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HAL Authorization

DIGEST: Safety and Performance Validation of an Ingestible Medical Device for Collecting Small Intestinal Liquid in Healthy Volunteers

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INTRODUCTION:

- The gut microbiome → **major role in maintaining health**.
- Stratification** through the gastrointestinal tract (micro-organisms and metabolites).
- Dysbiosis = unbalanced microbiome → linked to some cancers, inflammatory, metabolic, and neurological diseases...
- Current methods for studying the human intestinal microbiome: **not representative** of the entire gut microbiome.
 - Fecal analysis: common but do not fully represent the intestinal microbiome (only large bowel).
 - Endoscopy and colonoscopy: expensive, invasive and complex to implement on a large scale and could introduce a contamination bias during collection!

To overcome these issues, PELICAN HEALTH has developed a cutting-edge **ingestible device**, capable of performing **multi-sampling** in the **small intestine** (SI) to conduct **multi-omics analysis** (Figure 1).

POC clinical investigation (NCT05477069) promoted by Grenoble Alpes CHU on 15 healthy volunteers²



Figure 1: Structure and use of Pelican Sampler medical device (MD)

DIGEST clinical investigation



Primary objective: For at least 12 out of 15 volunteers

Safety

No adverse event of grade ≥3

Performance

- At least 1 module is analysable
- Found in feces within a 96h period
- Recovered volume ≥25µL
- Satisfactory visual condition



Secondary objectives:

- Verify the safety of the use of the MD for intestinal content collection.
- Verify the safe passage of the MD through the GIT.
- Evaluate the capture of intestinal liquid.
- Verify that the MD opened in the intestine.
- Verify the state of the MD after collection.
- Evaluate the sample's functional potential and identify biomarkers via metagenomics and metabolomics.
- Estimate volunteers' experience from MD ingestion and use.
- Obtain sample's functional potential via culturomics for two subjects.

16 volunteers, 1 excluded (feces collection error)

-	Description	N = 15
critère composite global		
FALSE	1 (6.7%)	
TRUE	14 (93.3%)	
(col %)		
critère composite de sécurité		
TRUE	15 (100.0%)	
(col %)		
critère composite de performance		
FALSE	1 (6.7%)	
TRUE	14 (93.3%)	
(col %)		
sous critère performance du délai		
FALSE	1 (6.7%)	
TRUE	14 (93.3%)	
(col %)		
sous critère performance du contenu		
FALSE	1 (6.7%)	
TRUE	14 (93.3%)	
(col %)		
sous critère performance de l'état visuel		
FALSE	1 (6.7%)	
TRUE	14 (93.3%)	
(col %)		

Table 1: Results obtained for the primary objective

SAFETY

-	Description	N = 15
Présence d'EI par patient		
FALSE	11 (73.3%)	
TRUE	4 (26.7%)	
(col %)		
Gravité		
N	3 (75.0%)	
Y	1 (25.0%)	
(col %)		
Catégorie de gravité		
hospitalisation	1 (100.0%)	
(col %)		
intensité		
légère	1 (50.0%)	
modérée	1 (50.0%)	
(col %)		
Evolution		
résolu sans séquelles	4 (100.0%)	
(col %)		
Causalité		
à un traitement de l'essai	2 (50.0%)	
autre(s)	1 (25.0%)	
autre(s) maladie(s) concomitante(s)	1 (25.0%)	
(col %)		
détails de la causalité		
Appréhension d'aller à la selle	1 (50.0%)	
Entorse	1 (50.0%)	
(col %)		

Table 2: Detailed results obtained for the primary objective and the safety

PERFORMANCE

-	Description	N = 41
Evaluation visuelle		
fatigue	32 (78.0%)	
non fatigé	9 (22.0%)	
(col %)		
Evaluation visuelle non satisfaisant : Déchirure		
non	2 (22.2%)	
oui	7 (77.8%)	
(col %)		
Evaluation visuelle non satisfaisant : Décollement		
non	6 (66.7%)	
oui	3 (33.3%)	
(col %)		
Evaluation visuelle non satisfaisant : autre		
non	9 (100.0%)	
(col %)		
Etat visuel du polymère : couleur		
jaune	33 (80.5%)	
marbré	8 (19.5%)	
(col %)		

Table 3: Detailed results obtained for the primary objective and visual conditions per module

Table 5: Primary objective: detail of sub-criteria by volunteer

-	Description	N = 41
volume >= 25 µl		
FALSE	3 (7.3%)	
TRUE	38 (92.7%)	
(col %)		
Volume récupérée µl		
Mean (SD)	74.00 (29.83)	
Median	78.00	
Q1-Q3	59.00 - 97.00	
Min-Max	8.00 - 129.00	
N	41	

