GC-MS Metabolomics of SCFAs for B-cell Epigenetic Control

Kim et al. (2019) Nature Communications 10:5850. DOI: 10.1038/s41467-019-13603-6

Our role: Absolute quantification of SCFAs (acetate, propionate, butyrate) in spleen, colon tissues, and mesenteric lymph nodes (MLNs) by GC–MS.

Background & Significance

Dietary fiber is fermented by gut microbiota to produce SCFAs that shape host immunity.

In B cells, SCFAs act as histone deacetylase (HDAC) inhibitors and modulate gene programs governing class switch recombination (CSR), somatic hypermutation, plasmablast differentiation, and antibody output.

Understanding tissue level SCFA exposure is essential to link diet, microbiome metabolism, and B cell–intrinsic epigenetic regulation with functional antibody responses.

Study Highlight

- The study demonstrates that physiologically relevant SCFA concentrations regulate B cell programs via an intrinsic, epigenetic mechanism.
- Dietary fiber restriction lowers intestinal/tissue SCFAs; exogenous propionate/butyrate supplementation modulates antibody responses in vivo.
- Effects extend to disease relevant contexts, underscoring translational potential of nutrition immune interventions

SCFA Quantification by Creative Proteomics

Absolute quantification of SCFAs in mouse spleen, colon tissue, and MLNs by gas chromatography–mass spectrometry (GC–MS), enabling direct tissue level exposure readouts that support mechanism and phenotype linkage.

Matrices

Spleen • Colon tissue • MLNs (mesenteric lymph nodes)

Analytes (typical panel)

Acetate (C2) • Propionate (C3) • Butyrate (C4) • Isobutyric acid (C4:0i)

• Valeric acid (C5:0) • Isovaleric acid (C5:0i) • Hexanoic acid (C6:0)

(Panel expandable to additional SCFAs/branched SCFAs upon request.)

Deliverables

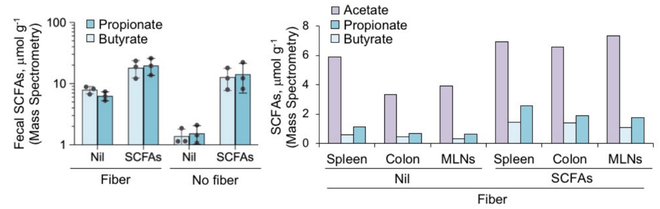
Raw files (.D/.mzData as needed) • Calibrated concentration tables (nmol/g tissue; optional µM for fluids) • QC summary • Publication ready plots and methods text.

Results

SCFA Levels Across Tissues

SCFAs in spleen, colon, and MLNs were quantified by GC–MS to assess local immune exposure.

- Fiber deprivation significantly reduces tissue butyrate and propionate.
- SCFA-supplemented water restores levels (e.g., spleen: 0.59 → 1.43 µmol·g⁻¹).
- Distinct SCFA profiles across tissues inform B-cell responses.



SCFA concentrations in spleen, colon, and MLNs under fiber or SCFA treatment. (Supp. Fig. 1a)

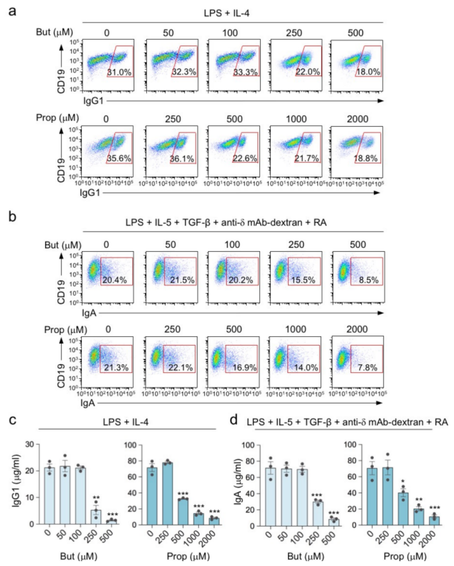
SCFAs Drive Epigenetic Reprogramming in B Cells

SCFAs act directly on B cells as HDAC inhibitors, increasing miRNAs that suppress Aicda and Prdm1, leading to reduced AID/Blimp-1 expression and antibody-class switching.

Functional Readouts Confirm SCFA Effects on Antibody Responses

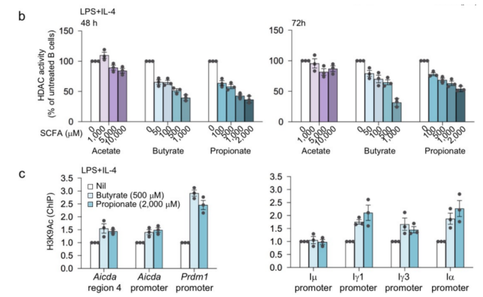
In vitro assays show dose-dependent suppression of IgG1/IgA CSR and antibody secretion by butyrate and propionate. Acetate has limited effect.

Butyrate/propionate reduce IgG1+/IgA+ B cells and antibody secretion in a dose-dependent manner. (Supp. Fig. 6a–d.)



Translational Relevance: Autoantibodies in Lupus

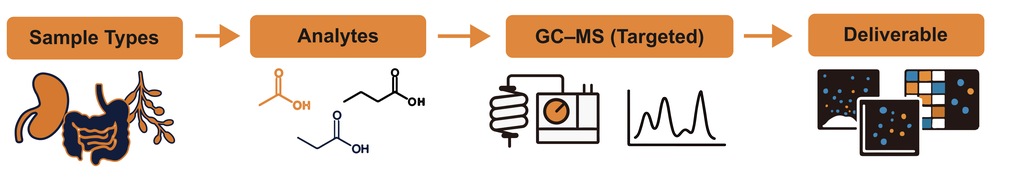
SCFA treatment in NZB/W F1 lupus mice reduces autoantibody titers and renal IgG deposition, supporting the therapeutic value of SCFA modulation.



SCFAs decrease HDAC activity and increase H3K9ac at Aicda/Prdm1 loci. (Supp. Fig. 8b–c.)

Methods (GC-MS)

1. Sample prep: Tissue homogenization (ice cold), protein precipitation, and targeted derivatization optimized for volatile SCFAs.
2. Quantitation strategy: Stable isotope internal standards + external calibration; 1/x weighted linear regression; report units normalized to tissue mass.
3. Instrument: GC coupled to single quadrupole MS in SIM mode for sensitivity and specificity.
4. QC architecture: Method blanks • Solvent blanks • Matrix matched QCs • Pooled biological QCs • System suitability checks (retention time windows, ion ratios) • Batch to batch drift correction.
5. Performance (typical): Low µM (fluids) / sub nmol·g⁻¹ (tissue) LOQs; intra /inter batch RSDs within accepted targeted metabolomics norms.



Interested in Quantifying SCFAs in Your Study?

Contact us to measure SCFA levels in immune tissues using GC–MS.

Support your mechanistic insights with absolute tissue exposure data.

Web: www.creative-proteomics.com

Email: info@creative-proteomics.com

Contact Us

Why Choose Creative Proteomics

- Optimized GC–MS method for volatile SCFAs in tissue matrices
- Broad dynamic range supports physiological to supplemented levels
- Minimal sample input: as little as 20–30 mg tissue per replicate
- Full QC coverage: blanks, pooled QCs, drift correction
- Proven reproducibility across multi-batch and multi-organ studies