Investigating biomarkers of the gut-brain axis and children's mental health in a post-COVID-19 urban clinic

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Background

- Viral infections during childhood can increase susceptibilities to neurodevelopmental and psychiatric disorders, leading to concerns about the current pandemic [1]
- Gut-brain axis (GBA) consists of bidirectional communication between the central and the enteric nervous system, linking the emotional and cognitive centers of the brain with peripheral intestinal functions [2]
- Some neurological disorders and mental health deficits may stem from gastrointestinal (GI) dysfunction, caused, or worsened by inflammation
- Children living in economically disadvantaged areas would be expected to show more GI problems
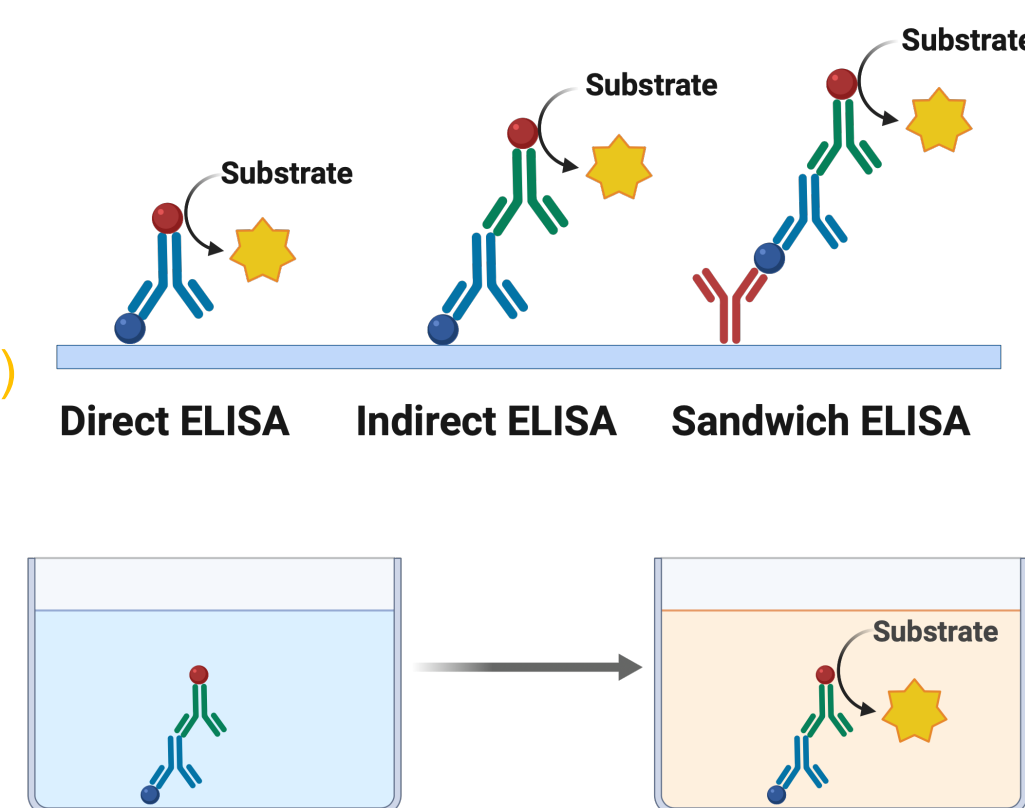

