

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

### **Lecture 6: Metabolism and inflammation during dietary interventions: lessons from transcriptomics**

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#### **Abstract**

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The excess of fat mass in obesity is associated with dysregulation of adipose tissue (AT) metabolism and inflammation. However, the interconnections between metabolic and inflammatory pathways and their impact on insulin sensitivity remain largely unknown. In a series of clinical studies, we have investigated the regulation of AT gene expression in relation to metabolic status and during dietary interventions with a special emphasis on metabolism and inflammation.

Transcriptomic analysis was performed using 44k DNA microarrays and RT-qPCR. The various cell types composing AT have been shown to play distinctive functions in AT biology. We therefore determined the transcriptomic profiles of human AT fat cells, macrophages, endothelial cells, progenitor cells and a fraction composed of other cells. Cell type-specific markers including a set of 31 macrophage-specific markers (MSG) were identified. The information on cell specificity was used to classify genes differentially expressed in subcutaneous and visceral AT from women with different metabolic status and in subcutaneous AT of obese women undergoing a multiple phase dietary weight loss program. Because of the importance of AT inflammation in obesity-related complications, gene expression of MSG was also determined.

In visceral and subcutaneous AT, MSG discriminate lean from overweight, obese and metabolic syndrome subjects and, obese from metabolic syndrome subjects. In both AT depots, expression of MSG was the lowest in the lean and the highest in the metabolic syndrome group. MSG expression in both AT depots was negatively correlated with insulin sensitivity and associated with several parameters of the metabolic syndrome. Supporting data analysis from DNA microarray analyses on metabolism and inflammation genes will be presented.

During the dietary intervention program, transcriptome profiling revealed two main patterns of variations. The first involved mostly adipocyte genes involved in metabolism downregulated during the initial very-low calory diet phase and upregulated during the weight stabilization phase. The second comprised mainly macrophage genes involved in inflammatory pathways not changed or upregulated during very-low calory diet and downregulated during weight stabilization. Accordingly, MSG were upregulated during very-low calory diet and downregulated during weight stabilization.

In subcutaneous and visceral AT, macrophage gene expression pattern differs according to obesity and metabolic status. The expression of macrophage markers is related to insulin sensitivity and metabolic syndrome. AT macrophages and adipocytes show distinct pattern of gene regulation during various phases of a dietary weight loss program depending on the energy status of the subjects. This suggests an in vivo crosstalk between the two cell types.