

# LpD64 REDUCES ADIPOSITY, IMPROVES GLUCOSE METABOLISM AND ALTERS GUT MICROBIOTA PROFILE

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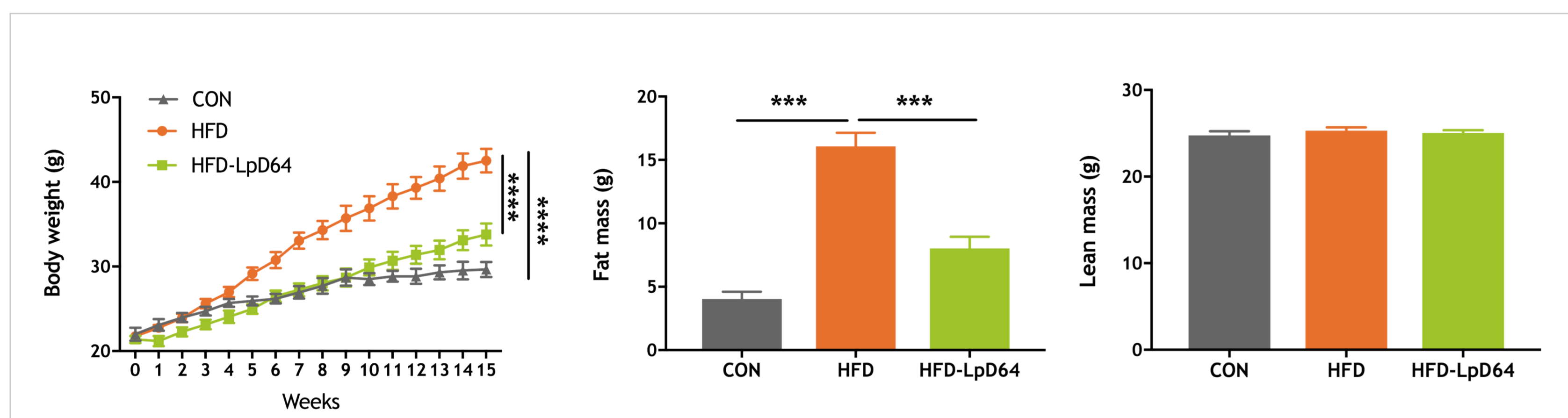
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## BACKGROUND

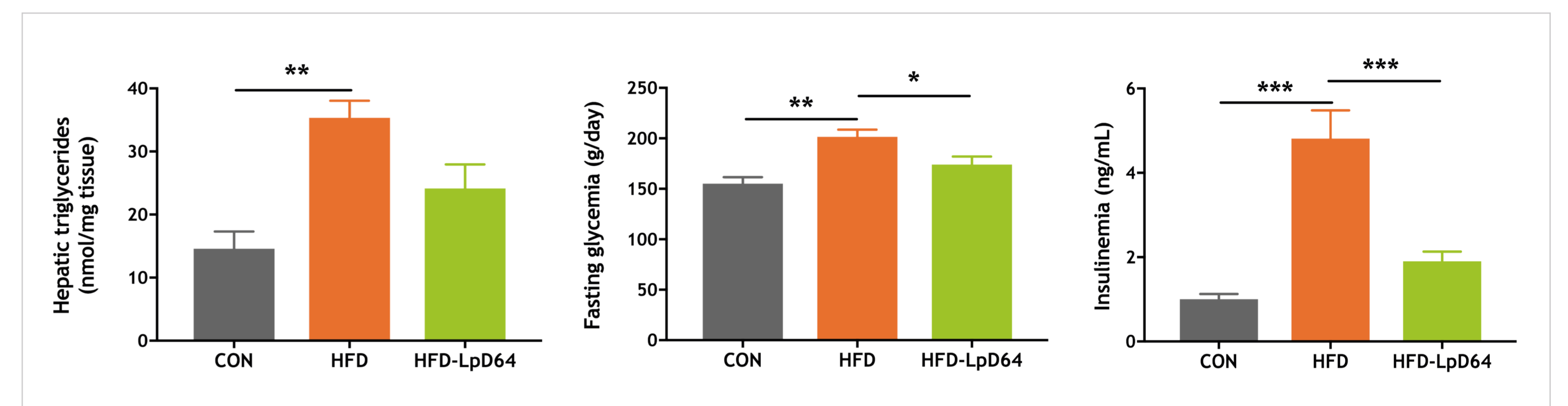
Obesity has been recognized as a global epidemic inducing serious health consequences often linked to metabolic syndrome, insulin resistance and type 2 diabetes. One therapeutic approach is lifestyle intervention. However, weight loss is generally difficult to maintain in the long-term. To prevent metabolic diseases development, we had tested a new complex (LpD64) that aims to reduce fat mass and to delay negative obesity outcomes.

