# Exercise partly protects against semaglutide-induced muscle loss in obese LDLR-/-.Leiden mice

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## 1. Background & aims

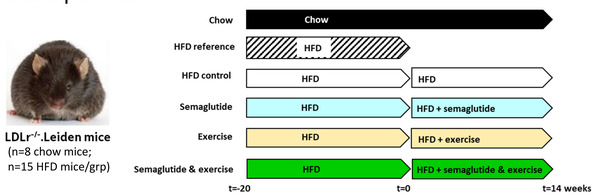
Semaglutide, a glucagon-like peptide-1 receptor agonist, is an antidiabetic medication that has recently been approved for treatment of obesity as well. While the benefits of semaglutide for weight management are encouraging, concomitant muscle loss can be a potential drawback.

Here, we evaluated the metabolic effects of semaglutide, exercise and the combination thereof in a translational model of obesity and associated complications.

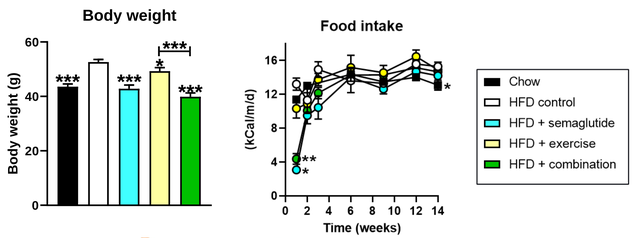
## 2. Methods & study design

Ldlr-/-.Leiden mice received a high fat diet (HFD) for 20 weeks to induce obesity, insulin resistance and hyperlipidemia. Mice were subsequently left untreated (control) or were treated for 14 weeks with semaglutide, exercise (running-wheel) or the combination thereof.

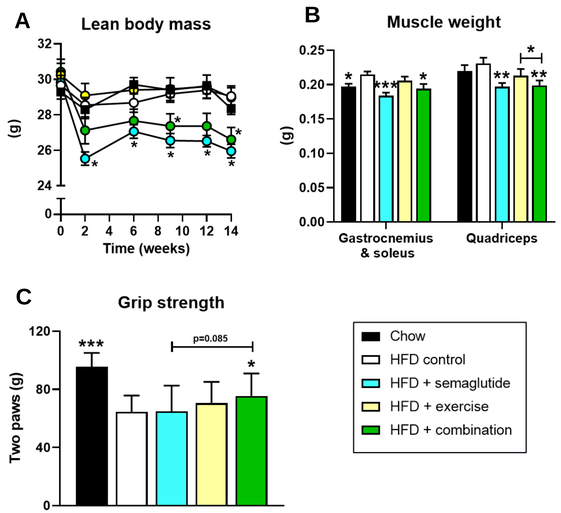
Body weight, lean body mass (EchoMRI) and plasma parameters were evaluated during the study and liver, muscles, adipose tissue depots, hearts and brain were collected at end-point for histological analysis and future transcriptomics.




## 3. Semaglutide decreased body weight and transiently decreased food intake

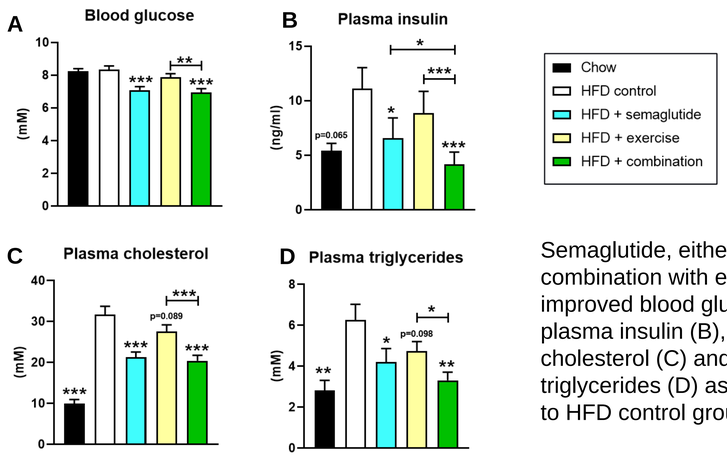



## 4. Semaglutide, either alone or in combination with exercise, decreased lean body mass and muscle weights



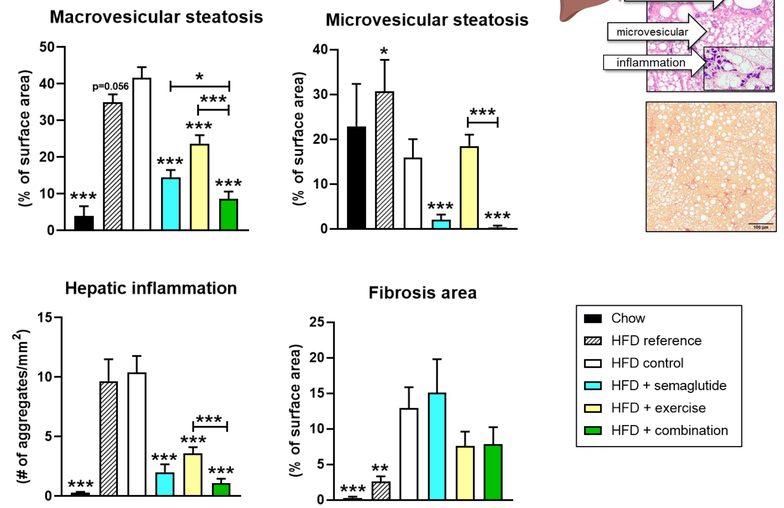

A. Lean body mass was decreased with semaglutide treatment and as well, but to a lesser extent, when combined with exercise
B. Muscle weights at sacrifice were significantly decreased as compared to HFD control group with semaglutide treatment, but also when combined with exercise
C. Absolute grip strength was improved as compared to HFD control group in combination treatment group only

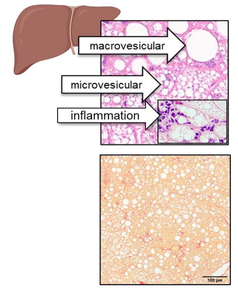
## 5. Semaglutide, either alone or in combination with exercise, improved metabolic parameters.




Semaglutide, either alone or in combination with exercise, improved blood glucose (A), plasma insulin (B), plasma cholesterol (C) and plasma triglycerides (D) as compared to HFD control group.

## 6. Liver steatosis and inflammation improved with interventions, but not liver fibrosis

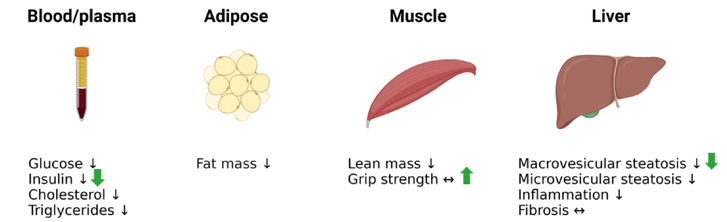



## 7. Conclusion

Using a translational model of obesity and the Metabolic Syndrome, we demonstrated that:

- Semaglutide has broad beneficial effects on plasma, adipose and liver parameters
- But decreased lean body mass and muscle mass.
- **Adding exercise** to semaglutide intervention further improved plasma insulin, muscle strength and liver steatosis.

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