

## **Parallel Session RTD Line 2 / Nutrigenomics**

### **Lecture 3: Adipose tissue gene expression profiling in the Diogenes study**

**Nathalie Viguerie**  
**INSERM Toulouse, France**

#### **Abstract**

Nutritional genomics has tremendous potential to change the future of dietary guidelines and personal recommendations; however, its use for the prevention of diet-related disease such as obesity remains distant. The physiopathology of obesity is complex and multidisciplinary investigations are required to decipher the mechanisms of obesity-related co-morbidities. One approach to understand the molecular mechanisms through which diet alters health is to identify diet-regulated genes that cause or contribute to the development of disease.

The RTD line 2 objective is the identification and characterization of molecular bio-markers of dietary intake and predictors of weight and metabolic variations. The regulation of the transcription of genes by food components may modify the phenotype of subjects. Indeed, nutrients can serve as important regulators of adipose tissue (AT) function. Therefore, AT gene profiling can identify key factors for weight control and dietary effect.

Regarding weight loss, the role of macronutrient content was assessed by comparing 2 groups of 24 obese women following 10-wk energy-restricted diets with moderate-fat or low fat content selected from the cohort of the Framework 5 European Project NUGENOB. DNA microarray analysis showed that energy restriction had a more pronounced effect on variations in human adipose tissue gene expression than macronutrient composition. However, the macronutrient-sensitive regulation of a small subset of genes may influence adipose tissue function and metabolic response.

In the Diogenes dietary program, subcutaneous AT biopsies were taken at the beginning (CID1), 2 days after starting low calorie diet (LCD) (CID1b), at the end of the 8-wk LCD period (CID2), and at the end (CID3) of the 6-mth weight maintenance phase. Total RNA was extracted and pangenomic DNA microarrays were used to profile adipose tissue gene expression for subsets of premenopausal women. Using these data, RTD2 collaborators are searching for AT transcriptional bio-markers of macronutrient intake as well as markers and predictors of weight changes.

For the weight loss phase of the Diogenes project, 10 subjects who lost above 13% of their initial body weight during LCD (good responders) and 17 who lost between 8-10% of their initial body weight (poor responders) were selected in order to assess whether AT gene expression can be used to predict a good from poor responders. Transcriptomic studies were performed at CID1 and CID1b. Building on previous research performed in the NUGENOB program, the prediction classifiers accuracy was 90%.

After LCD, subjects with more than an 8% weight loss were randomized in 4 weight stabilization diets differing in protein content and glycemic index (GI) for 6 months. 22 subjects succeeding weight maintenance (successful subjects) were compared to subjects regaining weight (unsuccessful subjects or weight re-gainers) among the 4 dietary arms. RTD2 is now assessing whether weight maintenance using differential gene expression between CID2 and CID3 can accurately predict weight regain. Transcriptomic studies in AT samples at both CID2 and CID3 showed 1800 genes that were differentially expressed between successful and unsuccessful subjects. These genes encoded proteins involved in fatty acid metabolism, immunity and defense, apoptosis and cell proliferation. The search for diet-sensitive genes was investigated on subjects with stable weight. It indicated that glycemic index rather than protein content have a discrete impact on AT gene expression.

To summarize, it appears that the ability to maintain weight and the macronutrient composition of the diets are reflected in specific patterns of AT gene expression. Further analyses are needed in order to assess the use of AT gene expression as a predictive tool for weight loss. The combination of transcriptomic with proteomic and genetic data collected on the same subjects may prove useful for the identification of bio-markers of macronutrient composition and predictors of weight variations.