DEVELOPMENT STRATEGY

FIRST-IN-CLASS EPIGENETIC ORAL PILL



High-Impact Commercial Value Propositions

Single-Pill Systemic Impact

- Consolidates mucosal integrity, metabolic control, lipid management, MASH reversal, and oncology prevention into one convenient oral capsule.
- Replaces complex multi-pill burdens and painful injections with a single, non-invasive therapeutic solution.

Zero-Toxicity Adherence

- Eliminates side effects of metabolic blockbusters, such as gastrointestinal paralysis and liver toxicity.
- Replaces the severe systemic toxicities and complex clinical schedules associated with traditional cancer regimens like FOLFOX.

Targeted High-Risk Prevention

- Delivers preventive effects for human and animal patients at risk for colitis, metabolic diseases, and digestive cancer.

Gut-Driven Immune Reprogramming

- Targets intestinal mucosal immunity to halt progressive local and systemic inflammation.

Epigenetic Disease Reversal

- Modulates key gene expression pathways to naturally correct cellular metabolism.

GLOBAL MARKET OPPORTUNITY

ANIMAL AND HUMAN HEALTH



- Animal Health & Intestinal Markets: Capitalizes on the expanding animal intestinal health market (\$5.16B, surging to \$9.37B) driven by consumer rejection of continuous livestock antibiotic use.
- Dual-Track Regulatory Monetization: Maximizes market capture through a high-value prescription pharmaceutical track and a fast-to-market medical nutrient/feed additive track.
- High-Growth Metabolic & Gut Immunity Sectors: Dominates major therapeutic areas across obesity, T2DM, hyperlipidemia, and inflammatory bowel disease.
- Massive Oncology & Prevention Potential: Taps into expansive colorectal cancer prevention and treatment markets by targeting high-risk populations (recurrent polyps, APC, and Crohn's disease).
- Venture-Scale Platform & Strategic Value: Drives continuous pipeline returns and positions the asset for lucrative licensing deals with global pharma seeking next-generation alternatives.

INTELLECTUAL PROPERTY POSITION

Invention Title: Compositions Comprising HDAC Inhibitors and Retinoids

US Patent 12,740,953

Date: September 22, 2026

Academic Provenance and Licensing

The patent is assigned to the University of California, providing strong academic backing and potential for exclusive licensing.

Follow-on Patent Opportunities

Patents may cover optimized conjugates, manufacturing processes, formulations, and new medical indications.

Venture Firm Considerations

This IP is crucial for assessing defensibility, freedom to operate, and long-term value creation for investors.

