USE CASE

Shotgun metagenomic sequencing of the SIMBA™ Capsule to supplement feces in microbiome research

Focusing on fecal samples for shotgun metagenomic sequencing disregards the importance of the small intestine and the distinct microbiome population in this influential regions of the gastrointestinal tract, with major roles in nutrient digestion, absorption, drug metabolism and immune system activity.

The SIMBA™ Capsule collects endoscopic quality intestinal liquid biopsies from the small intestine. DNA collected from the SIMBA™ Capsule has been validated for characterization of different bacteria, virus, fungi, archaea and protist populations in this region, allowing for the microbiome research community to integrate small intestine microbiome data to compliment traditional fecal microbiome profiling.

Problem Statement

The small intestine is a critical region of the gastrointestinal tract with several physiologic functions including nutrient digestion and absorption, drug metabolism and immunological activity. A distinct microbiome profile from feces populates the small intestine, therefore relying on analysis from fecal samples for microbiome research has the potential to miss key data. In addition, the presence of fewer microbial species in the small intestine reduces noise that can be seen in densely populated fecal samples, allowing for the potential for more meaningful results. Shotgun metagenomic sequencing for microbiome research is commonly done utilizing fecal samples, which are readily accessible compared relying on invasive procedures, such as endoscopies, to access samples from the small intestine.

Solution

The SIMBA™ Capsule allows for direct, passive sampling of the intestinal tract, in the region of the small intestine, and has been validated to collect samples at equivalent quality to endoscopy aspirates. Samples collected from the small intestine have been shown to have distinct microbiome profiles compared to feces. The ease of research participants taking and retrieving the SIMBA™ Capsule from their homes allows for a wide range of potential target populations to be studied. The SIMBA™ Capsule can be seamlessly integrated into existing microbiome research studies, allowing for access to a previously under investigated region and further characterization of the microbiome differences along the gastrointestinal tract.

The SIMBA™ Capsules are authorized for Investigational Use only.

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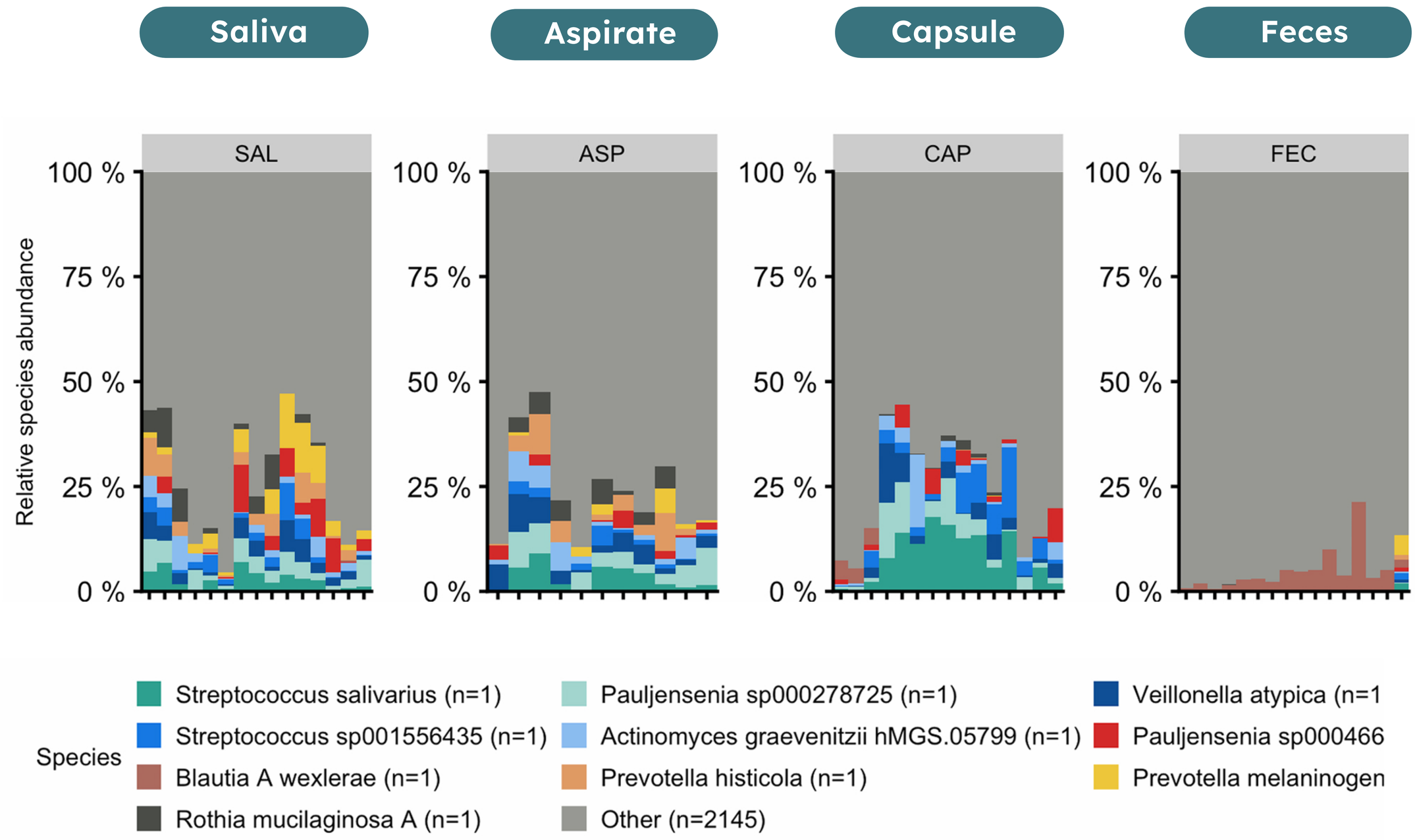
SIMBA™ Capsules in Action:

