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

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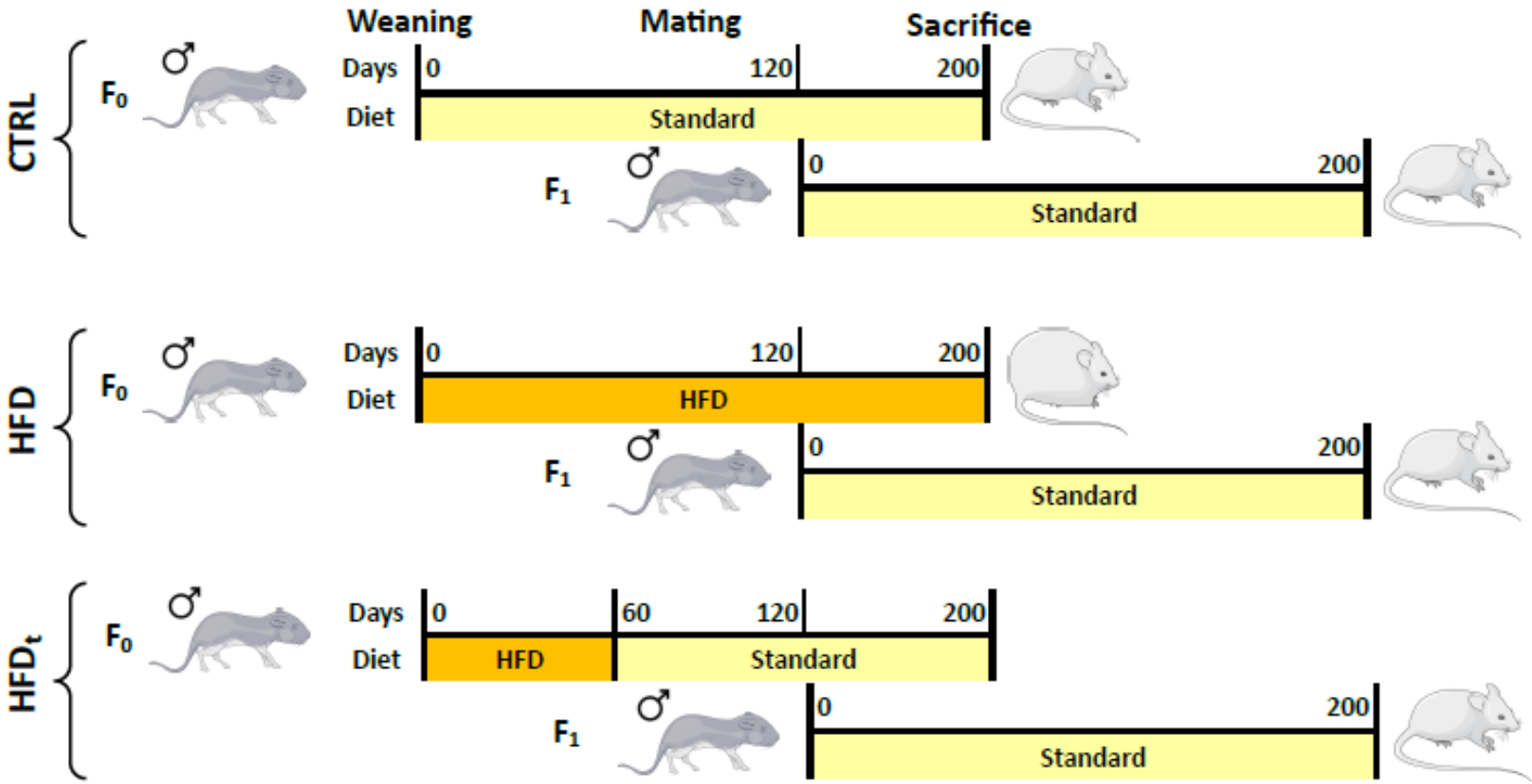
Abstract: The adoption of high-fat diets (HFD) is a major contributor for the increasing prevalence of obesity worldwide. Herein we study the impact of HFD from early age in testicular physiology and sperm parameters in two generations of mice, with focus on the testicular oxidative status. Mice of the 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
- GC-MS Lipidomics
- Sperm parameters
- Oxidative Stress and Mitochondrial activity
- NMR-based Metabolomics