Brain / Gut
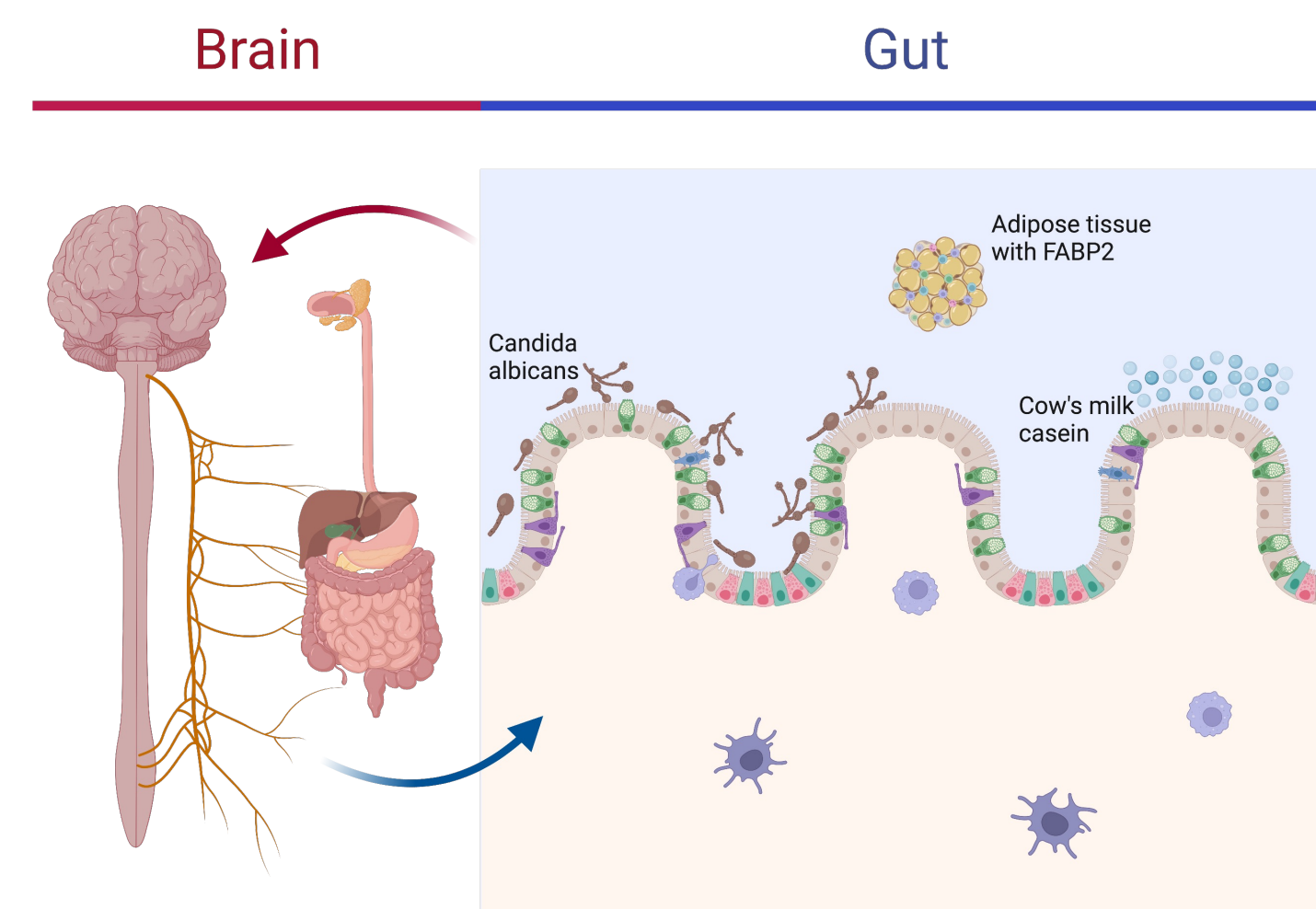
Methods & Design

- GI- or brain-derived products enter circulation when blood-GI or blood-brain barriers are damaged
- Enzyme-linked immunosorbent assays (ELISAs) for all biomarkers
- Child Behavioral Checklist (CBCL) to measure abnormal behavior
- Use STATA to test for significant associations with COVID-19 exposure

