Recombinant Human Lactoferrin (effera®) Increases SCFA Production and Outperforms Bovine Lactoferrin on Gut Barrier Function in an Ex Vivo Human Gut Model

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effera® HUMAN LACTOFERRIN

Background

Short-chain fatty acids (SCFAs), the metabolites gut microbes produce during fermentation, fuel the cells of the gut lining and help maintain a healthy inflammatory balance. **A well-maintained gut barrier is central to gastrointestinal function and to resilience under physiological stress such as intense exercise, heat, or travel.** Because lactoferrin is not inherently barrier-strengthening as an intact protein, its gut benefits may be microbiome-mediated. This study examined whether **effera®, a recombinant human lactoferrin,** shifts microbial metabolism and whether the resulting fermentation products support epithelial barrier integrity and immune signaling, **benchmarked against bovine lactoferrin.**

Methods

Test products underwent simulated **upper-gut digestion (INFOGEST 2.0)** followed by colonic fermentation in the **ex vivo SIFR® platform (Cryptobiotix)**, using fecal microbiota from six healthy adults (2 male, 4 female; ages 30 to 53). Fermentation products were then applied to intestinal cell models as shown in Figure 1,

- **Test arms:** effera® (50 to 1000 mg/day), bovine lactoferrin (100, 500, 1000 mg/day), human lactoferrin (1000 mg/day), skimmed milk (1000 mg/day), and a no-substrate control.
- **Fermentation measures:** Short-chain Fatty Acids
- **Barrier and immune measures:** transepithelial electrical resistance (TEER), a standard index of barrier strength where higher values indicate a tighter barrier, measured before and after an inflammatory (LPS) challenge; the inflammatory marker CXCL-10; and the tight-junction proteins ZO-1 and occludin.

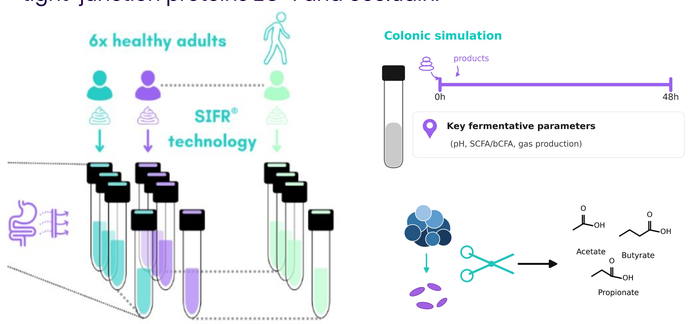
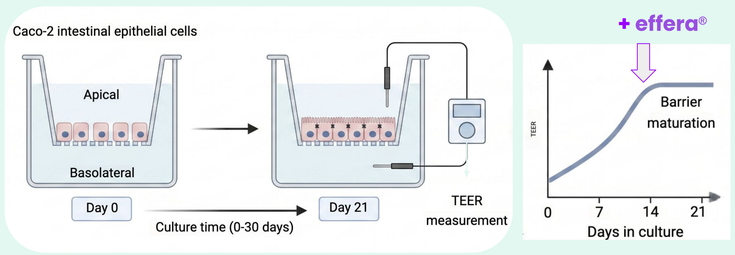


Figure 1a: (above): Ex vivo fermentation workflow (SIFR® platform).
Figure 1b (below): Caco-2 intestinal epithelial barrier model.



Results: Microbial SCFA production

effera® produced dose-dependent increases in total SCFAs, including acetate, propionate, and butyrate, starting at the lowest dose tested (50 mg/day) as shown in Figure 2 below.

Figure 2: effera® dose-response across short-chain fatty acids (50 → 1000 mg/day)

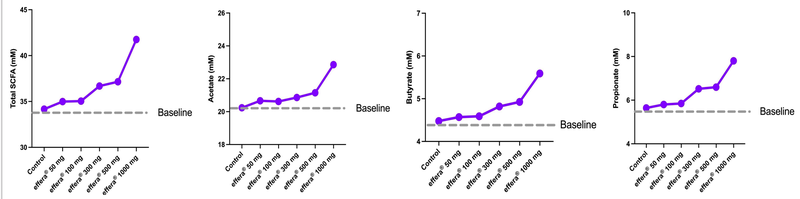


Figure 2a:Total SCFAs (mM) versus dose.
Figure 2b: Acetate (mM) versus dose.
Figure 2c: Butyrate (mM) versus dose
Figure 2d: Propionate (mM) versus dose.

