

Module 8: Metabolomics & Short-Chain Fatty Acids

Butyrate, propionate, acetate — the currency of host-microbe communication.

Tracks: Core, Clinical, Advanced | Duration: 50 min

KEY TAKEAWAYS

- SCFAs are the main output of colonic fermentation and the best-understood host-microbe communication channel.
- Butyrate is not just fuel — it's an HDAC inhibitor, Treg inducer, and barrier-integrity signal.
- TMAO connects diet, microbiome, and cardiovascular risk — but the clinical utility of measuring it is debated.

EVIDENCE-GRADED CLAIMS

Dietary fiber intake increases SCFA production	A — Clinically established	Well-established from feeding studies; dose-response relationship documented.
Butyrate is essential for colonocyte health and barrier integrity	A — Clinically established	Mechanistically validated; butyrate-deficiency models show barrier breakdown.
Elevated TMAO predicts cardiovascular events	B — Supported, context-specific	Prospective cohort data consistent; causal mechanism still debated.
TMAO testing should guide dietary counseling	D — Plausible, unproven	No guideline recommends TMAO measurement; clinical utility unestablished.

CLINICAL CASE

The TMAO-worried patient

A 60-year-old with a history of MI saw a wellness website offering TMAO blood testing (\$199) and was told his 'elevated TMAO' means he should stop eating eggs, red meat, and take their proprietary probiotic to 'lower gut TMAO production.'

How would you evaluate the clinical utility of TMAO testing, the dietary advice given, and the probiotic recommendation?

SUMMARIES

For Patients

When you eat fiber, your gut bacteria ferment it into short-chain fatty acids — especially butyrate. Butyrate is the main fuel for the cells lining your colon and helps keep your gut barrier strong. It also influences your immune system. This is one of the strongest arguments for eating a high-fiber diet.

For Clinicians

SCFAs (butyrate, propionate, acetate) are produced by microbial fermentation of dietary fiber and resistant starch. Butyrate serves as the primary energy source for colonocytes (~70% of energy), inhibits histone deacetylases (epigenetic regulation of gene expression), promotes Treg differentiation, and strengthens tight junctions. TMAO (trimethylamine N-oxide) is produced from dietary choline/carnitine by gut bacteria (TMA) → hepatic FMO3 → TMAO; elevated levels associate with MACE in prospective cohorts.

REFERENCES

- The impact of diet and lifestyle on gut microbiota and human health — Conlon MA & Bird AR, *Nutrients* 2015 [[Link](#)]