Table 4: Detailed results obtained for the primary objective and sampled volume per module

-	Description	N = 15
Nombre de capsules exploitables pour critère de performance par patient		
0	1 (6.7%)	
1	4 (26.7%)	
2	5 (33.3%)	
3	5 (33.3%)	
(col %)		
sous critère performance du délai		
FALSE	1 (6.7%)	
TRUE	14 (93.3%)	
(col %)		
sous critère performance du contenu		
FALSE	1 (6.7%)	
TRUE	14 (93.3%)	
(col %)		
sous critère performance de l'état visuel		
FALSE	1 (6.7%)	
TRUE	14 (93.3%)	
(col %)		

CLINICAL DATA

CULTUROMICS

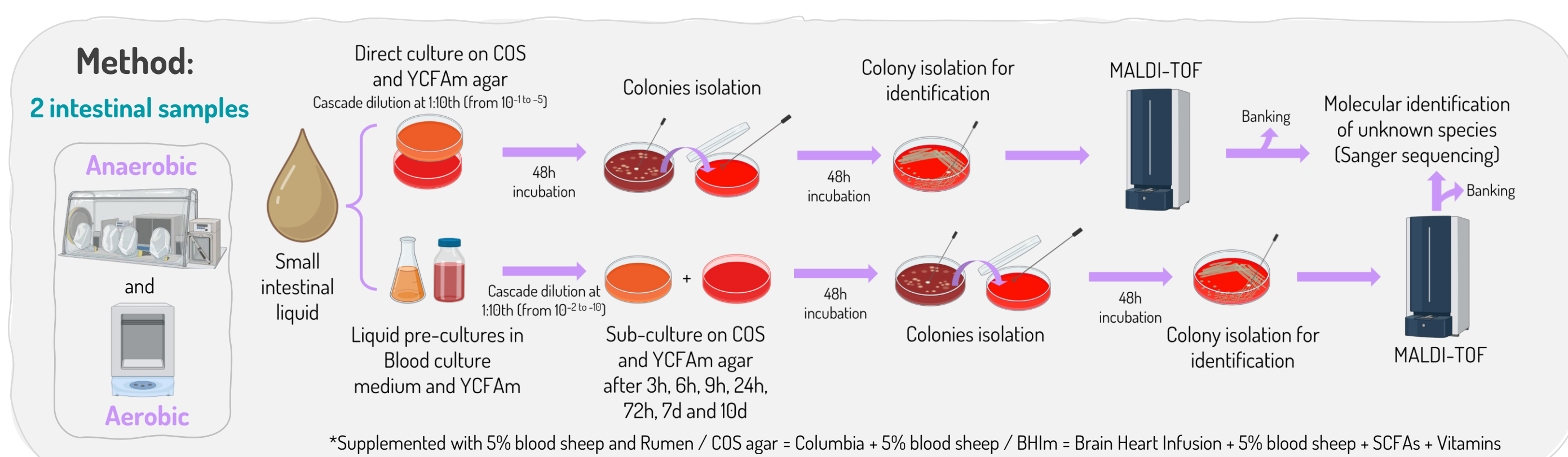
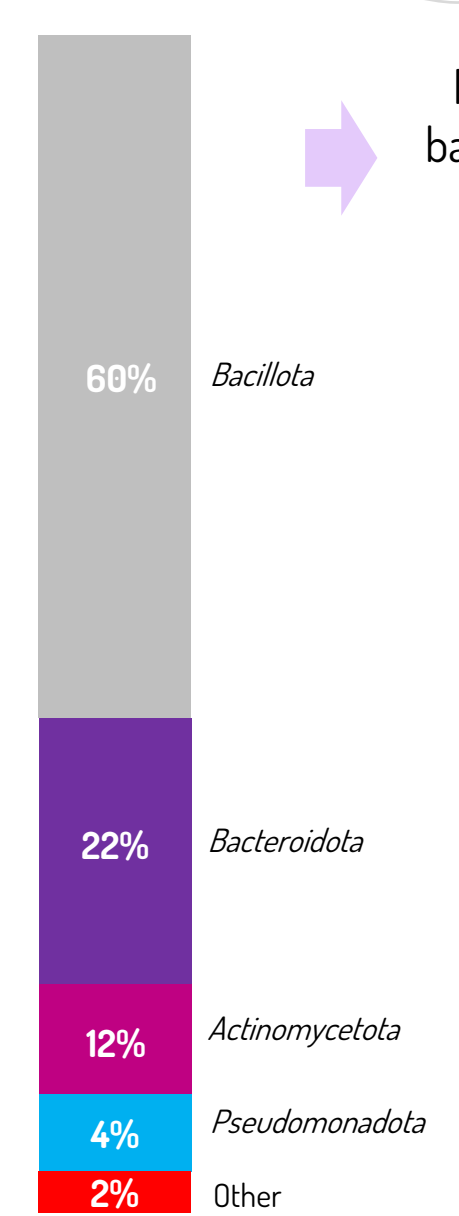