## METHODS

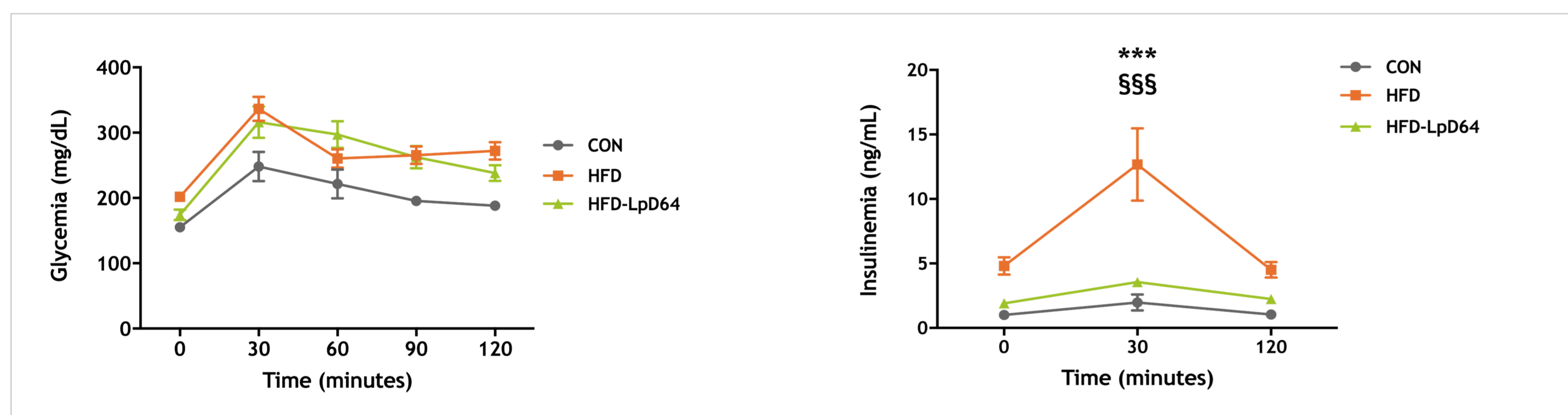
- Five-week-old mice were fed a standard diet (CON), a high-fat diet (HFD) or a HFD + LpD64 (HFD-LpD64, 2.7% diet) for 16 weeks, *ad libitum*.
- Whole body composition was determined by Echo MRI™ analyses, at the end of the experiment.
- Oral Glucose Tolerance Test (OGTT) was performed at the end of the experiment. Blood glucose was monitored before (0), 30, 60, 90 and 120 mn after an oral gavage of 2.3g of glucose/kg of lean mass.
- Plasma insulin levels were determined by ELISA (Alpco Diagnostics) before (0), 30 and 120 min after the oral gavage.
- Caecal content was harvested immediately after sacrifice of the animal and frozen into liquid nitrogen.
- Composition of fecal microbiota was assessed by 16S rDNA taxonomical metasequencing approach (Ondov et al, 2011; Schloss et al, 2009). Taxa represented in average in all samples at a threshold >0.5% or present in at least 10% of samples at a thresholds >0.5% are individually represented. In other cases, taxa are grouped and labelled as «others» in barplots.
- Caecal microbiota was analyzed by real-time qPCR (Cani et al, 2009; Everard et al, 2011).
- For the analysis of the relative abundances of taxa, a Benjamini & Hochberg procedure was applied to control the False Discovery Rate (FDR) due to multiple hypothesis tests on all taxa. For the other measurements, one-way ANOVA (or non-parametric Kruskal-Wallis test in case of non-gaussian distribution or heterogeneity of variances) will be applied followed by Tukey's or Dunn's post-hoc tests. As regard to parameters containing diets and time effects, repeated measures two-way ANOVA with Sidak's test will be used for multiple comparisons.



