

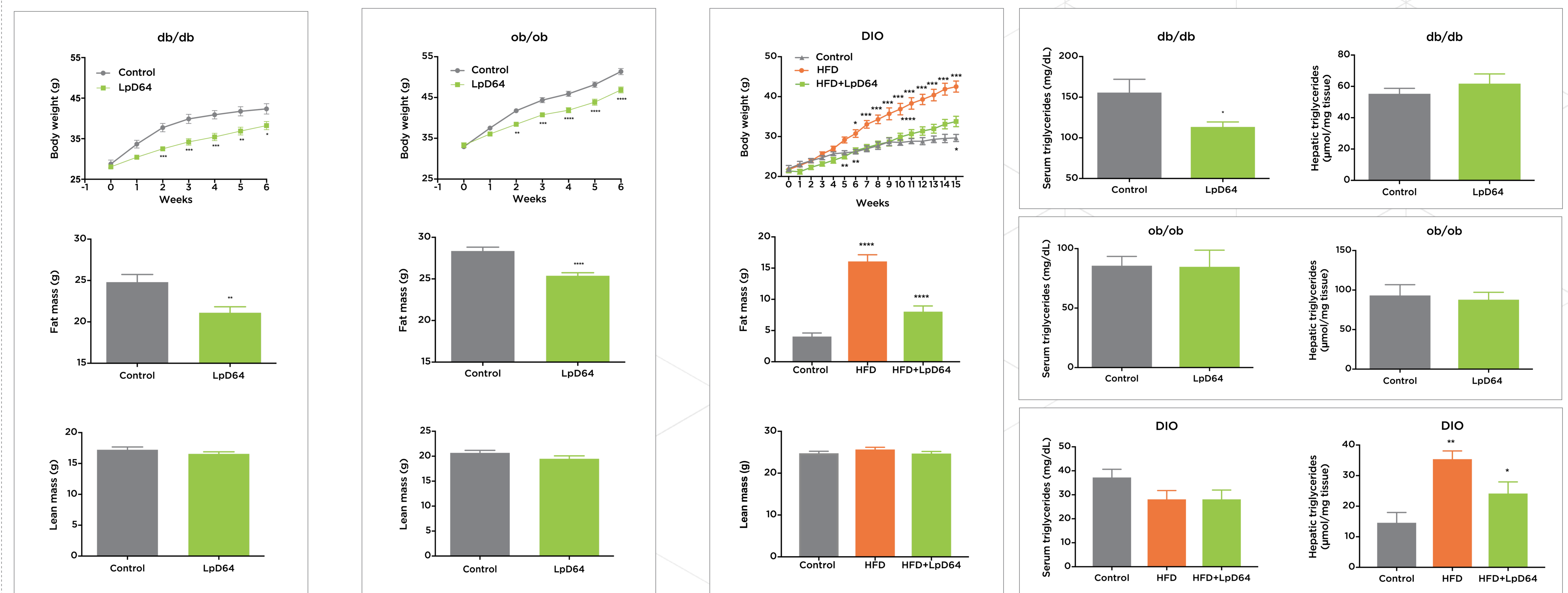
NEW COMPLEX LpD64 REDUCES ADIPOSITY IN db/db, ob/ob, AND DIO MICE

Y.F. Otero^{1*}, V. Chavanelle^{1,2}, G. Delcros², A. Teixeira¹, M. Etienne¹, P. Sirvent^{1,2}, S.L. Peltier²

¹AME2P Laboratory, Clermont Auvergne University, Clermont-Ferrand, France, ²Valbiotis, La Rochelle, France

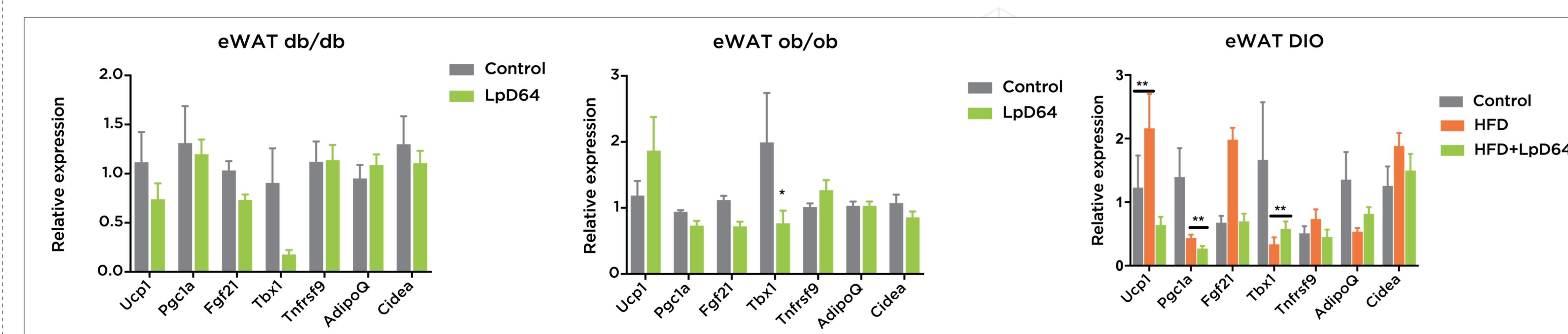
Background: Obesity has been recognized as a global epidemic, and it has serious health consequences often linked to metabolic syndrome, insulin resistance and type 2 diabetes. One of the main therapeutic approaches is lifestyle intervention. However, it is difficult to maintain the weight loss induced by changes in diet and exercise routine. We have developed a new complex (LpD64) that aims to reduce fat mass and to prevent negative obesity outcomes. We have tested LpD64 in three obese mouse models (db/db; ob/ob and C57Bl6 diet-induced obesity [DIO] mice).

