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Daily variations of gut microbial translocation markers in ART-treated HIV-infected people

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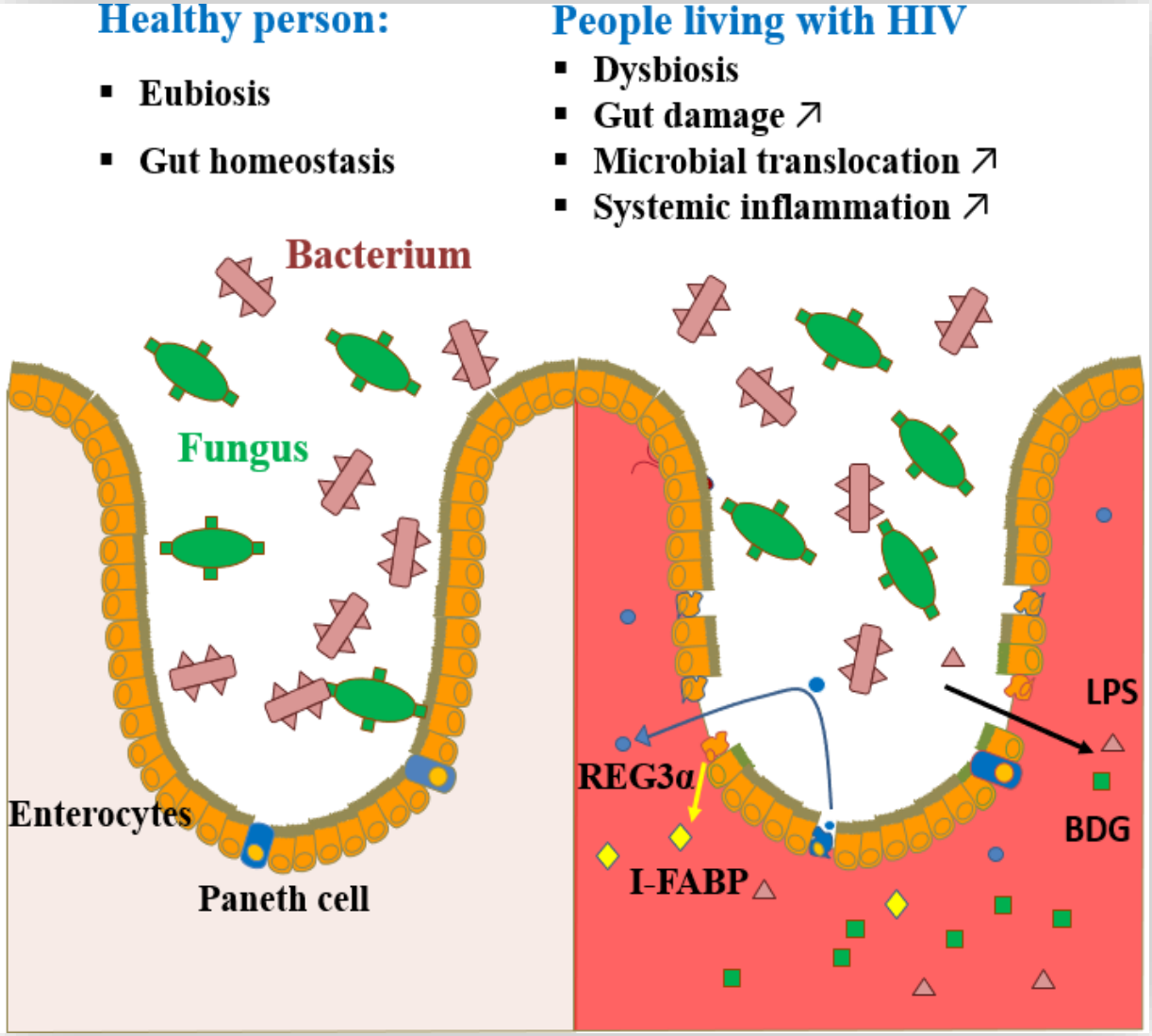
Conflict of Interest Disclosure: I have no conflicts of interest

BACKGROUND



Knowing daily variations of these markers could improve clinical care and research for PLWH

Microbial translocation markers:

- **LPS (Lipopolysaccharide):** Bacterial cell wall polysaccharide and a well-known inducer of innate immune activation.
- **BDG (β-D-Glucan) :** A major component of most fungal cell walls and serves as a potent pathogen-associated molecular pattern (PAMP) in triggering antifungal immunity.

Gut damage markers:

- **I-FABP (Circulating intestinal fatty acid binding protein):** An intracellular protein constitutively expressed in enterocytes, is released upon cell death.
- **REG3α (Regenerating islet-derived protein-3α):** An antimicrobial peptide secreted by intestinal Paneth cells into the gut lumen and upon gut damage, translocates into the blood.