Biomarkers:
- Fatty Acid Binding Protein 2 (FABP2)
- Soluble CD14 (sCD14)
- LPS-binding protein (LBP)
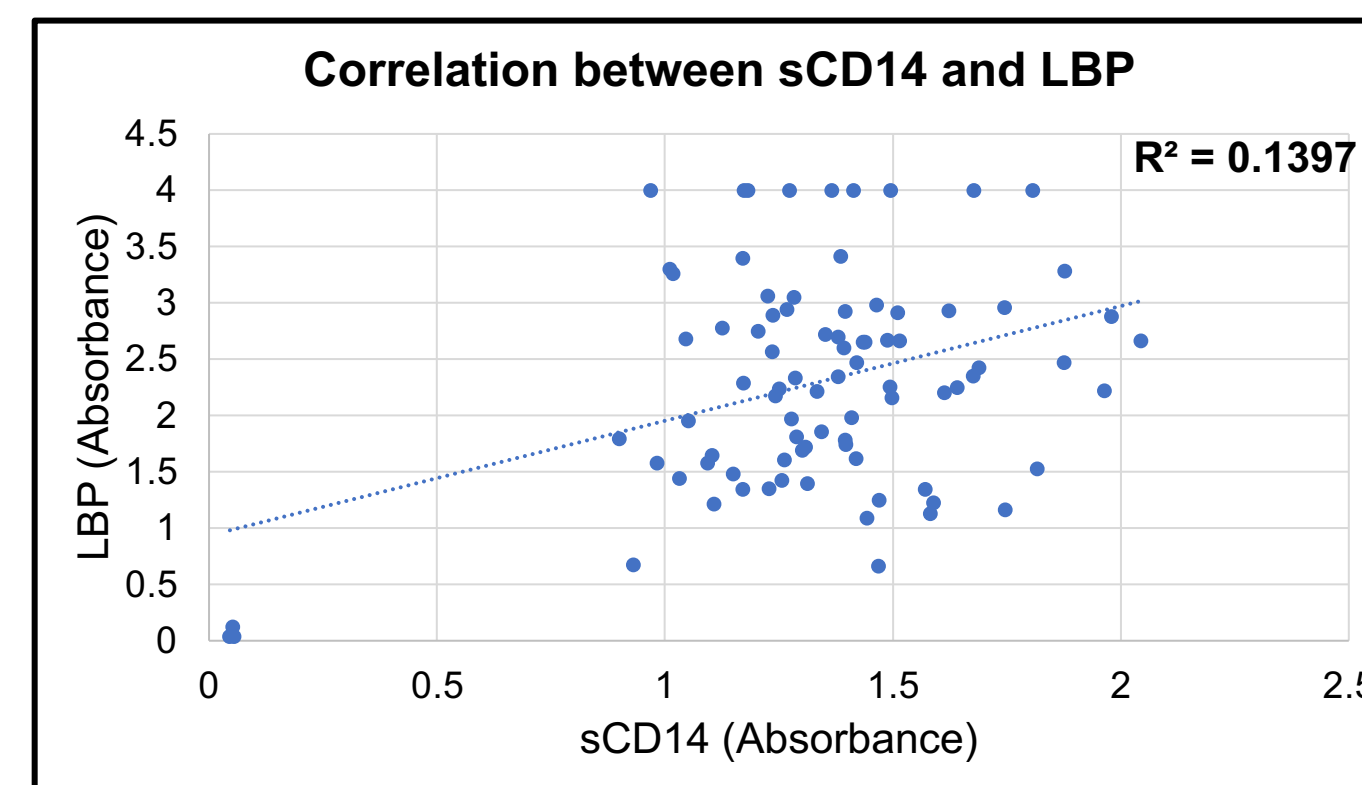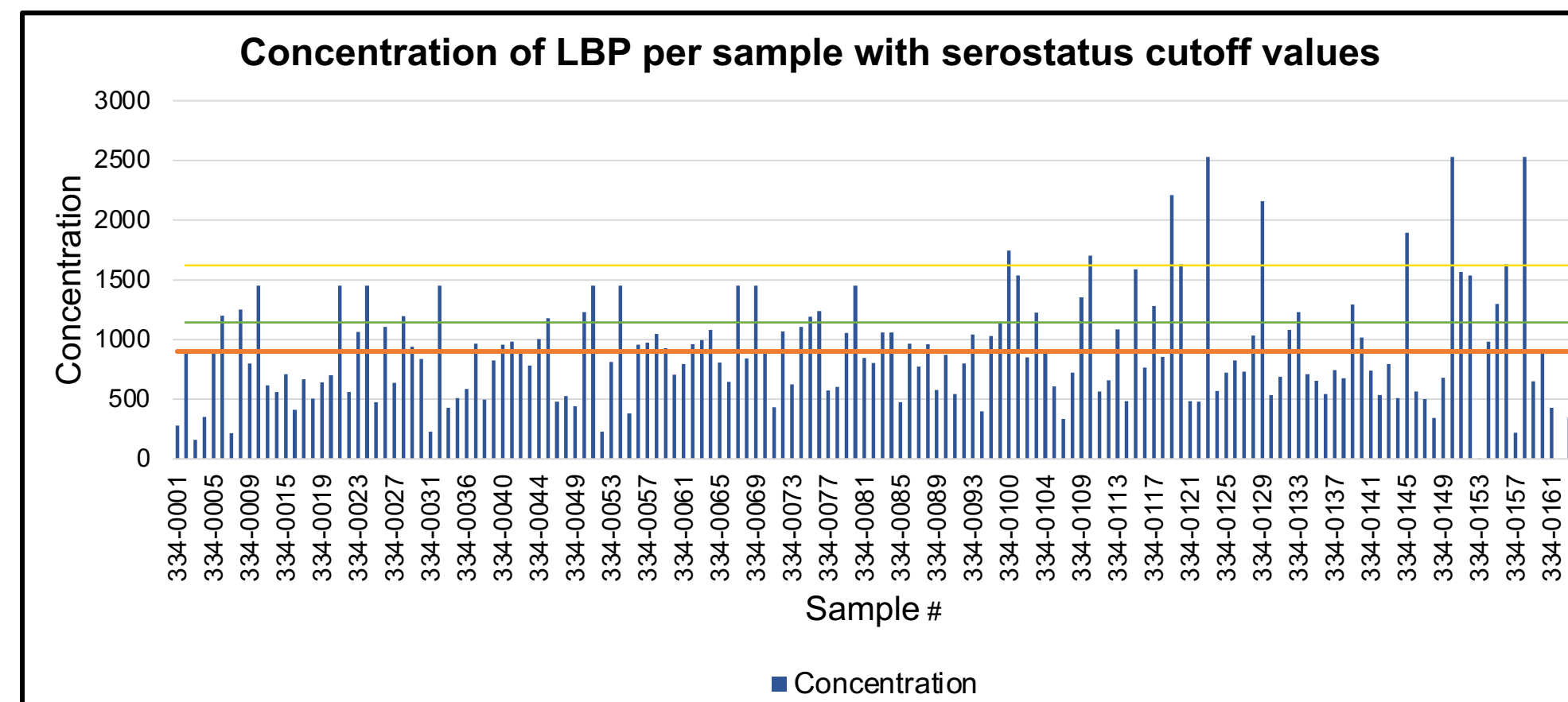- Calprotectin
- Casein
- *Candida albicans*

