High-fat diet promotes a pro-inflammatory environment in testis and inhibits antioxidant defenses in the progeny

Luís Crisóstomo¹, Romeu A. Videira², Ivana Jarak³, Kristina Starčević⁴, Tomislav Mašek⁵, Luís P. Rato⁶, João F. Raposo⁷,⁸, Pedro F. Oliveira⁹, Marco G. Alves¹,*

¹Department of Microscopy, Laboratory of Cell Biology, and Unit for Multidisciplinary Research in Biomedicine (UMIB), Institute of Biomedical Sciences Abel Salazar (ICBAS), University of Porto, Portugal;
²REQUINTE/LAQV, Laboratory of Pharmacognosy, Faculty of Pharmacy, University of Porto, Porto, Portugal;
³Department of Pharmaceutical Technology, Faculty of Pharmacy, University of Coimbra, Portugal;
⁴Department of Chemistry and Biochemistry, University of Zagreb, Faculty of Veterinary Medicine, Zagreb, Croatia;
⁵Department of Animal Nutrition and Dietetics, University of Zagreb, Faculty of Veterinary Medicine, Zagreb, Croatia; ⁶Health School of the Polytechnic Institute of Guarda, Guarda, Portugal;
⁷NOVA Medical School – New University Lisbon, Lisbon, Portugal;
⁸APDP – Diabetes Portugal, Lisbon, Portugal;
⁹QOPNA & LAQV, Department of Chemistry, University of Aveiro, Aveiro, Portugal

* Corresponding author: alvesmarc@gmail.com
Abstract: The adoption of high-fat diets (HFD) is a major contributor for the increasing prevalence of obesity worldwide. Herein we study the impact of HFD from early age in testicular physiology and sperm parameters in two generations of mice, with focus on the testicular oxidative status. Mice of the diet-challenged generation (F0; n=36) were randomly fed after weaning with standard chow (CTRL) or high-fat diet (HFD) for 200 days or transient high-fat diet (HFDt) (60 days of HFD+140 days of standard chow). The offspring generation (F1; n=36) were obtained by mating with normoponderal females with 120 days post-weaning and fed with chow diet. Mice fed with HFD for a lifetime have impaired insulin tolerance, a trait inherited by their sons. The sons of mice fed HFD inherited decreased catalase activity, displayed lower activities of mitochondrial complexes I and IV. Similar to their progenitors, fed with lifelong HFD, the sons of HFD had higher prevalence of pin head and bent neck defects. The adoption of HFD impairs testicular antioxidant defenses and mitochondrial function in the progeny, which is detrimental to sperm morphology.

Keywords: high-fat diet; pro-inflammatory state; intergenerational effects; antioxidant defenses; testis
Methods

- Biometric monitoring
- Glucose homeostasis
- Sperm parameters
- Oxidative Stress and Mitochondrial activity
- GC-MS Lipidomics
- NMR-based Metabolomics
Results

The offspring of HFD-fed mice display abnormal insulin tolerance

Two-way ANOVA corrected by Šidak’s method. Significance was considered when $p < 0.05$.

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$. * CTRL vs. HFD; # HFD vs. HFDt.
Results

The adoption of HFD inhibits testicular antioxidant defences even in offspring

Univariate ANOVA corrected by Tukey’s HSD. Significance was considered when p < 0.05. * p < 0.05; ** p < 0.01; *** p < 0.001. * vs. CTRL; # vs. HFD.
Results

*Testicular mitochondrial defects are only detected in offspring of HFD-fed mice*

Univariate ANOVA corrected by Tukey’s HSD. Significance was considered when p < 0.05. * p < 0.05; ** p < 0.01; *** p < 0.001. * vs. CTRL; # vs. HFD.
Results

*Paternal HFD causes intergenerational sperm defects*

Pearson’s Chi-square and z-test for column proportions corrected by Bonferroni’s method.

Significance was considered when p < 0.05. * p < 0.05; ** p < 0.01; *** p < 0.001. * vs. CTRL; # vs. HFD.
Discussion

• Acquired traits of metabolic syndrome are inherited by the offspring;
• Tissue-specific traits (e.g. catalase activity) may be inherited;
• Some effects of paternal exposure (to HFD) are just observable in the offspring – Intergenerational effects
• Despite the inhibition of AntiOx defenses and abnormal Mt. Activity, there is no evidence of oxidative stress in the sons of HFD mice;
• However, the sons of HFD mice have higher prevalence of sperm head and neck defects (lipid peroxidation of sperm cells’ membranes?);
• The father’s nutritional status at conception may be crucial for the health outcomes of the progeny.

Conclusions

The adoption of HFD causes intergenerational signatures in testis, which are associated with lower sperm quality.
Supplementary Materials

Links:


3. Sertoli Cell & Gamete Biology lab

4. UMIB - Unit for Multidisciplinary Research in Biomedicine
Acknowledgments

Sertoli Cell and Gamete Biology Lab

GIFT research grant 2019 - Marco G. Alves

Albert Renold Grant – Luís Crisóstomo

UID/Multi/00215/2019 and FEDER funds through POCI/COMPETE 2020 - UMIB