STUDY DESIGN AND METHOD

- A total of 11 male ART-treated PLWH were recruited for the study.
- Blood samples were collected every 4 hours over 24 hours before snacks/meals from 8:00 in the morning to 8:00 the next day.
- All participants consumed similar meals at set times, and had a comparable amount of sleep, physical exercise and light exposure.
- Translocation markers (LPS, BDG) and gut damage markers (I-FABP and REG3α) were assessed by ELISA or Fungitell® LAL assay.

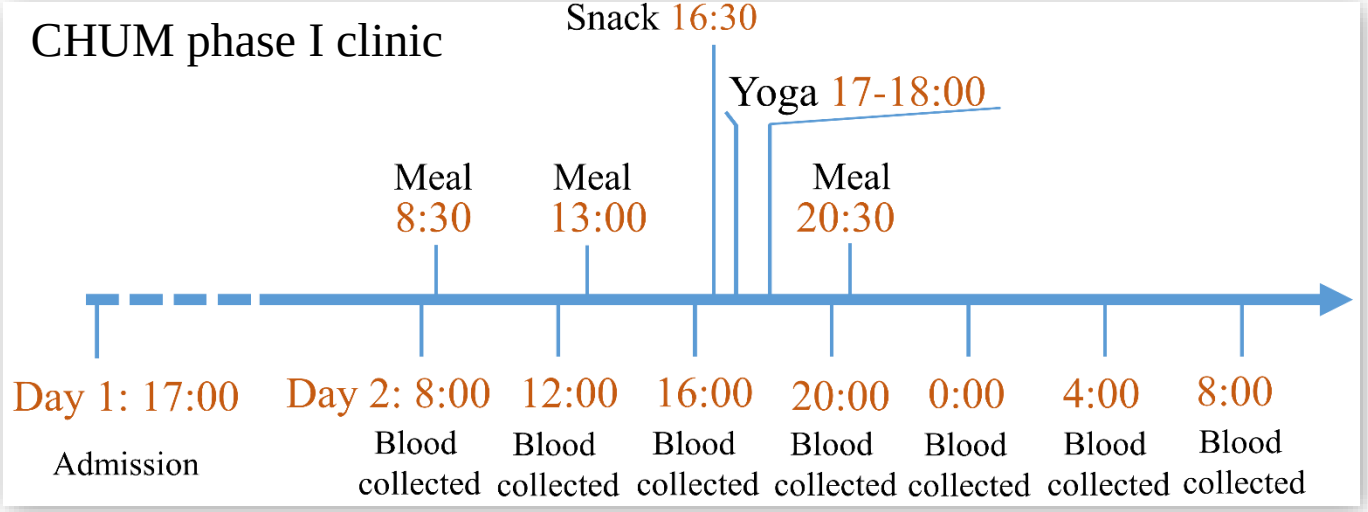


Fig. 1 Study timeline

Table 1 Participant Characteristics (n=11)

ID	Age	Body mass index (kg/m²)	CD4 count (cells/μL)	CD8 counts (cells/μL)	ART duration (years)	Viral load	Current ART medication
1	60	27.8	602	1321	10	undetectable	emtricitabine, TDF, raltegravir
2	52	27.1	491	613	21	undetectable	emtricitabine, TDF, raltegravir
3	57	28.4	606	855	12	undetectable	emtricitabine, TDF, raltegravir
4	57	32.9	846	901	22	undetectable	emtricitabine, TDF, darunavir, cobicistat
5	57	24.9	410	924	31	undetectable	emtricitabine, TDF, efavirenz
6	63	27.7	667	553	15	undetectable	abacavir, dolutegravir, lamivudine
7	50	34.9	379	498	19	undetectable	emtricitabine, TDF, raltegravir
8	58	26.1	311	331	21	undetectable	emtricitabine, TDF, elvitegravir, cobicistat,
9	57	24.6	800	597	13	undetectable	abacavir, dolutegravir, lamivudine
10	58	32.1	675	494	13	undetectable	abacavir, dolutegravir, lamivudine
11	54	23.9	1082	1425	17	undetectable	lamivudine, abacavir, raltegravir,

TDF = Tenofovir disoproxil fumarate

MAJOR FINDINGS

- Plasma levels of BDG and REG3α did not vary significantly over the course of the study.
- A significant increase of LPS was detected between 12:00 and 16:00 (Z-score: -1.15 ± 0.18 vs 0.16 ± 0.15, p=0.02), and between 12:00 and 24:00 (-1.15 ± 0.18 vs 0.89 ± 0.26, p<0.001).
- The plasma levels of I-FABP at 16:00 (-0.92 ± 0.09) were also significantly lower, compared to 8:00 the first day (0.48±0.26, p=0.002), 4:00 (0.73±0.27, p<0.001) or 8:00 on secondary day (0.88±0.27, p<0.001).