Direct ELISA   Indirect ELISA   Sandwich ELISA

Results

Concentration of LBP per sample with serostatus cutoff values

Correlation between sCD14 and LBP — $R^2 = 0.1397$

Table 1: Multivariate linear regression model with sCD14, LBP, Sex, and Age

Test	Value
Prob > F	0.0001
R^2	0.2279

Table 2: Seropositive and seronegative values for LBP

Type	Method	Calculation	Value	# of Seropositive	# of Seronegative
Conservative	Mean	900.32	900.32	67	88
Intermediate	Mean + one standard deviation	900.32 + 464.35	1364.67	23	132
Rigorous	Mean + two standard deviations	900.32 + 464.35*2	1829.02	6	149

Mean absorbance for each biomarker — COVID-19 - / COVID-19 +
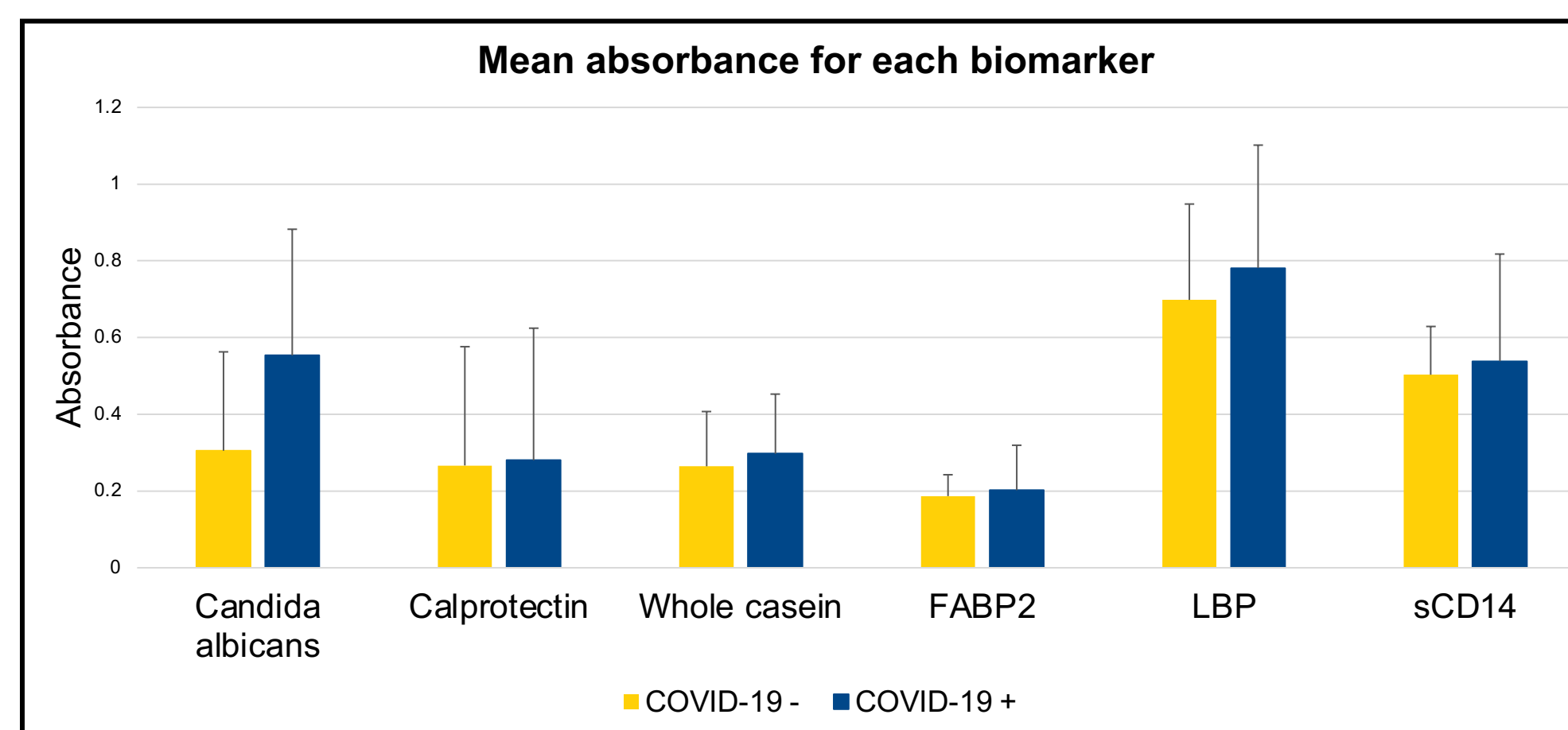
Conclusions

- Significant associations of the biomarkers, sCD14 and LBP, as consistent with previous studies and cellular pathways related to bacterial functions
  - Suggests some degree of bacterial translocation is occurring
- Patients with COVID-19 positivity have greater concentrations of antibodies to Candida albicans
  - Components of this relationship include antibiotics and bodily stress
- Other biomarkers thus far are inconclusive

Next Steps

- Compare the data presented to demographic factors and behavioral testing
- More ELISA experiments will be performed for biomarkers such as *Anti-Saccharomyces cerevisiae* IgG, matrix metallopeptidase 9 (MMP-9), gliadin, and Epstein-Barr Virus (EBV)
- Hypothesis: Children exposed to COVID-19 will have greater GI-related and neurological pathologies and subsequent mental health deficits

Neurological biomarkers
Glial fibrillary acidic protein
Neural cell adhesion molecule
Neurofilament light
Tau

CBCL measures
Aggression
Depression
Rules
Thought

References

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3. Ding, P. H., & Jin, L. J. (2014). The role of lipopolysaccharide-binding protein in innate immunity: a revisit and its relevance to oral/periodontal health. Journal of periodontal research, 49(1), 1–9. https://doi.org/10.1111/jre.12081
4. Figure under "Methods & Designs": Adapted from "ELISA Overview", by BioRender.com (2023). Retrieved from https://app.biorender.com/biorender-templates
5. Figure under "Results & Next Steps": Adapted from "Gut-Brain-Axis", by BioRender.com (2023). Retrieved from https://app.biorender.com/biorender-templates

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