Methods: Six week-old db/db and ob/ob male mice were fed with standard or LpD64-supplemented diet (2.7%) for 6 weeks. Six week-old C57Bl6 male mice were fed with high-fat diet or high-fat diet supplemented with LpD64 (2.7%) during 16 weeks. At the end of the study, body composition was measured by MRI. Moreover, plasma and tissue samples were collected. Liver and epididymal white adipose tissue gene expressions were measured using qRT-PCR. Serum and hepatic triglycerides levels were measured using colorimetric methods.

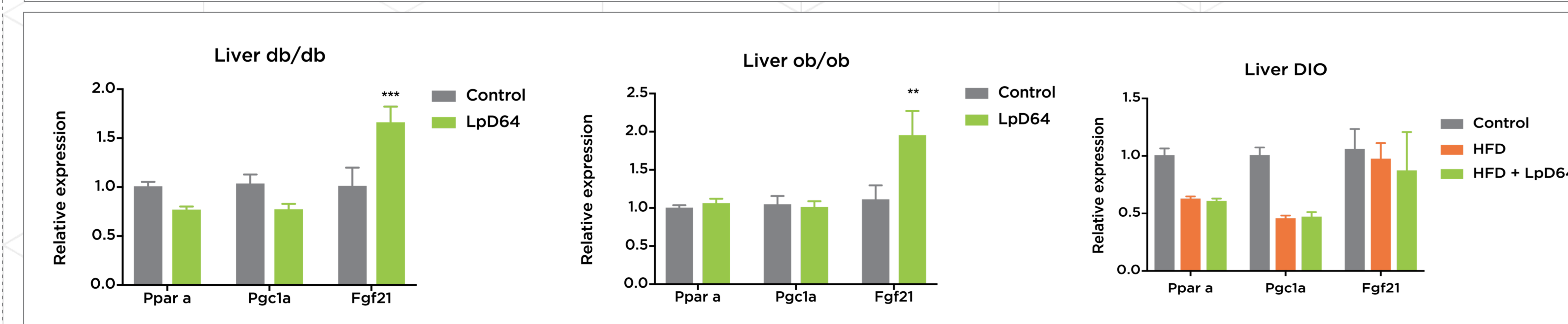


LpD64 supplementation reduced body weight gain on the three obese models studied. The difference in body weight was caused by lower fat mass at the end of the study, while lean mass was maintained. * p<0.05; **p<0.01; ***p<0.005; ****p<0.001.

Diet supplementation with LpD64 reduced serum triglycerides in db/db mice and hepatic triglycerides in C57BL6 mice fed with HFD. * p<0.05; **p<0.01.



The decrease in fat mass could not be explained by changes in the expression of « browning » markers gene expression in epididymal white adipose tissue (eWAT) from db/db mice (left panel); ob/ob mice (center panel) and C57Bl6 mice (right panel) fed with standard or LpD64-supplemented diet for 6 weeks (db/db and ob/ob) or 16 weeks (DIO). * p<0.05; **p<0.01.



Liver gene expression in db/db mice (left), ob/ob mice (center) and C57Bl6 mice (right) fed with standard or LpD64-supplemented diet during 6 weeks (db/db and ob/ob) or 16 weeks (DIO mice). Both genetic models showed increased FGF21 gene expression, while C57Bl6 mice fed with HFD or HFD+LpD64 showed no significant differences. **p<0.01, ***p<0.005.

Conclusion

LpD64 significantly reduces adiposity and improves lipid metabolism in three different mouse models of obesity. This phenotype might not be caused by direct alteration on adipose tissue browning. A phase I/II clinical trial is ongoing, to initiate LpD64 assessment in human subjects.