

Module 9: Sequencing & Diagnostics

16S, shotgun, metatranscriptomics — what each method tells you and what it can't.

Tracks: Clinical, Advanced | Duration: 55 min

KEY TAKEAWAYS

- 16S gives genus-level taxonomy cheaply; shotgun gives species/strain + function but costs more.
- Most consumer microbiome tests lack clinical validation — they can tell you composition but not what to do about it.
- Technical choices (DNA extraction method, sequencing platform, bioinformatics pipeline) can change results more than biology.

EVIDENCE-GRADED CLAIMS

Shotgun metagenomics provides species-level resolution	A — Clinically established	Well-validated against cultured isolates; strain resolution depends on read depth and reference database.
Consumer microbiome kits provide actionable health guidance	F — Misleading or false	No clinical validation, no FDA-cleared test, no consensus reference ranges.
DNA extraction method significantly affects results	A — Clinically established	MBQC demonstrated this is a major source of between-study variance.

CLINICAL CASE

Interpreting a consumer microbiome report

A 35-year-old brings in a consumer stool microbiome test report showing 'low Akkermansia,' 'high Proteobacteria,' and a 'microbiome health score' of 42/100. The company recommends a \$89/month supplement subscription to 'fix' these findings.

How would you interpret this report for the patient, explain the limitations of consumer testing, and advise on whether any action is warranted?

SUMMARIES

For Patients

Scientists study the microbiome by reading the DNA of all the organisms in a sample. There are different methods — some give broad overviews, others give detailed pictures. Consumer testing kits can tell you what bacteria you have, but they can't reliably tell you what to eat or which supplements to take.

For Clinicians

16S rRNA sequencing targets variable regions (V1–V9) and provides genus-level taxonomy at low cost (~\$50–150/sample). Shotgun metagenomics sequences all DNA, providing species/strain-level resolution and functional gene prediction but at higher cost (~\$200–500). Clinical validity: only specific pathogen detection (e.g., *C. diff* toxin, GAS) is clinically validated. Broad microbiome profiling lacks actionable reference ranges, and no consumer test is FDA-cleared for diagnostic use.

REFERENCES

- Assessment of variation in microbial community amplicon sequencing by the MBQC — Sinha R et al., Nat Biotechnol 2017 [\[Link\]](#)