Time-Restricted Eating Reprograms Immune Inflammatory and Lipid Pathways in Psoriatic Disease

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Rationale

Psoriasis is a chronic inflammatory disease with dysregulated immunity and metabolism. Current treatments address skin manifestations but fail to target underlying immunometabolic pathophysiology. Time-restricted eating (TRE) has demonstrated clinical evidence of dampening inflammation and improving metabolic health. **We hypothesized that TRE recapitulates fasting-induced immune suppression through metabolic reprogramming of CD4+ T cells.** This is the first human study to compare the effects of a dietary intervention on CD4+ T cell transcriptomics, lipidomics, and metabolomics in patients with psoriasis and healthy controls.

Clinical Protocol (NCT04728165)

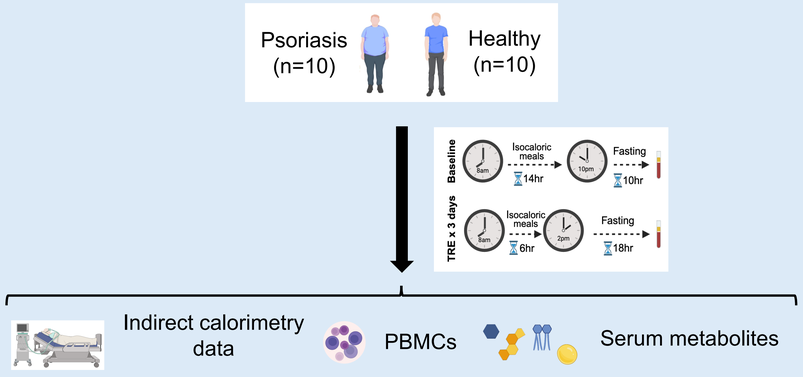


Figure 1. Clinical protocol and sample collection.
Patients with psoriasis and healthy controls underwent a 3-day TRE intervention, with fasting and eating windows indicated. Phenotypic data (indirect calorimetry and complete blood count), PBMCs, and serum metabolites were collected before and after the intervention.

Methodology

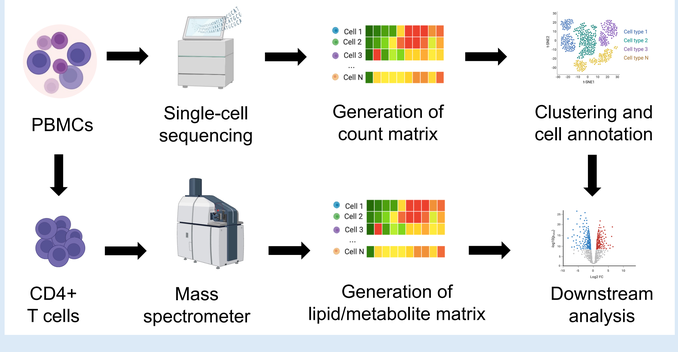


Figure 2. Multi-omics profiling workflow.
Top: PBMCs were processed for scRNA-seq. **Bottom:** CD4+ T cells underwent mass spectrometry-based lipidomics and metabolomics, enabling multi-omics TRE characterization.

Results

TRE Reduces CD4+ T Cell Cytokine Release

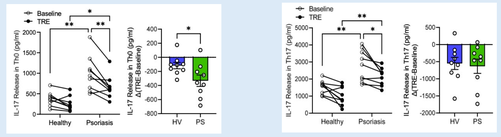


Figure 3. TRE reduces CD4+ T cell inflammatory cytokine release in psoriasis.
Left: IL-17 release from CD4+ T cells under Th0 conditions was reduced post-TRE, as quantified by ELISA in paired culture supernatants. **Right:** Differentiated Th17 cells also display post-TRE reductions in cytokine release, supporting functional suppression of CD4+ T cell activation in psoriatic disease.