SIMBA detects general microbiome differences between small intestine and feces



Methods

Participants (n=15) with paired samples for saliva, aspirate, capsule and feces. Taxonomic overview at species level per sample. Bar plots display the relative abundance of the ten taxa with highest average abundance across all samples. Light grey (Other) indicates the total relative abundance of species that are not among the ten most abundant taxa.

The overall microbiome composition of aspirate and capsule samples were very different from fecal samples

Unpublished data, 2024

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Shotgun metagenomic sequencing of the SIMBA™ Capsule to detect Bacteria, Archaea, Fungi, Protista and Viruses

Challenges in access to samples from the small intestine for microbiome research hinders the exploration of which microbes reside in this region, along with how they may change under different conditions. The abundance of different microbial species in fecal samples generates significant data and noise upon metagenomic sequencing, which can pose challenges in drawing meaningful conclusions.

The SIMBA™ Capsule can be utilized for microbiome discovery purposes through the collection of endoscopic quality intestinal liquid biopsies from the small intestine, and subsequent detection of various microbial populations. DNA collected from the SIMBA™ Capsule can identify different bacteria, viruses, fungi, archaea and protist populations in this region. The detection of these microbial populations enables the microbiome research community to discover and further investigate the small intestine, a physiologically important and dynamic region of the gastrointestinal tract.