Figure 2: Distribution of bacterial species identified during culturomics according to phyla



Collinsella aerofaciens *Sutterella wadsworthensis* *Eggerthella lenta*
Alistipes onderdonkii *Parabacteroides merdae* *Bacteroides ovatus*
Bifidobacterium longum *Clostridium scindens* *Alistipes communis*

98 different bacterial species

5 NEW BACTERIAL SPECIES

Blautia sp *Flintibacter* sp
Exlibacter sp *Megasphaera* sp
Traorella sp

Figure 3: Bacterial species found in both intestinal samples.

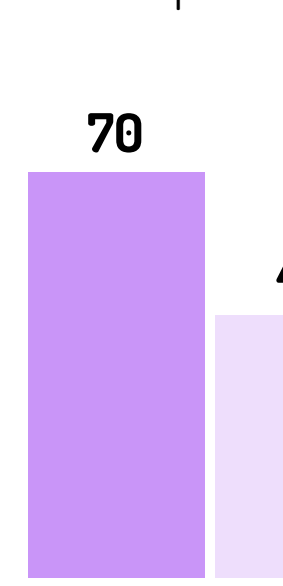


Figure 4: Total of bacterial species identified in subject 1 (S1) and subject 2 (S2). *Identification still in progress for some isolates

METABOLOMICS

Method: Feces and SI liquid from 14 subjects

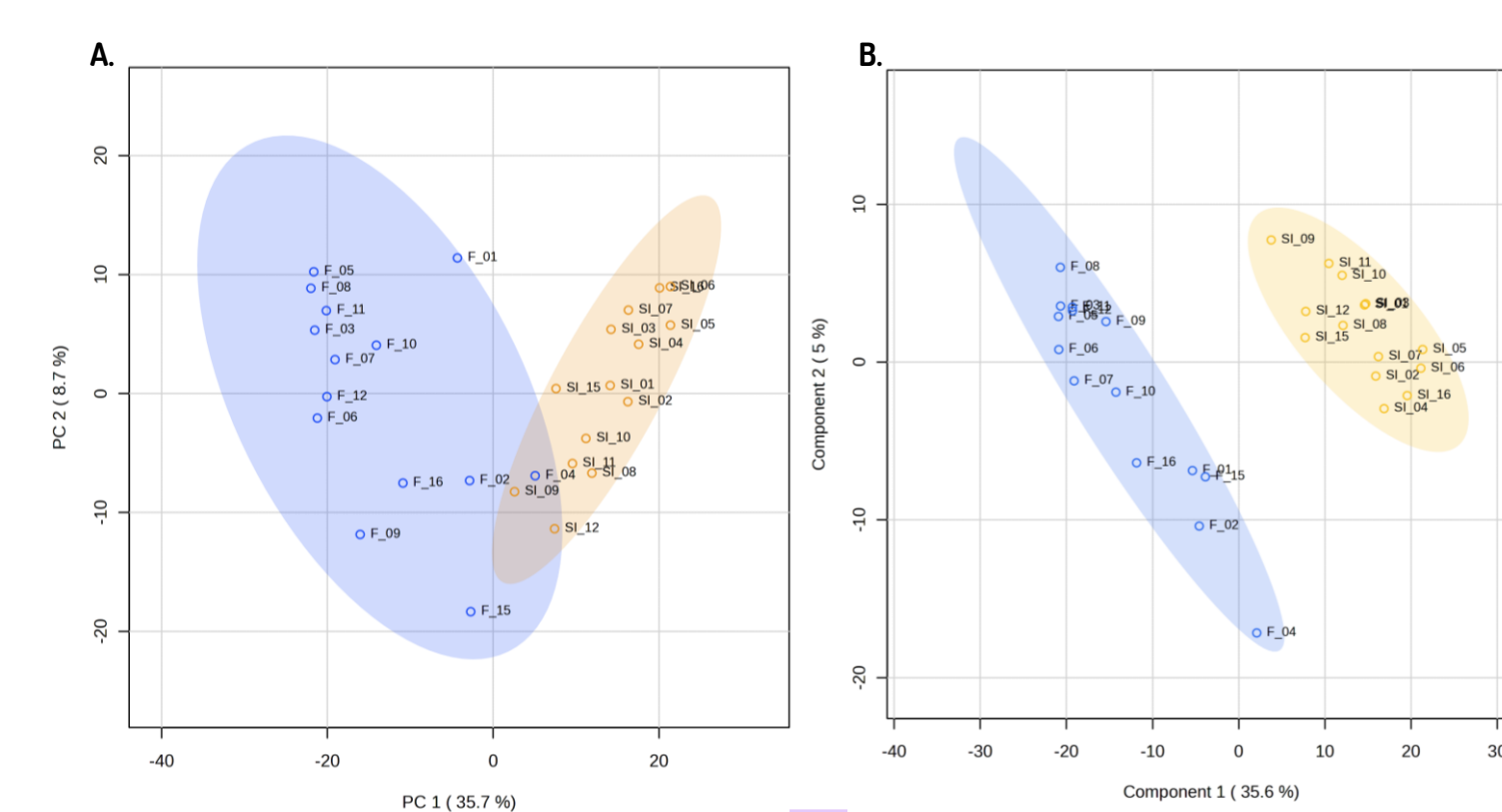
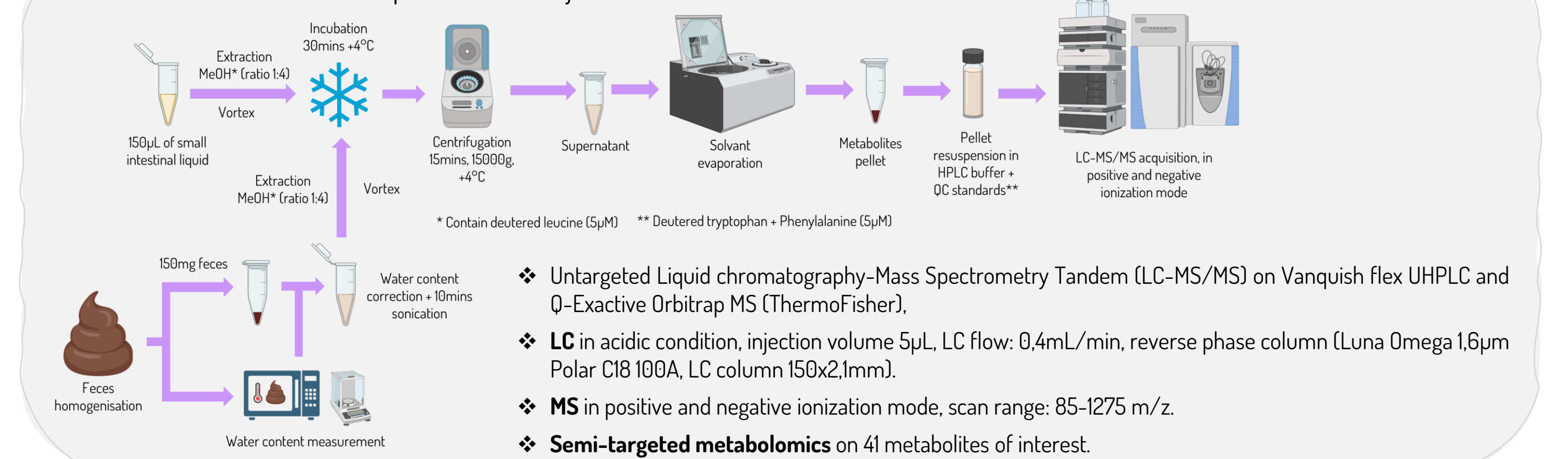
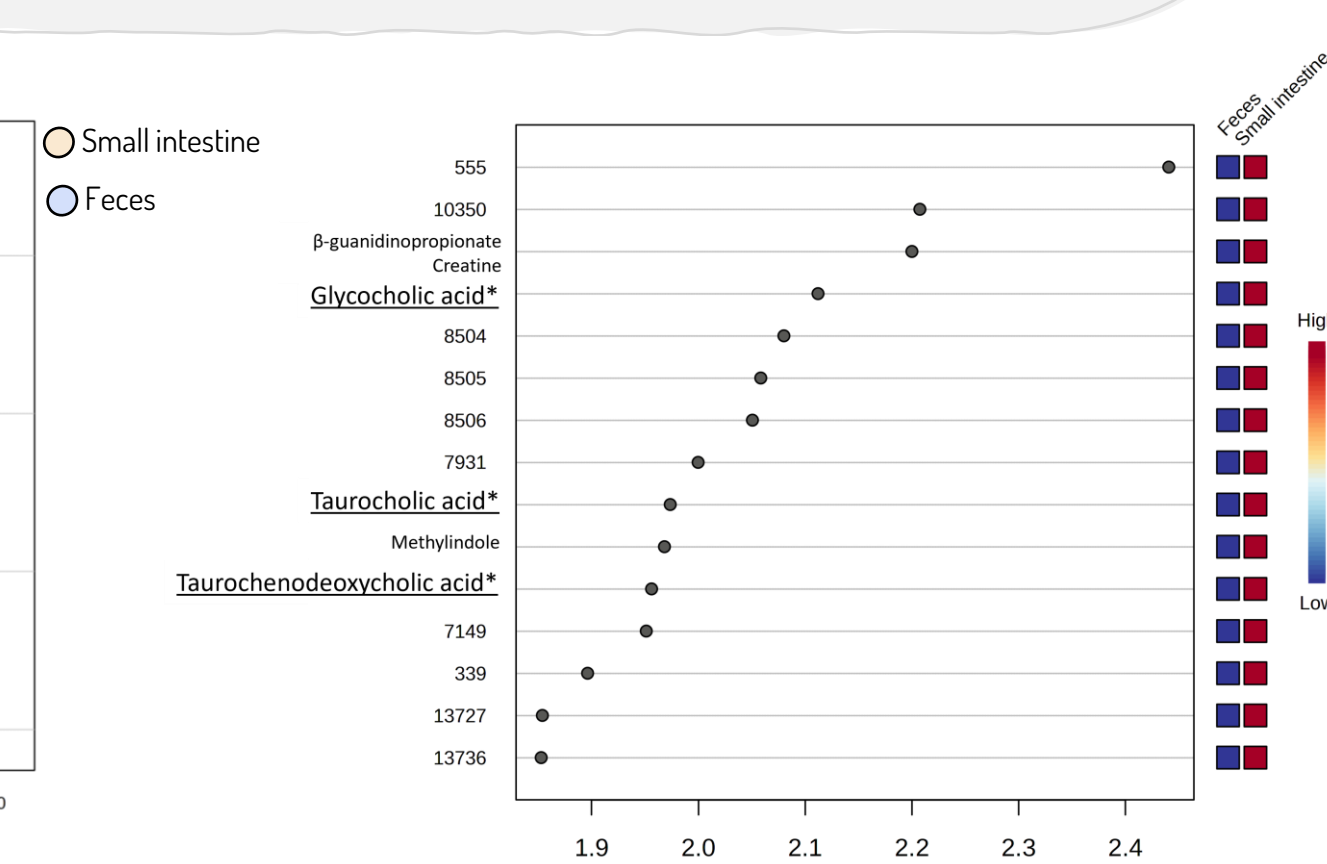


