Dissertation thesis „Effects of stable analogs of anorexigenic neuropeptides in models of metabolic syndrome" by Ing. Lucia Mráziková is well and clearly written, the results are or will be published in the near future in high quality journals. It deals with the effects of chronic administration of lipidated analog of anorexigenic neuropeptide prolactin-releasing peptide (palm^{11}-PrRP) on three rodent models of obesity with intact leptin signalisation or with leptin or leptin receptor defficiency.

The Thesis deals with a highly socially relevant topic of obesity treatment and all used methods are of high quality and common in this field of research. The results of the work suggesting a role for leptin signalisation in the effects of PrRP are original and novel. The formal quality is excellent.

Significance of this work for further development of the scientific field and possible applications in practice is very high. The use of lipidated analogues of PrRP certainly has great potential, as evidenced by the established commercial collaboration with Novo Nordisk A/S, in which the author participated.

This dissertation thesis definitely demonstrates the author's qualifications for independent scientific work and certainly meets the requirements for the award of Ph.D. degree.

Minor issues:

- It is not allways clear if the data cited in Introduction come from studies in humans or laboratory rodents.
- Why have you not shown representative histological microphotographs from all the groups within the study in Fig. 14 and 24?
- Why have you not included data from palm-PrRP31 treated group in Fig. 25?

Questions:

- Can you specify laboratory rodent models for diabetes? Is it possible to mimic diabetes in rodents only by using nutritional challenge?
- Can you comment on the fact stated in this Thesis that *ob/ob* mice have a defect in brown adipose tissue in light of the work Fischer, 2020, Endocr Rev, DOI: 10.1210/endrev/bnz016?
- Can you comment on the work of Zhao, 2019, Cell Metab, DOI: 10.1016/j.cmet.2019.08.005 , where a decrease in leptin plasma levels lead to an increase in leptin sensitivity? May you hypothetize how this increase in sensitivity to leptin would influence sensitivity to palm^{11}-PrRP?
- In which tissues NPFF is synthetized?
- How have you assessed subthreshold levels of leptin interventions to 5 or 10 μg/kg of body weight? Can you compare the effect with the work of Burnett, 2017, Int J Obes, DOI: 10.1038/ijo.2016.238? Why you choose different lengths of leptin treatments in this study (2 and 8 weeks)? Why have you used 10 ug/kg of body weigth as compared to 5 ug/kg of body weight in combination with palm11-PrRP?

[redacted]