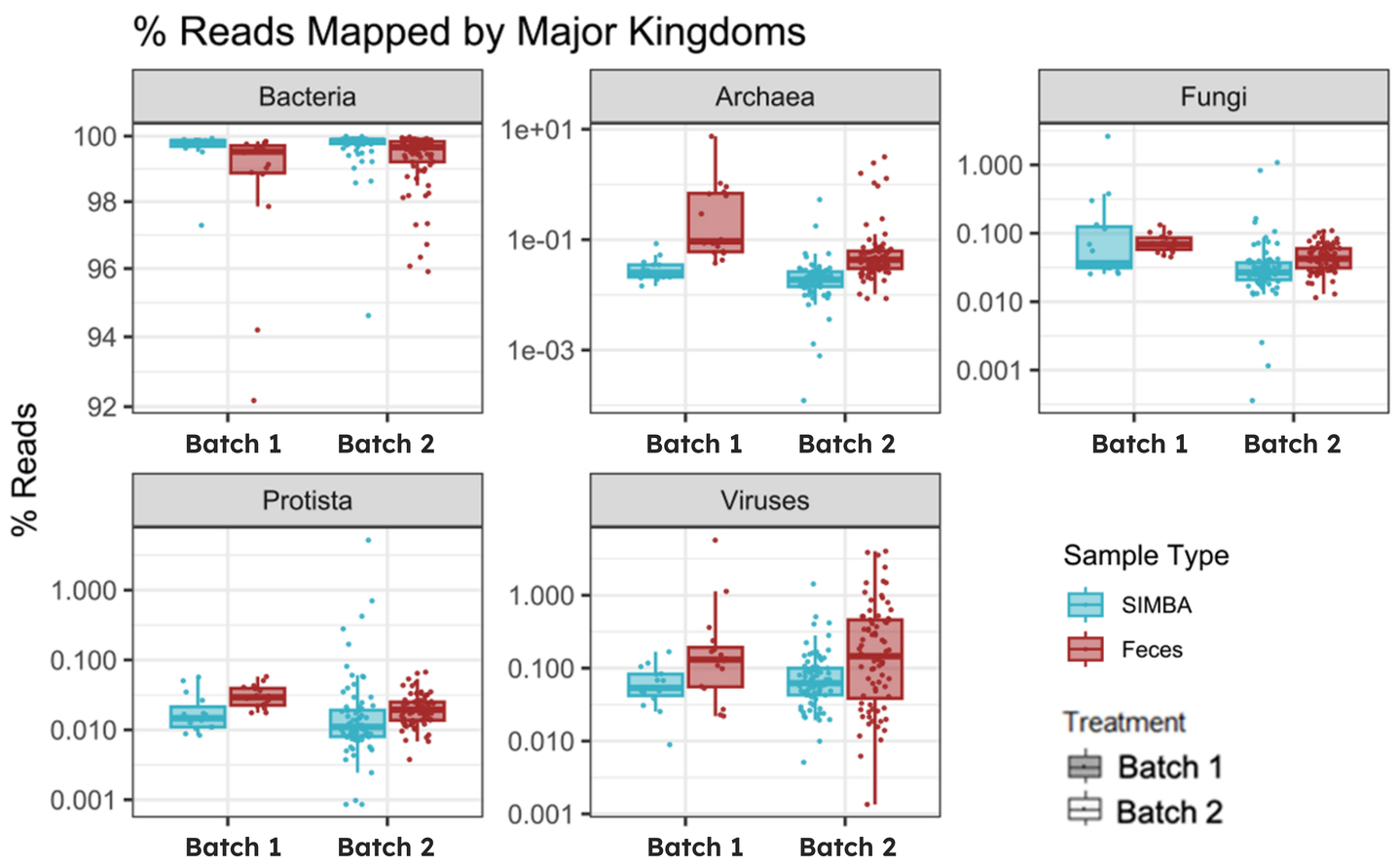
Validation has been performed on SIMBA™ Capsule liquid with low microbiome concentrations, and is still rich in readings of the different microbial populations. The addition of the SIMBA™ Capsule to supplement fecal microbiome research studies can determine general microbiome profile differences between small intestine and feces.

SIMBA™ Capsules in Action:
DNA from SIMBA detects bacteria, archaea, fungi, protists and viruses

Methods

• Multiple library prep protocols were tested on the low-biomass sample from the SIMBA™ Capsule

• The consistent % reads of major phyla (bacteria, archaea, fungi, protista, and viruses) demonstrates the high sample quality for shotgun metagenomic sequencing



The quality of DNA extracted from SIMBA™ Capsule has been validated for shotgun metagenomic sequencing.

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SIMBA™ Capsule for investigating drug metabolism in the small intestine: Characterization of *tdc* processing species

The small intestine is a consequential region for drug metabolism. Sampling of the small intestine with the SIMBA™ Capsule allows for more targeted and sensitive analysis of drug metabolism due to the presence of fewer microbial species relative to fecal samples.

Investigating the small intestine for understanding interactions between the microbiome and drug metabolism may have implications in drug development, how drugs are processed, how different microbial species may be interacting or interfering with drug action and may provide information on targeted probiotic treatment in combination with different medications.