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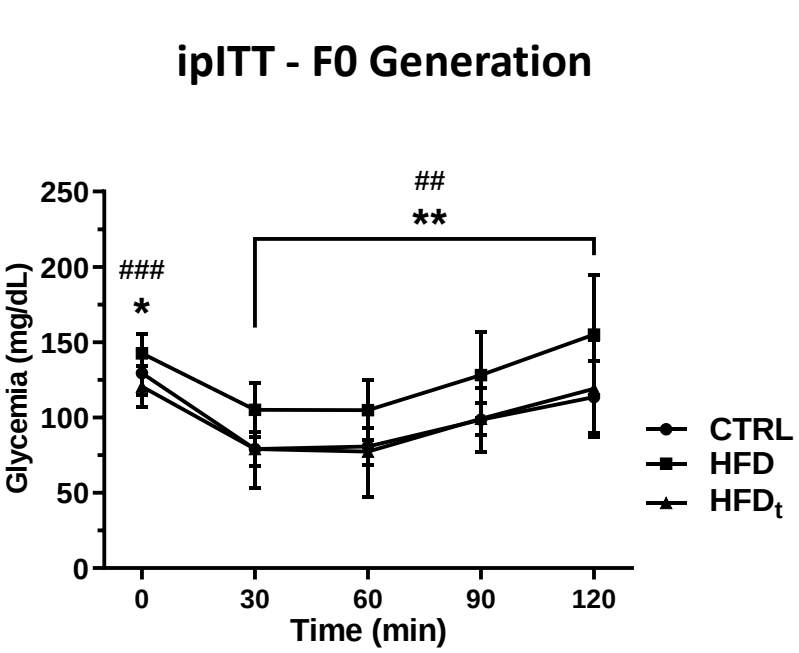
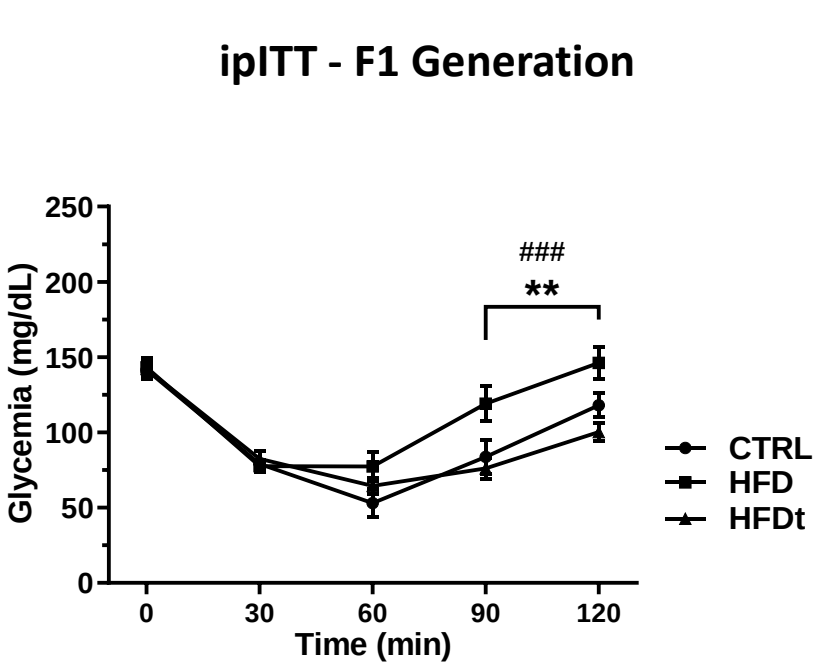
Results

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.