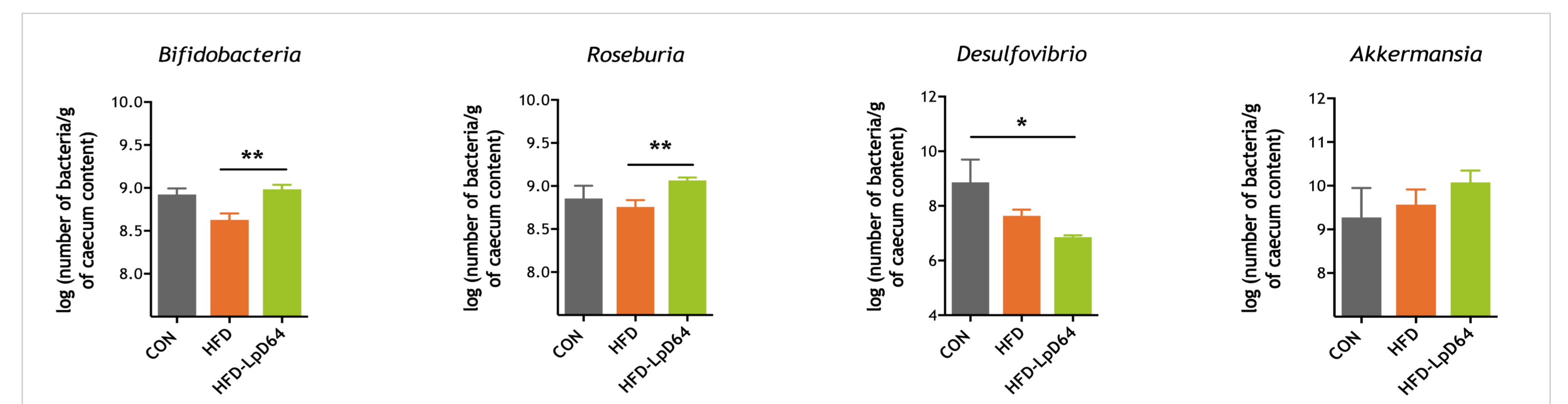
LpD64 diet supplementation had a beneficial effect on body weight gain. This reduced body weight was caused by lower fat mass at the end of the study. \*\*\*p<0.005; \*\*\*\*p<0.001



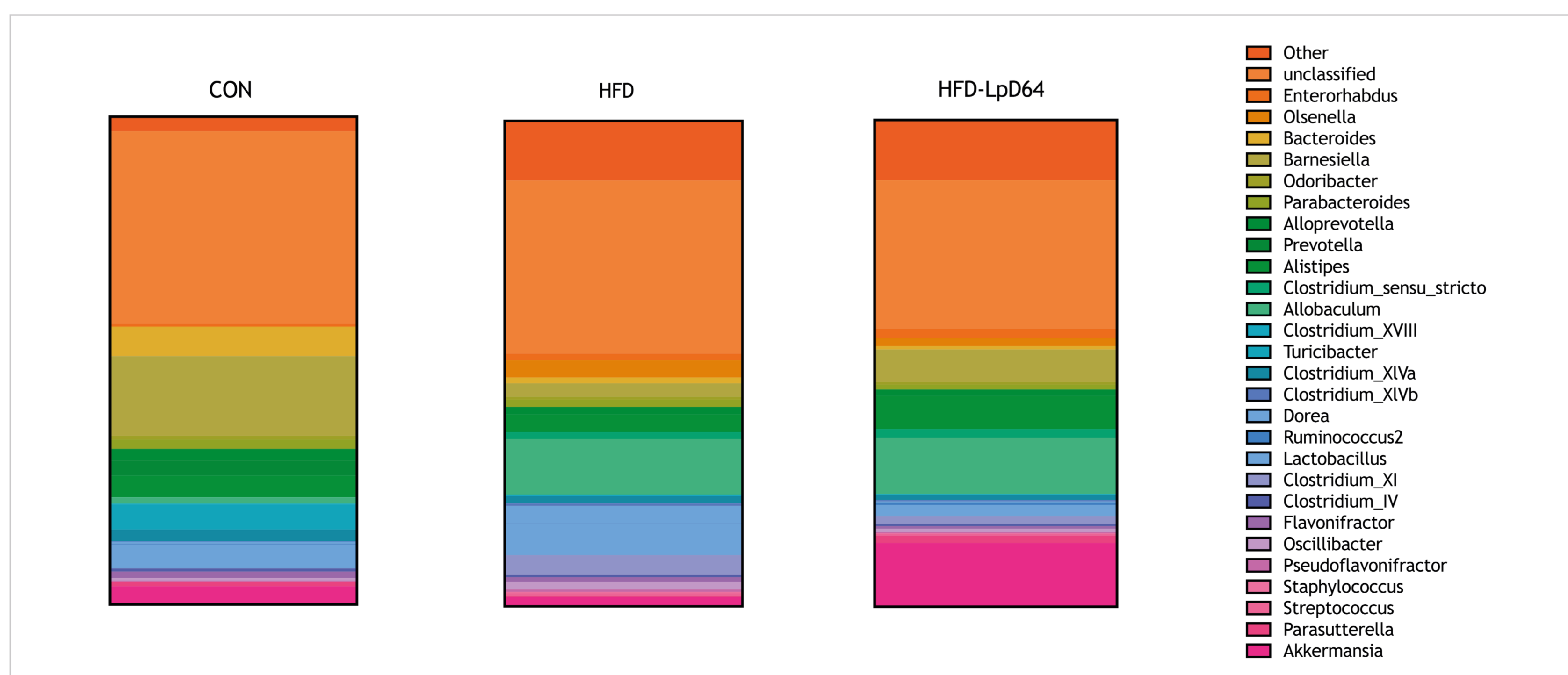
Diet supplementation with LpD64 reduced hepatic triglycerides, fasting glycemia and plasma insulin levels. \* p<0.05; \*\*p<0.01