TRE Suppresses TNF-α/NF-κB Signaling

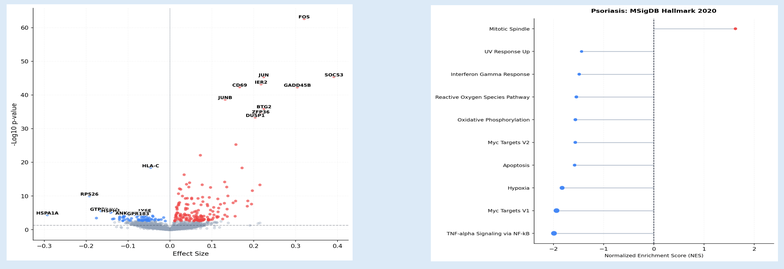


Figure 4. TRE suppresses TNF-α/NF-κB signaling in psoriatic CD4+ T cells.
Left: Volcano plot of paired pre- vs. post-TRE differential expression in CD4+ T cells from patients with psoriasis. **Right:** GSEA identifies TNF-α signaling via NF-κB as a strongly depleted inflammatory pathway following TRE.

TRE Depletes LacCer Lipids and Amino Acids

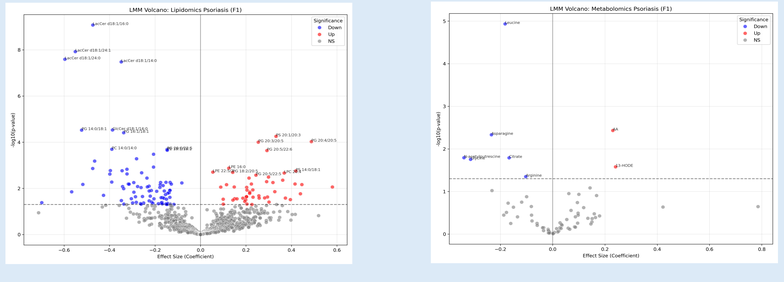


Figure 5. TRE depletes LacCer lipids and amino acids in psoriatic CD4+ T cells.
Left: Lipidomics identifies post-TRE reductions in LacCer species, including LacCer d18:1/16:0, d18:1/24:1, and d18:1/24:0. **Right:** Metabolomics shows reduced leucine, asparagine, arginine, and citrate following TRE.

Integrated Multi-Omics Reveals Coordinated Lipid-Metabolite-Transcriptome Remodeling by TRE

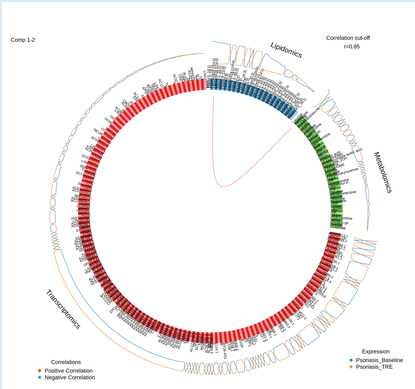


Figure 6. DIABLO multi-omics integration reveals coordinated transcriptomic, metabolomic, and lipidomic remodeling by TRE.
Circos plot showing high-confidence cross-omics correlations linking lipidomic and metabolomic changes to NF-κB transcriptional suppression.

Arginine changes covary with TNFRSF-family transcription

LPC lipids associate with immune signaling features

Amino acid metabolism is coordinated with transcriptional remodeling

Proposed Mechanism & Take-Home Message

TRE → ↓ amino acid abundance → ↓ mTOR/translation
TRE → ↓ LacCer glycosphingolipids → ↓ NF-κB nuclear translocation
Combined → ↓ CD4+ T cell activation and inflammatory output

A 3-day TRE intervention coordinately suppresses CD4+ T cell inflammatory signaling, LacCer lipid abundance, and amino acid availability in psoriatic disease.

Summary

- TRE reduces CD4+ T cell inflammatory cytokine release in psoriasis.
- Transcriptomics identifies suppression of TNF-α/NF-κB signaling and protein synthesis pathways.
- Lipidomics and metabolomics reveal depletion of LacCer species and amino acids.
- Multi-omics integration links lipid, metabolite, and transcriptional remodeling after TRE.

Future Directions

To further dissect the mechanism, future work will validate protein-level changes by CyTOF immunophenotyping, assess functional T cell activation and cytokine output, and map the LacCer–NF-κB mechanistic axis in CD4+ T cells.