P19-3
Gestational diabetes and obesity: role of oxidative stress and inflammation

M. P. R. Alvarez[1], M. Viana[1], M. A. Díaz-Mor[1], V. E. Bolado[1], J. P. Santibáñez[1], M. Espino[2], M. Albi[2] and I. Sánchez-Vera[3]
[1]Farmacia, Universidad San Pablo-CEU, Madrid, Spain, [2]Hospital Universitario Fundación Alcorcón, Madrid, Spain, [3]Medicina, Universidad San Pablo-CEU, ES, Madrid, Spain

Previous studies from our group have shown that Gestational Diabetes Mellitus (GDM) is associated with an increased oxidative stress, determined as susceptibility of LDL to oxidation. Otherwise, oxidative stress plays an important role in the pathogenesis of obesity. Therefore, the coexistence of both conditions, obesity and GDM, may aggravate the oxidative injury produced in lipids and proteins, and exacerbate the inflammatory process observed in these women. To test this hypothesis we compared in pregnancies complicated by GDM, with and without obesity, and normal pregnancies, oxidative stress, and their correlation with some inflammatory parameters.

During a period of three years women attending the Obstetrics Clinics of Hospital Universitario Fundación Alcorcón were asked to participate in the study. From 2000 gestations we obtained samples from 64 pregnancies complicated by GDM. Between them, 30 were obese (BMI = 31.25 ± 0.7 kg/m^2), and 34 were non-obese (BMI = 23.05 ± 0.4 kg/m^2). Besides, 39 pregnant women without complications were randomly selected as a control group (BMI = 22.28 ± 0.4 kg/m^2). In all women, blood was drawn at 15, 24 and 30 gestational weeks. Vitamin E (vitE), malondialdehyde (MDA), advanced oxidation protein products (AOPP), and inflammatory parameters such as C-reactive protein (CRP) were determined.

In the control group the vitE concentration in the 1st, 2nd and 3rd trimester was 3.2 ± 0.3, 3.1 ± 0.2 and 3.5 ± 0.2 μg/mg lipids, compared with 3.9 ± 0.5, 3.8 ± 0.3 and 4.5 ± 0.4 μg/mg lipids in lean GDM and 3.7 ± 0.5, 4.6 ± 0.6 and 4.3 ± 0.3 μg/mg lipids in the obese GDM group. In control pregnant MDA did not change during pregnancy, whereas AOPP were significantly higher in the 3rd trimester of gestation than in the first part of pregnancy. Similar results were obtained in non-obese GDM. However, in the obese GDM both MDA and AOPP were significantly higher than in the other groups. The AOPP levels in the first and second trimester were positive correlated with the CRP ($p < 0.001$ and $p < 0.05$, respectively).

Our results show that, even in the first trimester, prior to the diagnosis of diabetes, obesity before GDM is associated with an exacerbation in both oxidative stress and inflammation, that could contribute to the complications associated with GDM.

P19r-4
Neuronal differentiation promoted by oleic acid is impaired in TgDyrk1A primary neuronal culture

M. Hijazi[1], C. Fillat[2], J. M. Medina[1] and A. Velasco[1]
[1]Instituto de Neurociencias de Castilla y León (INCYL), Salamanca, Spain, [2]Instituto de Investigaciones Biomédicas August Pi i Sunyer (IDIBAPS), Barcelona, Spain

Down syndrome (DS) is a genetic disease characterized by the presence of an extra copy of chromosome 21, resulting in a trisomy. Histological brain studies of individuals with DS have revealed an aberrant formation of the cerebral cortex. Some authors attribute this effect to the lack of suitable substrates that direct the migration of neurons. Previous works in our laboratory have shown that oleic acid is a neurotrophic factor that induces neuronal differentiation. Dyrk1A (Dual-specificity tyrosine (Y)-regulated kinase) is one of the genes on human chromosome 21 and mouse chromosome 16 that has aroused most interest, owing to its relationship with the brain functions that are altered in DS. Dyrk1A is overexpressed in DS brains and is involved in neurogenesis and learning/memory. Here we show that oleic acid fails to induce neuronal differentiation in primary neuronal culture from transgenic mice overexpressing Dyrk1A (TgDyrk1A) because the cell clustering and axonal elongation were sharply reduced. Interestingly, the expression of GAP-43, a marker of axonal growth, was increased in the presence of oleic acid in normal neurons but not in TgDyrk1A neurons. To study the mechanism by which oleic acid do not promote cell differentiation in DS models, we used a cell line (CTb) derived from the cortex of trisomic (Ts16) mice where neither oleic acid induces cell differentiation. Dyrk1A was downregulated in CTb by siRNA. In these conditions, oleic acid gave rise to cell clustering and rescued ChAT expression, a marker of cholinergic differentiation, up to similar levels to that of normal cells. Therefore, we can suggest that oleic acid effect is mediated by overexpression of Dyrk1A.

P19-5
Mitochondrial metabolism and hormone action is regulated by proteins participating in mitochondrial dynamics

A. Zorzano
IRB Barcelona, University of Barcelona and Ciberdem, Barcelona, Spain

Mitochondria are dynamic subcellular organelles that convert nutrient intermediates into readily available energy equivalents. Optimal mitochondrial function is ensured by a highly evolved quality control system, coordinated by protein machinery that regulates a process of continual fusion and fission. Recent work has revealed that proteins participating in mitochondrial dynamics regulate metabolism. Thus, the mitochondrial fusion protein Mfn2 plays an essential role in metabolic homeostasis. Liver-specific ablation of Mfn2 in mice leads to glucose intolerance, and enhanced hepatic gluconeogenesis. Similarly, muscle-specific Mfn2 ablation caused susceptibility to glucose intolerance in response to a high fat diet. Mfn2 deficiency also impaired insulin signaling in liver and muscle due to enhanced ROS production and to ER stress.

The ATP-independent metalloprotease OMA1 plays an essential role in the proteolytic inactivation of the mitochondrial fusion protein OPA1. OMA1 deficiency also causes a profound perturbation of metabolic homeostasis. Thus, ablation of OMA1 in mice results in increased body weight due to increased adipose mass, hepatic steatosis, decreased energy expenditure and impaired thermogenenesis.

Data on the metabolic role of the mitochondrial fission protein Drp1 will be also discussed. All these results reinforce the importance of mitochondrial quality control for normal metabolic function.