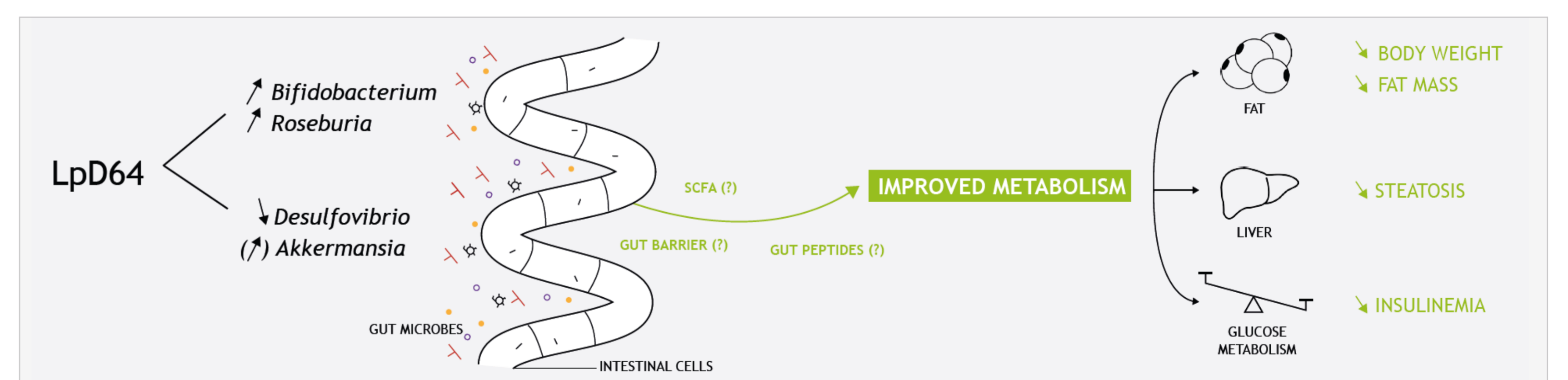
C57Bl6 mice fed with LpD64-supplemented diet for 16 weeks showed reduced insulin levels during the glucose challenge. \*\*\*p<0.001 vs CON; \$\$\$ p<0.001 vs HFD-LpD64



Quantitative qPCR of specific bacteria from caecum content revealed significantly increased levels of *Bifidobacteria* and *Roseburia* in mice fed HFD-LpD64, while a similar trend was observed for *Akkermansia*. Conversely, *Desulfovibrio*, which are considered opportunistic pathogens, are decreased by LpD64 consumption. \* p<0.05; \*\*p<0.01



Bacteria relative abundance measured by DNA sequencing from feces showed differences with the dietary treatment. Mice fed with LpD64 supplemented-HFD showed an increase in *Bacteroidetes*, while *Firmicutes* were decreased. Interestingly, *Akkermansia* was also increased.



Graphical summary of LpD64 effects and possible mechanisms of action that could explain the improved metabolism.

## CONCLUSION

LpD64 reduces weight gain and fat accumulation in mice, improving glucose metabolism. This is associated with changes in gut microbiota profile, showing the proliferation of bacteria previously linked to improved metabolic health. The underlying mechanisms of action are under investigation. A Phase I/II clinical trial is ongoing.