USE CASE

Use of the SIMBA™ Capsule for analysis of short-chain fatty acid composition in the small intestine

Short-chain fatty acids (SCFAs) are products of bacterial fermentation in the gut and have been established to play a key role in both health and disease states. The current understanding of the role of SCFAs is largely limited to readily accessible stool samples, leaving a gap in the knowledge of the role and composition of SCFAs in other regions of the gastrointestinal tract. Nimble Science addresses this gap with the SIMBA™ Capsule, an advanced capsule sampling technology that passively and directly collects endoscopic quality intestinal liquid biopsies from the small intestine.

Problem Statement

SCFAs have been established to play a vital role in both gut health and immunity, and have been demonstrated to be involved in infections, inflammation, autoimmunity, allergies, responses to cancer treatments and certain metabolic diseases [1, 2]. SCFAs are produced by bacterial fermentation of dietary fiber, and key SCFAs of interest are butyrate, propionate and acetate. The importance of these SCFAs, and their role in both health and disease states is ongoing. However, the majority of current research on SCFAs focuses on those produced and active in the colon.

Current sampling of the microbiome and the associated metabolites is primarily done through stool samples, which allows for relatively simple and non-invasive access to samples from various populations. However, this only allows for a small picture of what is happening, and at the end of the GI tract, which ignores the dynamics of other regions and potentially more active sites of the GI tract. One such region is the small intestine, the primary site for digestion and absorption, and a key immunological site. The presence of both dietary fiber, the substrate for SCFA production, and the small intestine microbiome, suggests that SCFAs would be present and active in the small intestine. However, lack of access to the small intestine limits researchers to groups undergoing endoscopies, sudden death victims, or animal models, missing a comparatively large group of the population that can be studied through stool sampling.

Solution

Nimble Science and the SIMBA™ Capsule allow for researchers to study the small intestine microenvironment and associated SCFAs of specific populations in a simpler way. This reduces the limitations previously placed on detecting and exploring SCFAs in fecal samples. SCFAs have previously been detected and identified through targeted metabolomics using the SIMBA™ Capsule, with significance to endoscopic samples collected at the same time. This demonstrates the potential value to researchers to utilize the SIMBA™ Capsule to answer various research questions for the roles of SCFAs in the small intestine. Direct sampling of the small intestine with the SIMBA™ Capsule, has the potential to:

- Accurately detect SCFAs produced and active in this region.
- Provide results that are more sensitive due to the smaller and distinctive microbial populations and associated metabolites in the small intestine and has the potential for greater impact.

The SIMBA™ Capsule can be integrated into existing fecal-based clinical studies, where it will capture complementing, real time data on the microbiome and associated SCFAs to support evidence-based findings. The capsule kit is shipped to the home of the participant and is taken in the morning on a fasted state, allowing for a wide range of populations to easily be studied.