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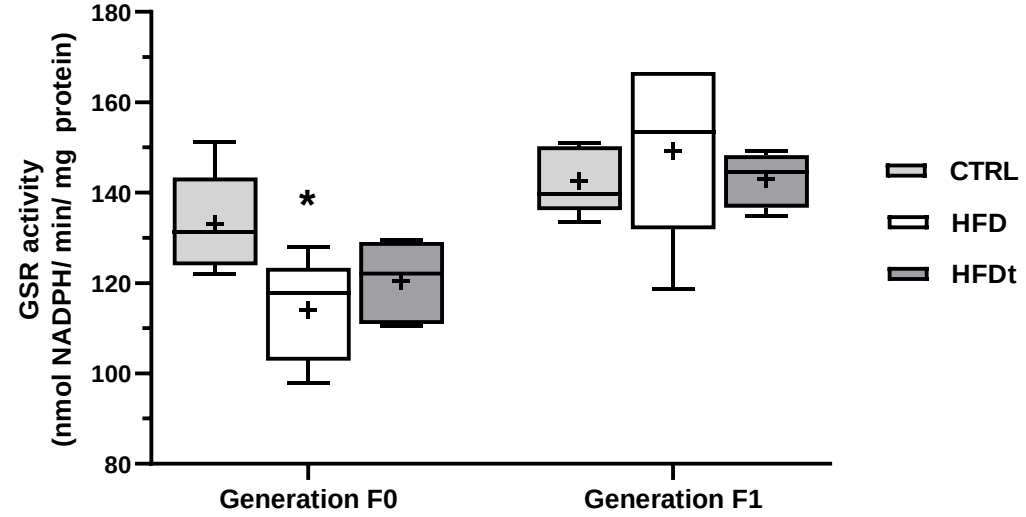
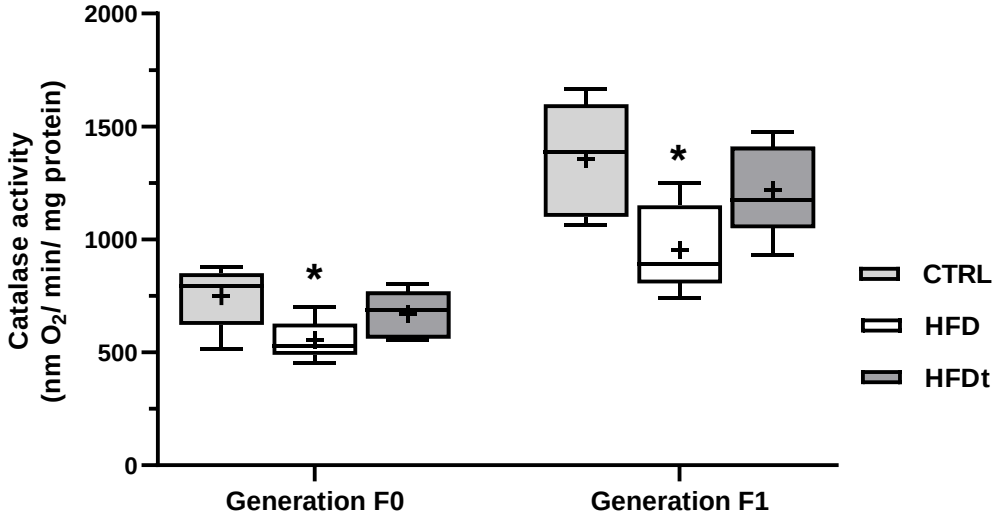
Results

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.

