Search for prediabetes markers: comparison of muscle methylome of lean and obese women with or without type 2 diabetes

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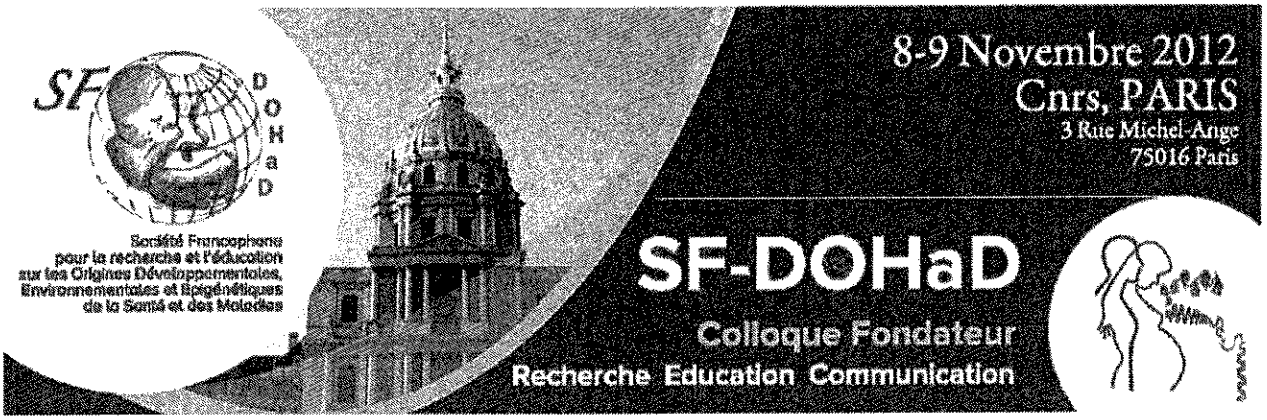

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signals induced by stress are transmitted to the transposons. We have investigated this question using *Drosophila* as a *model organism.*

Key words: epigenetic, stress, transposable element

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

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POSTER N°60

Search for prediabetes markers: comparison of muscle methylome of lean and obese women with or without type 2 diabetes

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There is convincing experimental evidence to suggest that stable changes in epigenetic marks act as a memory of exposure to unbalanced nutrition or metabolic disturbances during crucial developmental periods and throughout life.[1] These marks induce long-term changes in gene expression, thereby influencing the susceptibility to mental and physical health, including obesity and type 2 diabetes (T2D).[2] Until now, only one large-scale epigenome-wide study investigated how the epigenome changes were mediated by hyperglycemia in primary vascular cell[3]. So far, there has been no such study comparing T2D and non-T2D obese patients. Our aim was to identify genome-wide differentially methylated DNA sites in abdominal muscle from operated patients and to test their involvement in obesity and T2D. We selected from the ABOS (Atlas Biologique de l'Obésité Sévère) collection of biological samples obtained during bariatric surgery[4] muscle samples (80 mg) from obese women without T2D [25, body mass index (BMI) = 48.1 + 6.9], and obese women with T2D (25, BMI = 48.6 + 6.0), and lean control (15, BMI = 22.7 + 2.4). Using Illumina Infinium 450K Methylation Beadchip, which allows the simultaneous quantitative monitoring of more than 480,000 cytosines across the genome, we identified sequences with methylation differences. Data normalization and analyses with bioinformatics tools including IMA and SWAN were performed. Some differentially methylated CpG sites were validated by pyrosequencing. Furthermore, the expression of genes close to these sites was investigated by RT-qPCR. For example, hypomethylation of some CpG within the promoter region of SIM1 was found in obese groups but especially in the obese and diabetic group. A differentially methylated region was found in chromosome 17q21, in which HOXB gene family and two HOX-related miRNA-encoding genes map. Interestingly, some CpGs within this region were hypomethylated, whereas some others were hypermethylated in obese groups. Data will be presented to show the differentially methylated regions, the genes and the potential networks concerned. The author(s) declare that they have no competing interests.

Key words: CpG, DNA methylation, gene expression, methylome, obesity, type 2 diabetes

Statement of interest: Authors report no conflict of interest.

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POSTER N° 76

Fetal programming of β-cell dysfunction in type 2 diabetes: implication of the glucocorticoids and their signalling pathway

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Several studies have shown that many adult diseases originate from adverse foetal environment that alters organ development and programs their dysfunction later in adult life. The risk to develop type 2 diabetes, a metabolic disease characterized by peripheral insulin resistance and insufficient insulin secretion by pancreatic β cells, is, for example, increased in individuals with low birth weight.[1] To explain this association, we and others have proposed that perturbations of the foetal environment alters the development of pancreatic β cells that will not be able to secrete insulin properly in adult life. We developed murine models of altered foetal environment through caloric restriction of pregnant females. Offspring submitted to this abnormal foetal environment develop glucose intolerance as adults with decreased β-cell mass and function. In those models, we observed that caloric restriction in pregnant females led to