Differentially Expressed Genes in Microarray Analysis of Rheumatoid Arthritis Disease
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Background
Rheumatoid arthritis (RA) is a chronic systemic disease that affects mainly the joints. The RA is characterized by inflammation in the synovial membranes and articular structures. Their clinical manifestations are predominantly noted in the muscle-skeletal system. The new techniques in bioinformatics enabled the possibility to study diseases in genomic scale. There are several technologies for determining gene expression, like cDNA microarrays. This technique provides data that can be used to develop a more complete understanding of the role of regulation and interaction of genes. The aim of this work was to find differentially expressed genes in microarray data from patients with rheumatoid arthritis and control individuals.

Materials and Methods
Gene expression data from microarray image quantification were provided by the Laboratory of Molecular Immunogenetics, Department of Genetics, Ribeirao Preto School of Medicine, University of Sao Paulo. The microarray analysis included 17 adult patients with RA and 9 control adult subjects (without RA). Data normalization was carried out using the R platform. The normalized data were statistically analyzed by the significance analysis of microarray (SAM) using the MeV software with false discovery rate \( \leq 0.01 \) and fold change \( \geq 1.0 \). The data regarding gene annotation were obtained at the SOURCE [http://smd.stanford.edu/cgi-bin/source/sourceSearch], ACEVIEW [http://www.ncbi.nlm.nih.gov/IEB/Research/Acembly/] and DAVID [http://david.abcc.ncifcrf.gov/home.jsp] databases.

Results and Conclusion
The most significant differentially expressed genes (\( n = 100 \)) were selected by the SAM analysis. The hierarchical tree shows that the control cases and patients were clearly clustered in separated groups. More than half of the genes studied (55\%) were not categorized according to biological processes and function (see Figure 1). The metabolism category is the most representative, and together with gene expression category they comprise 30\% of the studied genes. Within the known categories 6 induced and 16 repressed genes are related to other diseases. In the induced genes it was highlighted one gene responsible for the expression of the human glutathione transferase A4-4 isoenzyme (hGSTA4) that protects against oxidative stress by removing electrophilic compounds like 4-hydroxynonenal (HNE). In the downregulated genes it was highlighted the adiponectin receptor 2 (ADIPOR2), which encodes a receptor of adiponectin that is involved, in lipid and glucose metabolism, energy homeostasis, and inflammatory pathways. Researches with type 2 diabetes show that downregulation of the ADIPOR2 receptor may be responsible for development of insulin resistance in peripheral tissues.

References