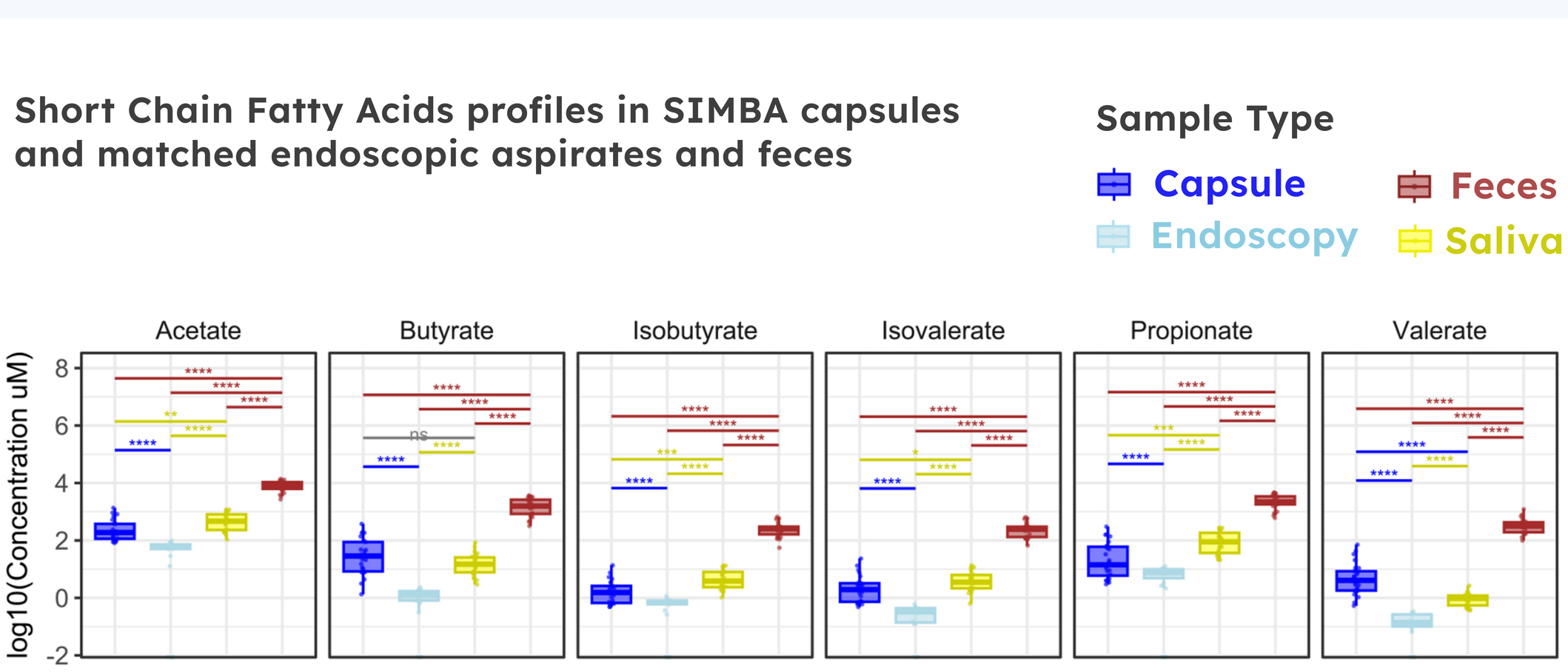
The SIMBA™ Capsules are authorized for Investigational Use only.

403-862-5777 info@nimblesci.com www.nimblesci.com

SIMBA™ Capsules in Action:

Detection & Identification of SCFA in SIMBA™ Capsules

Short Chain Fatty Acids profiles in SIMBA capsules and matched endoscopic aspirates and feces



Methods

Participants (n=30) underwent an esophagogastroduodenoscopy (EGD) procedure to collect a duodenal aspirate, duodenal cytological brush, and saliva sample, and ingested two capsules two days following the procedure. Stool samples were collected with retrieval of capsules.

SIMBA™ Capsule successfully detected SCFAs, with significance to endoscopy aspirate.

Capsule: dark blue, Endoscopy: light blue, Saliva: yellow, Feces: red. Short-Chain Fatty Acid absolute concentrations across sample types with and significant pairwise differences.

Image adapted from [3]

[1] Mann, Elizabeth R., Lam, Ying Kam., & Uhlig, Holm H. Short-chain fatty acids: linking diet, the microbiome and immunity. Nature Reviews Immunology. Volume 24, August 2024, 577–595

[2] Xiong, Ruo-Gu., Zhou, Dan-Dan., Wu, Si-Xia., Huang, Si-Yu., Saimaiti, Adila., Yang, Zhi-Jun., Shang, Ao., Zhao, Cai-Ning., Gan, Ren-You., & Li, Hua-Bin. Health Benefits and Side Effects of Short-Chain Fatty Acids. Foods. Volume 11(18), September 2022, 2863. doi: 10.3390/foods11182863.

[3] Gang Wang, Cedoljub Bundalovic-Torma, Sharanya Menon, Sabina Bruehlmann, Lynn Wilsack, Renata Rehak, Sahar Bagheri, Mohammad M. Banoei, Lawrence Lou, Yasmin Nasser, Matthew Woo, Ian Lewis, Kathy D. McCoy, Christopher N. Andrews, Clinical Sampling of Small Intestine Luminal Content for Microbiome Multi-omics Analysis: A Performance Analysis of the Small Intestine Microbiome Aspiration (SIMBA) Capsuel and Benchmarking Against Endoscopy, medRxiv 2024.04.04.24305299; doi: https://doi.org/10.1101/2024.04.04.24305299

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