Interactions between the gut microbiome and novel type 2 diabetes medications in type 2 diabetes

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Rationale

Commonly used medications are known to affect the gut microbiome composition, and microbiome can modify medication effectiveness [1-2].

Sharp increase in the prevalence of type 2 diabetes (T2D) has resulted in the need for novel medications, such as glucagon-like peptide-1 receptor agonists (e.g. semaglutide) and sodium-glucose cotransporter-2 inhibitors [3].

However, little is known about how these drugs affect the gut microbiome and how microbiome impacts the treatment effect.

Study questions

1. How do semaglutide and empagliflozin affect the gut microbiome composition in T2D patients?

2. How does baseline gut microbiome predict T2D treatment effect?

Results

No significant changes in the alpha (**Figure 2A**) nor beta diversity (PC1-PC2) (**Figure 2B**) (Aim 1).

Significant changes in the abundance of genera after treatment initialization (**Figure 2C**) (Aim 1).

Microbiome predicts treatment effect (**Figure 3**) (Aim 2).

Conclusions and implications

Microbiome could be a part of the drug action, which needs further studies.

As microbiome predicted changes in treatment outcome, we might be able to personalize the treatment in future.

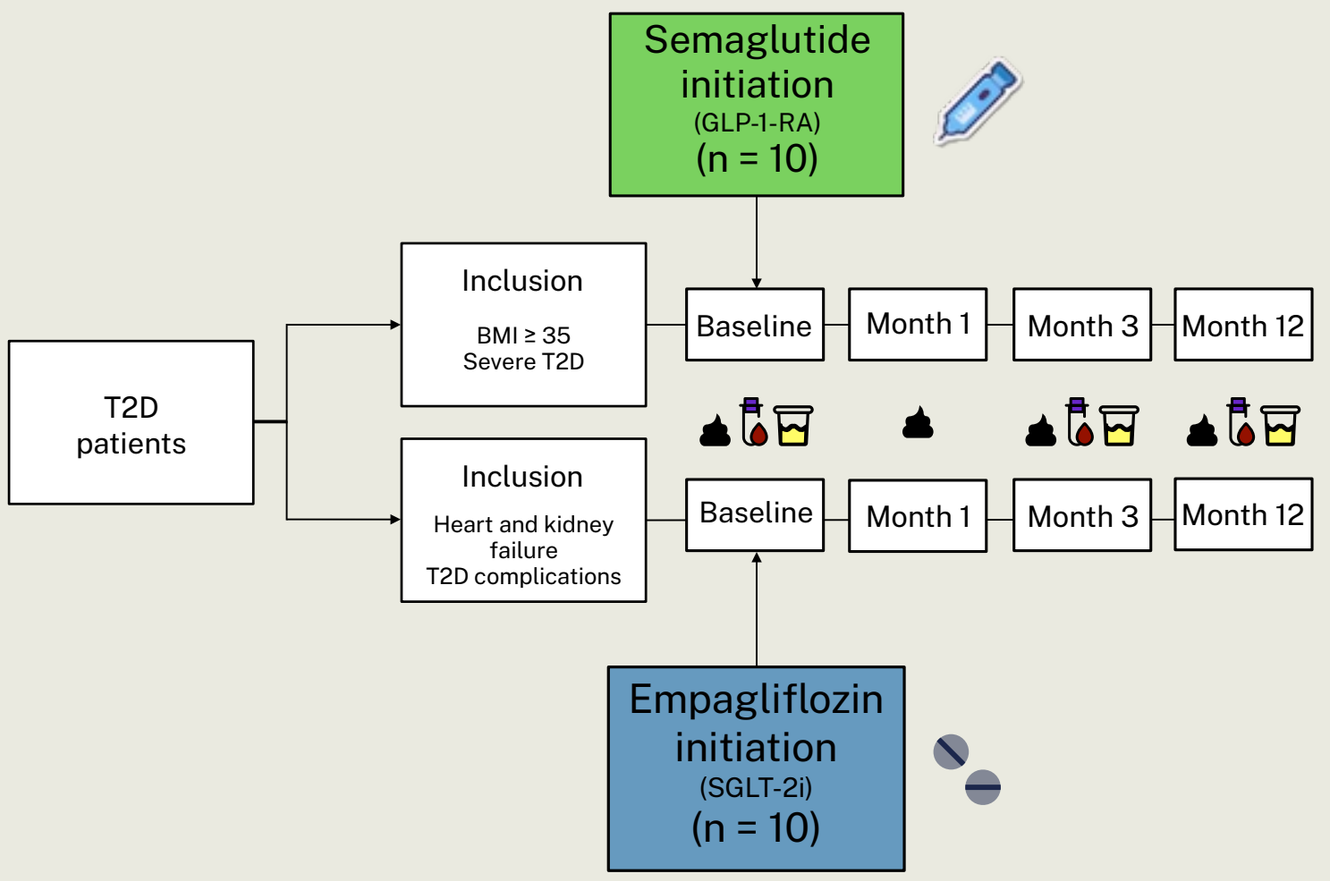

Figure 1. Study design and sample collection. Stool microbiome samples were collected at baseline and at 1 month, 3 months, and 12 months after treatment initialization. Microbiome was then sequenced and changes in the microbiome composition were analyzed.
GLP-1-RA - glucagon-like peptide-1 receptor agonist, SGLT-2i - sodium-glucose cotransporter-2 inhibitor.