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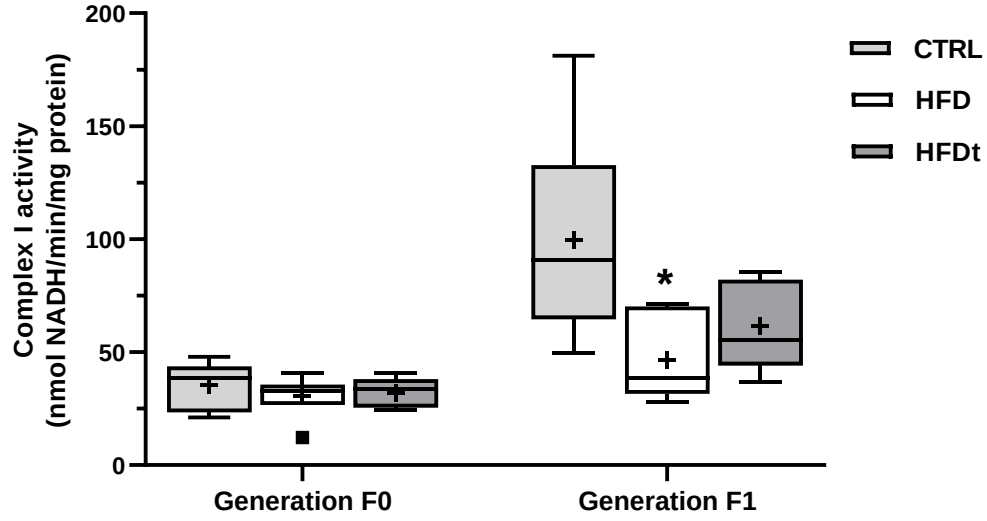
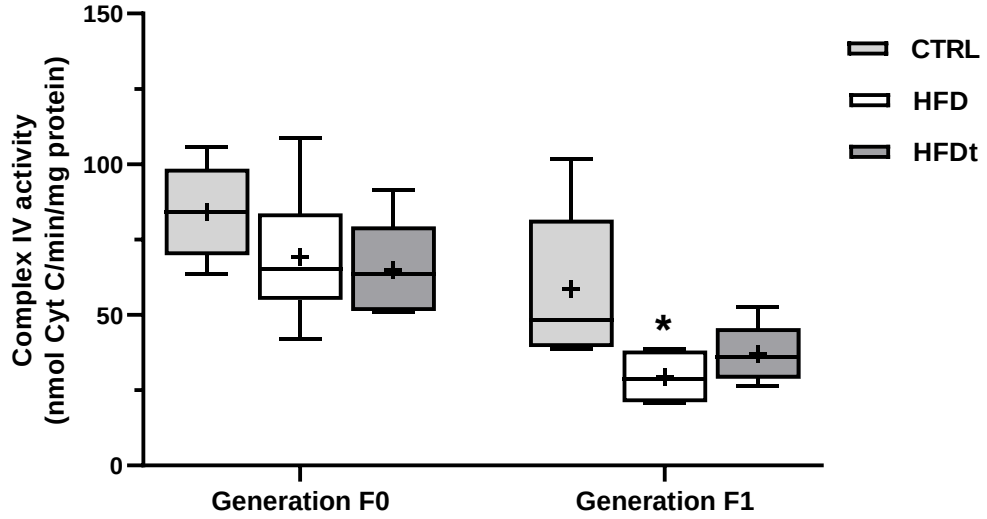
Results

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.

