Objective

- Previous reports demonstrated that erythropoietin (EPO) induces body weight loss and improves insulin resistance in obese mice. As part of its mechanisms, the lowering of white adipose tissue (WAT) induced by high dose EPO treatment (3,000 IU/kg) contributes the improvement of obesity.
- The aim of this study is to elucidate the mechanism of thermogenesis in the classic brown adipose tissue (classical BAT, cBAT).

Materials and Methods

- Four-week-old male C57BL/6J mice were fed a high fat diet (HFD) and injected with recombinant human (rh)EPO. EPO (100 IU/kg, Epoetin-a, JCRPharma, Japan) was administered three times per week for 4 weeks by intraperitoneal injection.
- Oxygen consumption (VO2) was measured to estimate the metabolic rate. And also, surface temperature on the interscapular BAT (iBAT) was used to quantify heat generation a thermal imaging camera.
- Metabolic parameters were measured at 8 weeks.
- Intraperitoneal glucose tolerance tests (IPGTT) (glucose, 1 g/kg) were performed in the overnight-fasted mice. And measurements of the levels of blood glucose and serum insulin.
- We also analyzed the expression of genes and proteins related to thermogenesis and that associated signal pathway on iBAT (By the methods of quantitative realtime PCR and western blot analysis).

Discussion

- We have investigated that EPO treatment significantly reduced the body weight and improved glucose intolerance in the HFD mice. WAT mass volume was decreased and iBAT mass volume was increased by the effect of EPO treatment.
- Kate O. J. Endocrinol 2010
- Meng B. Post one 2011
- Woo M. Diabetes 2014
- Our study identified that the mRNA expression and protein of UCP1 were increased in the HFD group in comparison with the control group. Furthermore, the expression of UCP1 protein was upregulated with EPO treatment under the HFD condition. We considered that EPO treatment could have synergistic effect under the condition such as the adrenergic stimulation. The biological markers for BAT-specific differentiation (PRDM16, PPARα, PPARγ and PGC1α) were also increased in the interscapular BAT (iBAT).
- We confirmed that classical BAT expresses EPO receptor (Epor). EPO has a direct effect through Epor/STAT3 signaling pathway on the regulation of UCP1 in iBAT and related to differentiation pathway that Myomi13 regulates brown fat differentiation through Prdm16. Further investigation is required for these signals in detail by EPO.
- Li W et al. Diabetes 2013
- Sally Y et al. Diabetes 2014

Conclusion

- EPO treatment, even at a lower dosage, activates heat production and lipolysis in cBAT through Epor/STAT3 and MEIF2-nur3r13/PRDM16 conditions. This mechanism leads to improve obesity and insulin resistance.

We have nothing to disclose.