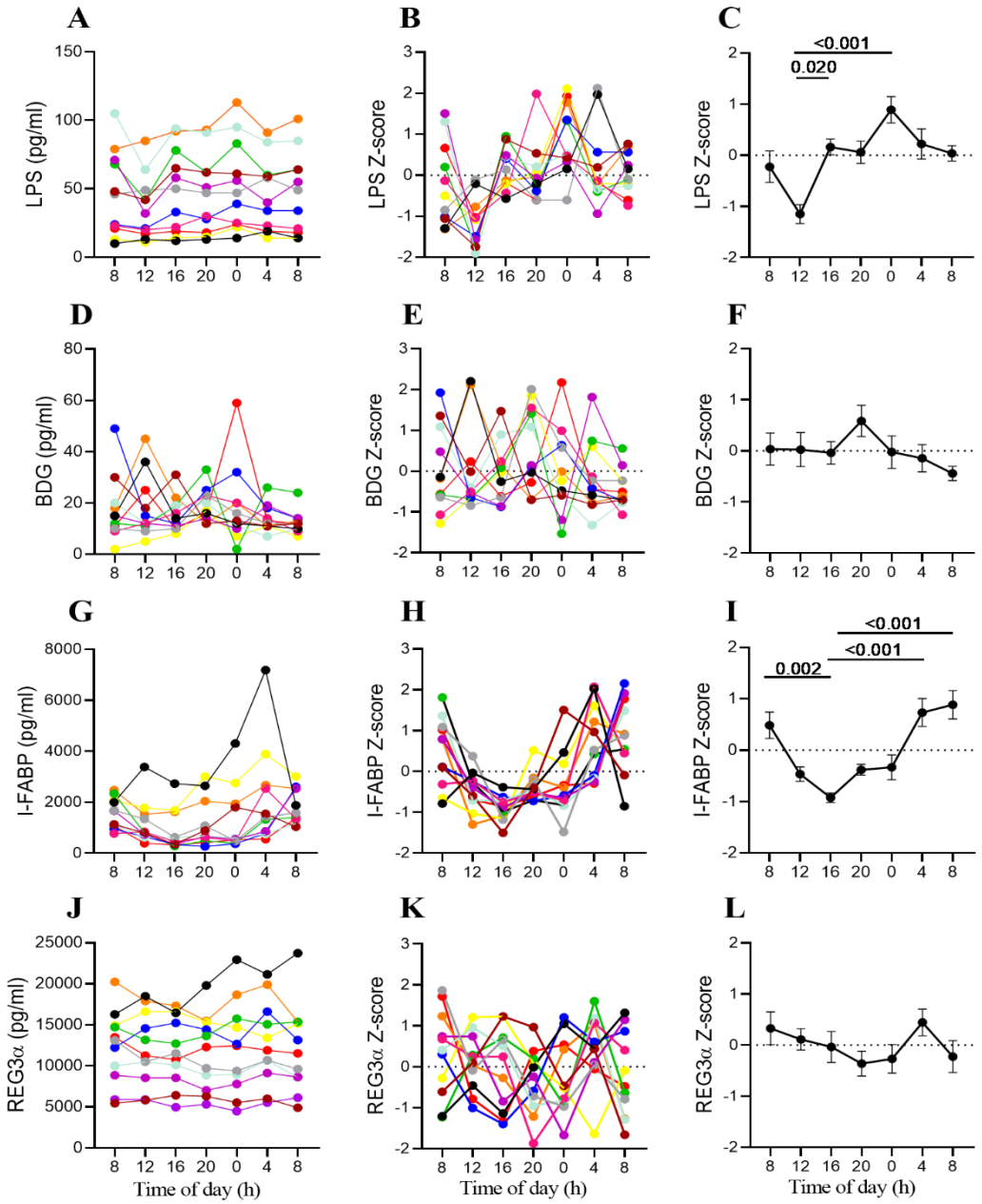


Fig. 2 Daily variation of gut damage and translocation markers.

CONCLUSIONS

1. We are the first to report the daily variation of different microbial translocation with gut damage markers in ART-treated PLWH.

2. We showed that conversely to I-FABP and LPS, plasma levels of REG3α and BDG can be considered as reliable markers of gut damage and fungal translocation respectively, and are not influenced by food intake, time of sampling, or day/night shifts in ART-treated PLWH.

3. Our findings provide reference for clinical research, focusing on the assessment of blood markers of gut damage and microbial translocation.

4. The clinical implications of the daily variation of these markers should be assessed in larger cohorts of ART-treated PLWH, including male and female participants from different ages and ethnicity.