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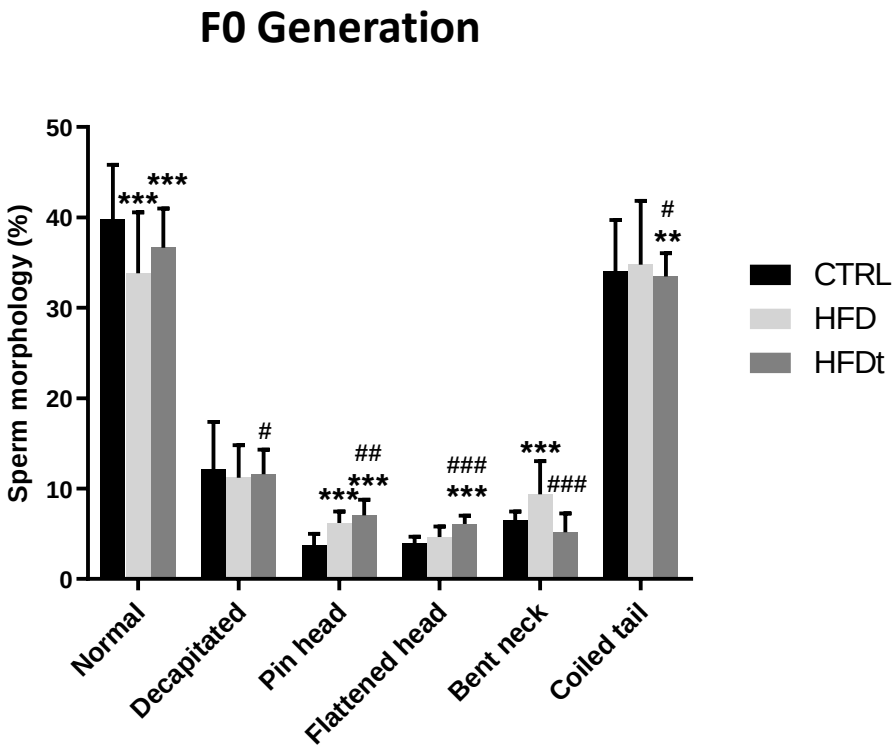
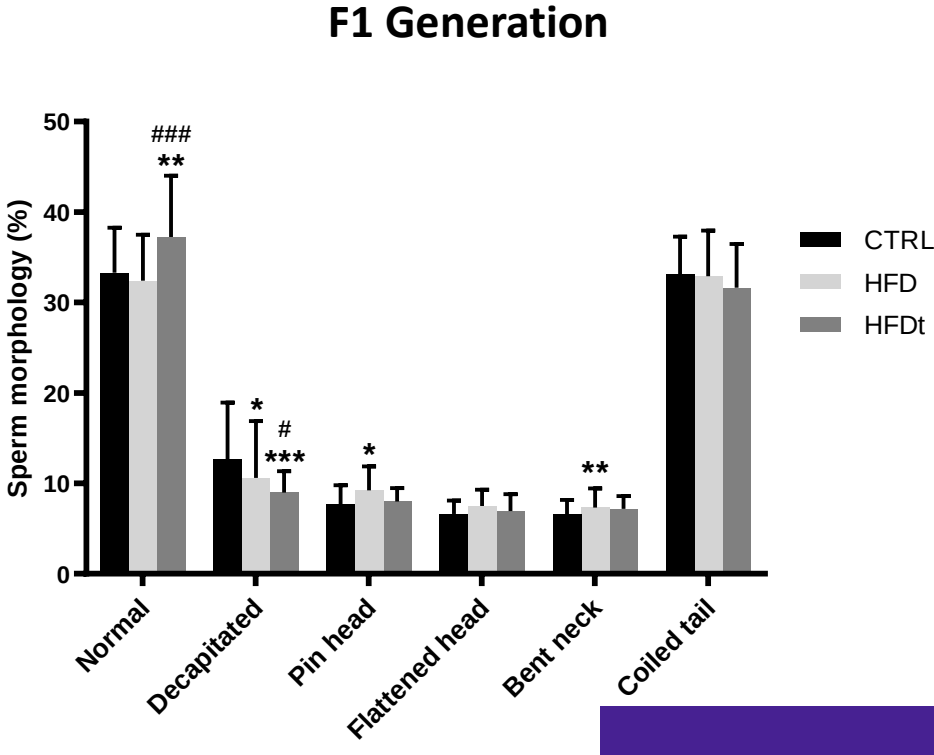
Results

Paternal HFD causes intergenerational sperm defects





Pearson's Chi-square and z-test for collumn 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.

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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.

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Supplementary Materials

Links:

1. Crisóstomo, L.; Rato, L.; Jarak, I.; Silva, B.M.; Raposo, J.F.; Batterham, R.L.; Oliveira, P.F.; Alves, M.G. A switch from high-fat to normal diet does not restore sperm quality but prevents metabolic syndrome. *Reproduction* **2019**, *158*, 377–387, doi:10.1530/REP-19-0259.

2. Crisóstomo, L.; Videira, R.A.; Jarak, I.; Starčević, K.; Mašek, T.; Rato, L.P.; Raposo, J.F.; Batterham, R.L.; Oliveira, P.F.; Alves, M.G. Diet during early life defines testicular lipid content and sperm quality in adulthood. *American Journal of Physiology-Endocrinology and Metabolism* **2020**, *(article in press)*, doi:10.1152/ajpendo.00235.2020.

3. Sertoli Cell & Gamete Biology lab

4. UMIB - Unit for Multidisciplinary Research in Biomedicine

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Sertoli Cell and Gamete Biology Lab

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