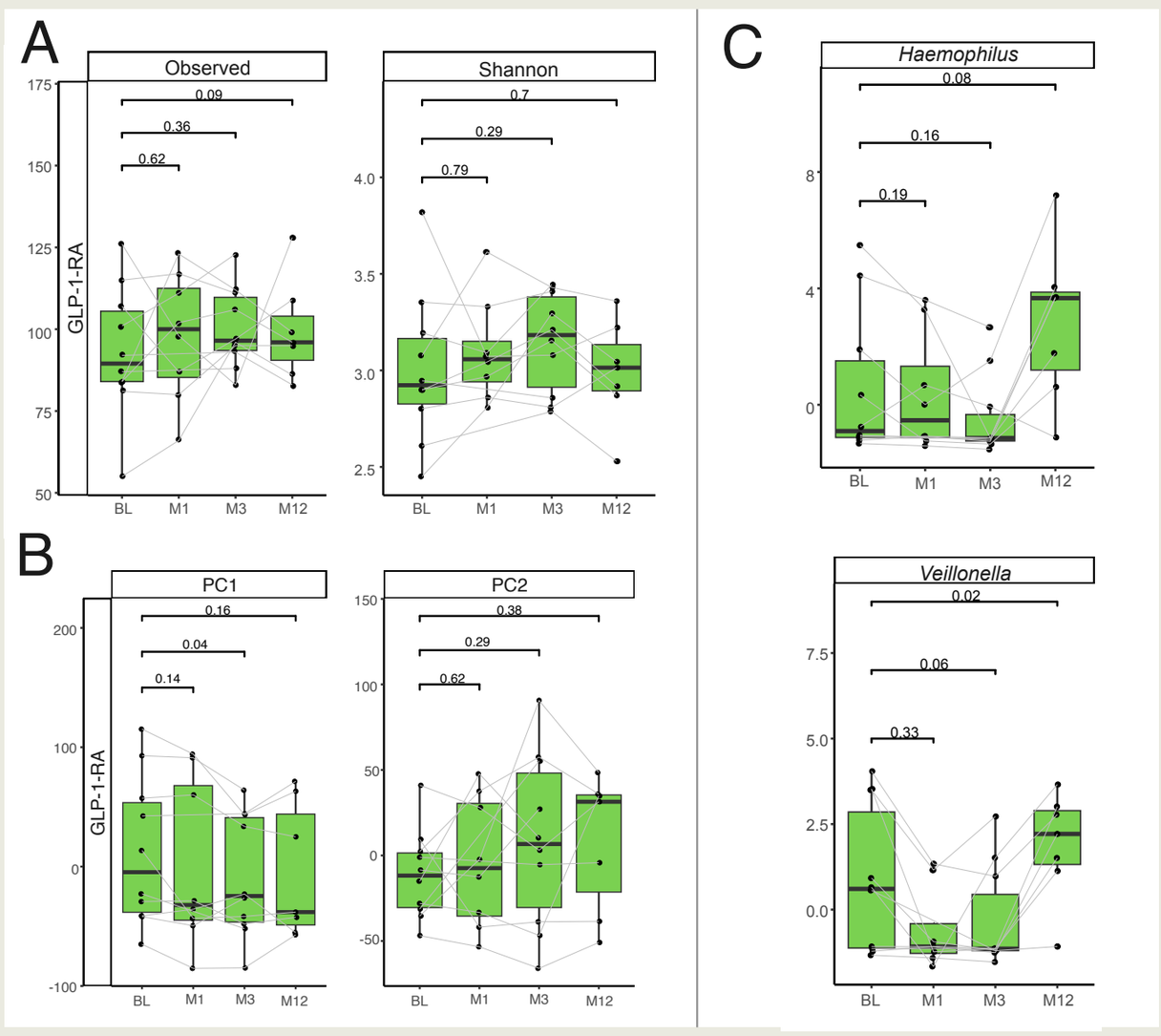

Figure 2. Effect of semaglutide (GLP-1-RA) on baseline (BL) gut microbiome and after treatment initialization. Comparisons were perfomed with paired t-tests and using FDR-correction (FDR <= 0.05).
M1 - Month 1, M3 - Month 3, M12 - Month 12.
A - microbiome alpha diversity, B - beta diversity, C - CLR-values of prevalent bacterial genera.

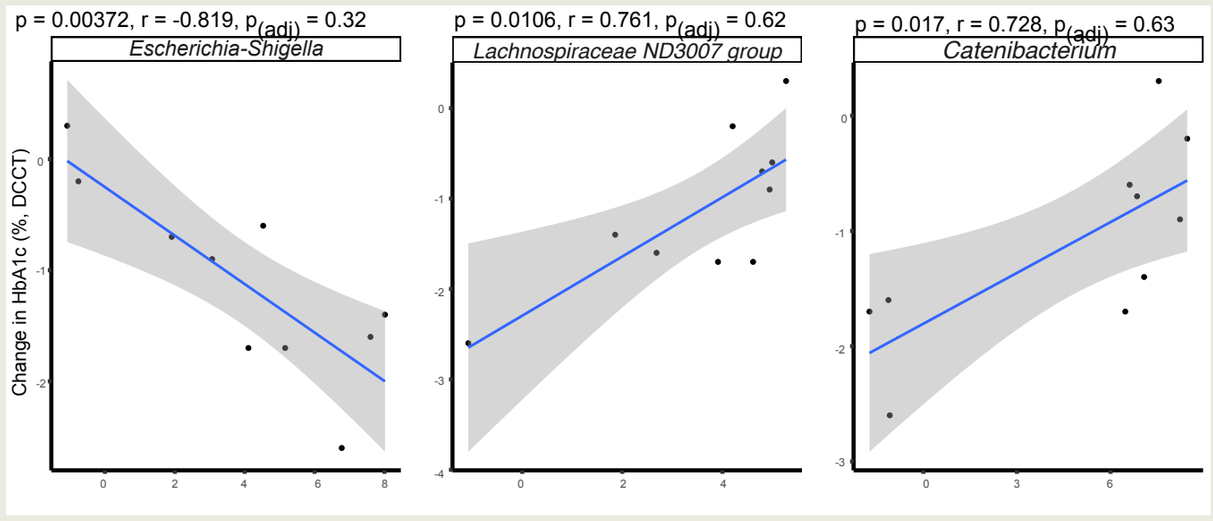

Figure 3. Associations between the baseline CLR-values of prevalent genera and changes in glycohemoglobin (HbA1c) by 3rd month in the semaglutide study group.
p - uncorrected p-value, r - Pearson correlation coefficient, p(adj) - FDR-corrected p-value, DCCT - Diabetes Control and Complications Trial units (HbA1c).

[1] Aasmets, O., Krigul, K. L et al. Gut metagenome associations with extensive digital health data in a volunteer-based Estonian microbiome cohort. Nat Comm 13, 1–11 (2022).

[2] Forslund, K. et al. Disentangling type 2 diabetes and metformin treatment signatures in the human gut microbiota. Nature 528, 262–266 (2015).

[3] Palmer, S. C. et al. Sodium-glucose cotransporter protein-2 (SGLT-2) inhibitors and glucagon-like peptide-1 (GLP-1) receptor agonists for type 2 diabetes: systematic review and network meta-analysis of randomised controlled trials. BMJ 372, m4573 (2021).

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