Figure 5: Principal component analysis (a) and PLS-DA (b) of the intestinal and fecal samples

Figure 6: VIP features for the differentiation feces vs small intestinal liquid. *Validate features (in MS2), part of the 41 metabolites of interest



CONCLUSION:

- Primary objective reached:** the MD is **SAFE** (no adverse events observed).
- Performance was validated for 14/15 healthy volunteers (93.3%). Mean collected volume: **74µL** per module ; **78%** of the modules presented good visual condition (no fecal contamination).
- Multi-omics analyses have been performed. Functional potential was evaluated using metabolomics, metagenomics, and culturomics. Potential biomarkers of the small intestinal liquid have been detected such as glycocholic acid or taurocholic acid (primary conjugated bile acids). 98 bacterial species have been isolated from 2 intestinal samples and offering a potential source of new live biotherapeutic products.

References:

- Villmones, H. C. *et al.* The cultivable microbiota of the human distal ileum. *Clin. Microbiol. Infect.* **27**, 912.e7-912.e13 (2021).
- Tronel, A. *et al.* Pilot Study: Safety and Performance Validation of an Ingestible Medical Device for Collecting Small Intestinal Liquid in Healthy Volunteers. *Methods Protoc.* **7**, 15 (2024).

Organizations:

- University Grenoble Alpes, CNRS, UMR 5525, VetAgro Sup, Grenoble INP, CHU Grenoble Alpes, TIMC, 38000 Grenoble, France
- University Grenoble Alpes, Inserm, CHU Grenoble Alpes, CIC, 38000 Grenoble, France
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