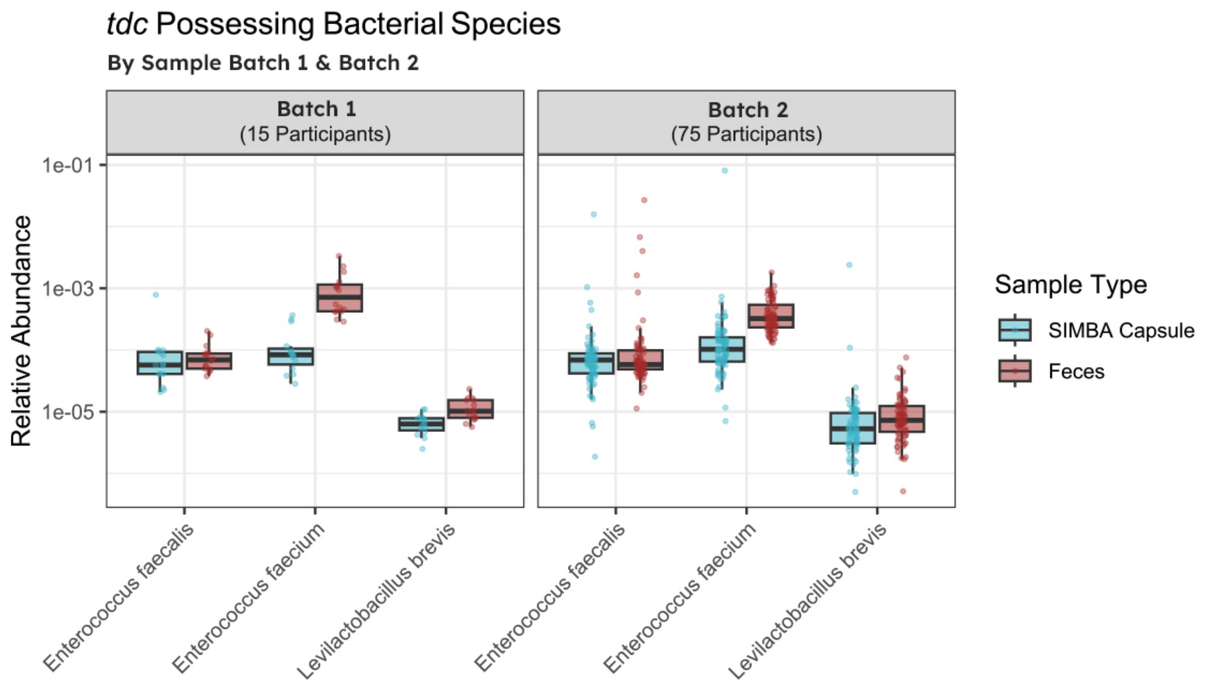
The SIMBA™ Capsule allows for direct, passive and relatively easy access to the small intestine in a wide range of different potential study populations to research the effects of different medications. This access allows for researchers to address several important questions, in determining what bacterial populations are present in both responders and non-responders to certain medications, investigating bacterial modification of drugs in the small intestine, which could allow researchers to investigate whether certain bacteria play a role in drug activity or modifications, and whether specific bacteria are involved in different patient outcomes on the same medications. Research into drug activity in the small intestine could help in understanding why certain people respond or not respond to certain medications, and what conditions lead to which response.

One such example of use of the SIMBA™ Capsule for detection of bacterial species implicated in drug metabolism are tyrosine decarboxylases (*tdc*) processing species and the Parkinsons drug levodopa. The small intestine is a critical region for understanding how the microbiome metabolizes levodopa, as the *tdc* processing species are more abundant in the small intestine, and have less interference compared to fecal samples [1]. The SIMBA™ Capsule has been successfully used to detect *tdc* processing species in the small intestine.

SIMBA™ Capsules in Action: *tdc* processing bacterial species are detected using the SIMBA™ Capsule

Methods

Detection of relative abundance of *tdc* processing bacterial species in SIMBA vs Feces in participants (n=15) in BEST study and (n=75) in OPEN study



Tdc processing bacterial species

Unpublished data, 2024

[1] Cirstea, M.S., Creus-Cuadros, A., Lo, C. et al. A novel pathway of levodopa metabolism by commensal Bifidobacteria. Sci Rep 13, 19155 (2023). https://doi.org/10.1038/s41598-023-45953-z. https://www.nature.com/articles/s41598-023-45953-z

[2] van Kessel SP, Frye AK, El-Gendy AO, Castejon M, Keshavarzian A, van Dijk G, El Aidy S. Gut bacterial tyrosine decarboxylases restrict levels of levodopa in the treatment of Parkinson's disease. Nat Commun. 2019 Jan 18;10(1):310. doi: 10.1038/s41467-019-08294-y. PMID: 30659181; PMCID: PMC6338741. https://pmc.ncbi.nlm.nih.gov/articles/PMC6338741/

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