Supporting Muscle Health Through a Gut–Centric Lens

Clinical Takeaways from *New Frontiers in Functional Medicine Podcast:* When High Protein Backfires in the Gut with Dr. Tom Fabian, science advisor at Diagnostic Solutions Laboratory.

Patients are increasingly encouraged to consume higher protein diets to support muscle health, yet many struggle to meet targets or achieve expected outcomes. This raises an important clinical question:

Is the issue protein intake or the patient's ability to digest, absorb, and utilize it?

The Gut–Muscle Axis

Muscle health is influenced by more than protein intake alone. The gut microbiome, through its diverse metabolites and signaling pathways, plays a central role in muscle repair and recovery.

- Short-chain fatty acids (SCFAs) and secondary bile acids help regulate immune balance and control inflammation
- Regulatory T cells originating in the gut may support muscle regeneration following stress or injury
- Fermentation of undigested protein can increase production of pro-inflammatory metabolites

Why Higher Protein Intake May Fall Short

Even with increased protein intake and resistance training, some patients fail to build or maintain muscle mass.

Common contributing factors include:

- Impaired digestion → incomplete protein breakdown
- Slow transit → prolonged microbial fermentation
- Low fiber intake → reduced beneficial microbial activity
- Microbiome imbalance → altered protein metabolism

These factors can impair protein utilization and increase the risk of excessive protein fermentation.

Clinical Considerations

- Assess for signs of impaired digestion, including postprandial bloating, heaviness, or food intolerance

- Evaluate stool testing markers (e.g., elastase-1, patterns of commensal and opportunistic overgrowth)
- Review bowel habits and assess for slow transit or constipation
- Evaluate fiber intake and overall dietary pattern
- Consider whether GI symptoms worsen as protein intake increases

Protein Fermentation vs. Fiber Fermentation: Why Balance Matters

Excess protein reaching the colon due to high intake or impaired digestion can shift microbial metabolism toward protein fermentation, producing metabolites such as ammonia, phenols (e.g., p-cresol), and biogenic amines (e.g., histamine).

These compounds are associated with increased intestinal permeability, immune activation, and systemic inflammation, and may exert neurotoxic effects in certain contexts.

In contrast, fermentation of carbohydrates, particularly a diverse range of fibers, promotes the production of beneficial SCFAs such as butyrate. These metabolites support gut barrier integrity, regulate immune function, and create an environment that discourages excessive protein fermentation.

Fiber also “sponges” excess amino acids by fueling microbial growth, while polyphenols further modulate microbial activity. Together, adequate fiber and polyphenol intake help rebalance colonic fermentation, mitigating the adverse effects of excess protein fermentation.

Clinical Considerations

- Recognize that excess protein in the colon can drive production of harmful metabolites
- Consider both digestion and total protein load when evaluating risk
- Prioritize adequate and diverse fiber intake to support SCFA production
- Use fiber and polyphenol-rich foods to mitigate protein fermentation
- Balance protein prescriptions with overall dietary pattern, not protein in isolation

Special Considerations: Aging & GLP-1 Therapies

Aging and GLP-1 receptor agonists may increase susceptibility to protein fermentation by impairing digestion and slowing gastrointestinal transit.

Age-related declines in stomach acid and pancreatic enzyme output can reduce protein breakdown, allowing more undigested protein to reach the colon. Similarly, GLP-1 therapies

delay gastric emptying and may slow overall motility, increasing transit time and promoting proteolytic fermentation.

Additionally, reduced appetite, which is common in both scenarios, may lead to lower intake of fiber-rich foods, compounding the imbalance.

Together, these factors create a higher-risk environment for pro-inflammatory protein fermentation, particularly when fiber intake is insufficient.

Clinical Considerations

- Monitor total dietary intake, not just protein targets
- Assess for reduced meal frequency and overall nutrient density
- Screen for signs of slowed motility or constipation
- Support both protein intake and digestive capacity
- Ensure adequate fiber intake despite reduced appetite

Testing to Guide Clinical Decisions

Targeted, comprehensive stool testing can help determine a patient's capacity to effectively process dietary protein and identify areas requiring support.

- **GI-MAP (Diagnostic Solutions Laboratory):** provides insight into digestion, microbiome balance, and markers influencing protein metabolism
- **StoolOMX (Diagnostic Solutions Laboratory):** evaluates microbial metabolites, including SCFAs and secondary bile acids, offering a functional view of gut ecosystem activity

These tools can help identify patterns impacting digestion, absorption, and gut-mediated signaling relevant to muscle health.

Clinical Considerations

- Use testing to assess digestion, absorption, and microbiome balance before increasing protein intake
- Identify patterns suggestive of protein maldigestion or excessive fermentation
- Evaluate SCFA and bile acid profiles as markers of gut ecosystem function
- Reassess following interventions to guide ongoing care

Key Clinical Takeaway

Muscle health is not determined by protein intake alone.

The gut ecosystem plays a central role in how effectively protein is digested, absorbed, and utilized for repair, recovery, and optimal function.