Results: Stronger gut barrier (TEER)

- effera® fermentation metabolites **significantly increased TEER** versus control, in a dose-dependent manner.
- The barrier benefit was most pronounced under inflammatory challenge, **indicating stronger activity when the gut is stressed** (Figure 3a).
- Dose for dose, effera® produced **higher TEER than bovine lactoferrin at every dose tested**. Most strikingly, 50 mg of effera® exceeded both 100 mg and 500 mg of bovine lactoferrin on barrier strength (Figure 3b).

Figure 3: effera® fermentation metabolites strengthen the gut barrier (TEER)

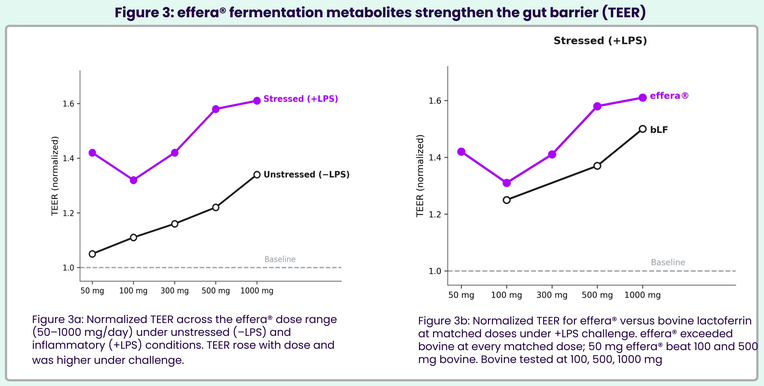


Figure 3a: Normalized TEER across the effera® dose range (50–1000 mg/day) under unstressed (−LPS) and inflammatory (+LPS) conditions. TEER rose with dose and was higher under challenge.

Figure 3b: Normalized TEER for effera® versus bovine lactoferrin at matched doses under +LPS challenge. effera® exceeded bovine at every matched dose; 50 mg effera® beat 100 and 500 mg bovine. Bovine tested at 100, 500, 1000 mg

50 mg of effera®

outperformed 100 mg and 500 mg of bovine lactoferrin on gut barrier integrity.

A human-identical protein doing more, at a lower dose, than the animal-derived incumbent.

Results: Balanced inflammatory response

- effera® reduced the inflammatory marker CXCL-10.
- It supported expression of the tight-junction proteins that keep gut cells sealed.
- Effects were seen across doses as shown in Figure 4.

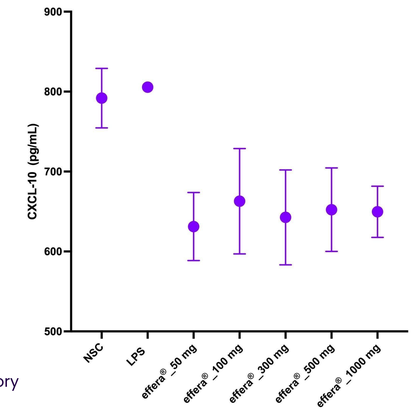


Figure 4: effera® lowers the inflammatory chemokine CXCL-10 across all doses

Conclusions

In an ex vivo human gut model, effera® acted as a microbiome-responsive substrate, in a dose-dependent manner.

Gut microbes fermented it into metabolites that **increased beneficial SCFAs** from the lowest dose (50 mg/day) and, through those products, **strengthened the gut barrier** and supported a balanced inflammatory response.

Barrier benefits exceeded dose-matched bovine lactoferrin at every dose and were **strongest under inflammatory stress**.

These findings support further investigation of effera® for microbiome modulation and gut barrier support.

Key takeaway

effera® triggers SCFA production in ex vivo human donated microbiome even at the lowest (50mg) dose.

effera® fermentation metabolites, produced after colonic fermentation, improved gut barrier integrity (TEER) starting at the 50 mg dose, with a linear increase in improvements through dose escalation.

effera® was superior to bovine lactoferrin across all matched doses in improving gut barrier integrity.

effera® decreased CXCL-10 across all doses providing MOA in regulating inflammatory response.