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Sexual dimorphism of hepatic epigenetic marks and machinery in offspring of obese and diabetic mothers fed a control diet during periconceptional/gestation/lactation period

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R_m diet could allow reducing the duration of force-feeding. These results are currently under confirmation by replicating the experiment.

Key words: DNA methylation, duck, foie gras, hepatic steatosis, methionine restriction

Statement of interest: Authors report no conflict of interest.

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ORAL N°10

Lessons in epigenetics from the human parasite *Schistosoma mansoni*: sexual differentiation under environmental stress

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Schistosomes are parasitic plathyhelminthes that are responsible for schistosomiasis (bilharziosis), an important parasitic human disease.¹ The life cycle of the parasite is characterized by passage through two obligatory hosts: a fresh-water snail for the asexual larval stage; and humans or rodents as hosts for the sexual adult stage. Male individuals are homogametic (ZZ), whereas female individuals are heterogametic (ZW). We used massively parallel DNA sequencing to identify unambiguously Z-specific, W-specific and pseudoautosomal regions of the *Schistosoma mansoni* sex chromosomes. We showed that more than 90% of *S. mansoni* W and Z are pseudoautosomal. The W-specific region is composed almost entirely of 36 satellite DNA families. Transcription and chromatin status of female-specific repeats are correlated to life stage; for example, if repeats were transcribed, transcription would be restricted to the larval stages lacking sexual dimorphism. In addition, levels of histone modifications typically associated with transcriptionally active euchromatin decreased around the W-specific repeats, as assayed by ChIP and ChIP-Seq. Our study provides evidence for the hypothesis that repeat-induced chromatin changes may have been an initial event in sex chromosome emergence. These chromatin structure changes have probably an effect in *cis* and/or *trans* and control (pseudo)autosomal genes that are responsible for sexual dimorphism.^{2,3} To investigate how the epigenome of the parasite reacts to environmental stress, we conducted experimental evolution experiments in which the larvae were exposed to two different snail host strains.

We measured life history traits, and used RNA-Seq and ChIP-Seq to follow changes in gene expression and chromatin structure through three generations. We show that stress-induced bias towards females in sex ratio occurs, and that transcriptional changes are correlated with modifications in chromatin structure. We hypothesize that chromatin structure provides a link between the environment and the development of females.

Key words: developmental programming, epigenetics

Statement of interest: The authors declare not to have competing interests.

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POSTER N°58

Sexual dimorphism of hepatic epigenetic marks and machinery in offspring of obese and diabetic mothers fed a control diet during periconceptional/gestation/lactation period

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Early nutritional events may have an influence on later life health mainly through epigenetic processes.¹ In our two-generation mice model, providing obese and diabetic mice with a control diet during the periconceptional/gestation/lactation period led to a pronounced sex-specific shift from susceptibility to resistance to a high-fat diet (HFD) in the female offspring only.^{2,3} The aim of this study was to detect sex-specific differences in the expression of candidate genes and epigenetic marks and machinery in the liver of both sexes and both generations. As a key organ for lipid processing and detoxification, liver plays a major role in conditions of chronic lipid oversupply. According to the sex, female (F) or male (M), the generation, first (F1) or second (F2), and diet types, CD or HFD, mice were divided into eight groups (F-F1-CD, F-F1-HFD, M-F1-CD, M-F1-HFD, F-F2-CD, F-F2-HFD, M-F2-CD and M-F2-HFD). Body weight, blood glucose level and blood cholesterol levels were measured. Liver morphology was identified by hematoxylin-eosin staining and oil red O staining. Heparosteatosis was found to be more common in all HFD groups with adaptation of

the liver phenotype in F2 females but not in males, in parallel with obesity and cholesterol levels.⁴ Global DNA methylation and histone modifications were investigated by LUMA and Western blot analysis, respectively. Interestingly, although no significant difference was found within groups, global DNA methylation level was significantly negatively correlated to steatosis percentage. Using RT-qPCR, sexual dimorphism was observed for the gene expression of 12 genes encoding enzymes of the epigenetic machinery. These marks may help us to understand the sex-specific epigenetic mechanisms of the underlying sex-specific responses to HFD and improve the early life nutritional environment in a sex-specific manner. The author(s) declare that they have no competing interests.

Key words: epigenetics, gene expression, hepatocellular carcinoma, hepatosteatosis, high-fat diet, histone modification, methylation, obesity, sexual dimorphism, type 2 diabetes

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POSTER N°68

Exposure to the diabetic intrauterine environment, growth in infancy and childhood and development of adiposity at 7 years

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Recent meta-analyses pointed out inconsistent evidence of an association of gestational diabetes mellitus (GDM) with offspring overweight and obesity.^{1,2} Our objective was to examine the associations of maternal gestational glucose tolerance with child growth trajectory from birth, and child body composition at 7 years. Among 914 women in the pre-birth cohort Project Viva, maternal glucose tolerance was assessed in the second trimester by non-fasting 1-h glucose challenge test (GCT), followed, if needed, by fasting 3-h glucose tolerance test (OGTT). We categorized women as normoglycemic (Norm: 83.3%) if GCT was normal, isolated hyperglycemia (9.1%) if GCT was abnormal but OGTT was normal, impaired glucose tolerance (IGT: 3.3%) if one abnormal value on OGTT and gestational diabetes (GDM: 4.5%) if women had two or more abnormal OGTT values.

We obtained child weight and height from medical records and research examinations, and body composition at 7 years using DXA (*n* = 760). We modeled growth trajectories. We adjusted the multivariate linear regressions for parental body mass index, gestational weight gain, child age, race/ethnicity and socio-demographic characteristics. Boys born to GDM mothers were heavier throughout infancy and childhood. At the age of 7, they had a higher overall adiposity (1.89 kg; 95% CI: 0.33, 3.45) compared with boys of Norm. Girls born to GDM mothers did not show a different growth trajectory compared with Norm. Yet, girls of IGT mothers showed a slower growth in infancy, followed by a steep acceleration in early childhood that resulted in a higher overall adiposity at 7 years (+2.23 kg; 95% CI: 0.12, 4.34), compared with girls of Norm. The exposure to maternal glycemia of fetuses of IGT and GDM mothers may differ in timing and intensity. This, combined with a different sensitivity of male and female fetuses *in utero*, may result in different programming and metabolic consequences in the long run.

Key words: body composition, child growth, developmental programming, gestational diabetes, human

Statement of interest: The authors declare that they have no competing interests.

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ALLEVIATION OF PROGRAMMING DYSFUNCTIONS

9 – A. Vambergue and L. Storme

Evidence indicates that the consequences of programming dysfunctions can be partly corrected. In an experimental model of metabolic syndrome obtained in the offspring of undernourished rats, lactation by adoptive mothers is able to prevent occurrence of metabolic syndrome later in life. In the same way, extracted polyphenolic compounds from seeds, teal and grapes in the maternal diet may modulate DNA methylation and chromatin accessibility, suggesting potential perspectives for modulating programming.

ORAL N°40

Role of postnatal leptin on organ maturation and development

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