Effects of high-fat diet-induced obesity and metabolic disorder on sperm small RNA profile and offspring phenotype in mice

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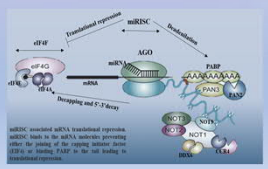
MOLECULAR SYSTEMS BIOLOGY

Introduction

Excessive fat accumulation in the body increases the risk of metabolic diseases. Acquired paternal obesity does not only affect the health of exposed individuals, but it can also induce changes in offspring phenotype through epigenetic mechanisms. High-fat diet (HFD) is known to affect sperm small non-coding RNA (sncRNA) levels, and these changes can transmit to offspring.



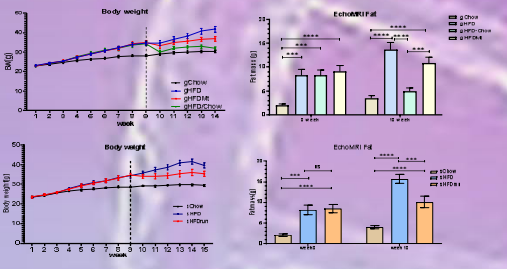
Aim

1. The main objective is to determine how paternal high-fat diet-induced obesity
2. treating obesity with different interventions, influences the small RNAs profile of spermatozoa.
3. Soma-to-germline small RNA are also tracked to trace the origin of sperm small RNA changes induced by high-fat diet

Result

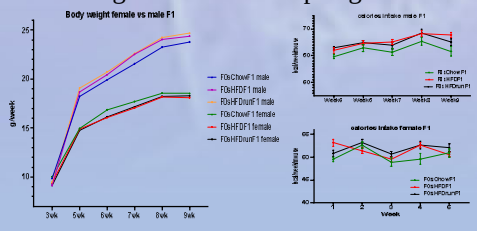
1. Obese phenotype can be treated by diet and exercise

Our result indicated that healthy diet and exercise interventions after HFD treatment decreased the weight (*p*-values 0.0008 and <0.02, respectively) and fat mass (*p*-values < 0.0001 and 0.0003, respectively), while metformin intervention did not have significant effects.



2. Both male and female offspring of either obese fathers or exposed interventions fathers did not show any differences in gaining weight

Although the calories intake of offspring exceeded control, these extra calories did not cause any significant differences in body weight. It is also interesting to mention that female offspring gained less weight than male offspring.

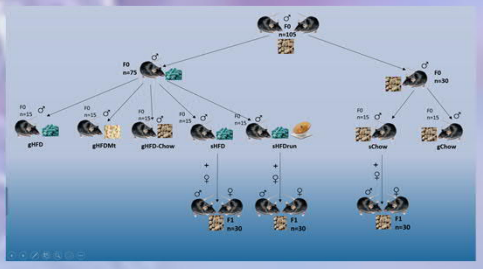


3. Optimization of RNA protocol of sperm resulted in intact RNA

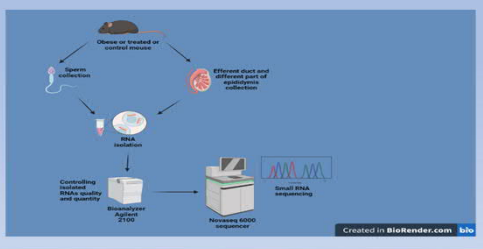
RNA extraction from sperm and efferent ducts and different parts of the epididymis resulted in good quality with high integrity values. RNA sequencing of these samples will reveal interesting novel information on the HFD-induced changes in small RNAs, as well as the effects of interventions on sperm sncRNA profiles.

Method

1. Adult male C57BL/6 mice were fed with an HFD for eight weeks to induce obesity. Control mice were fed with chow diet.
2. HFD-induced obesity was then treated by healthy diet (n=15), metformin medication (n=15), or exercise (n=15). Control mice kept eating HFD (n=15) or chow (n=15) without intervention.
3. Before sacrifice males were mated with females that were fed on Chow diet for the assessment of the offspring phenotype.
4. The pups were weaned from mothers at 21 days of age and fed on a chow diet for eight weeks



5. Subsequently, sperm and different parts of the reproductive tract were collected for the assessment of sncRNA expression patterns by deep sequencing



Conclusion

This study showed that exercise and diet alone are capable to restore phenotypic metabolic changes induced by high-fat diet. Ongoing experiments will reveal interesting novel information on the HFD-induced changes in small RNAs in both sperm and reproductive tract.