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Effect of milk fermentation on gene expression in human blood cells

F. Sagaya[a,b], M. Bellis[c], B. Walther[a], R.F. Hurrell[b], G. Vergères[a]

[a]Agroscope Liebefeld-Posieux Research Station ALP, Berne, Switzerland, [b]Laboratory for Human Nutrition, ETH Zurich, Zurich, Switzerland, [c]Centre de Recherche de Biochimie macromoléculaire (CRBM), Montpellier, France

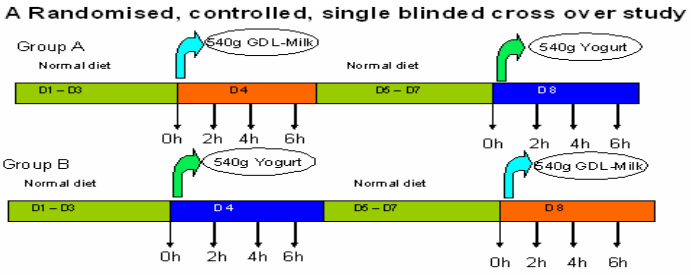
francina.sagaya@alp.admin.ch

Introduction

Dairy products with live bacteria are able to confer health benefits through several mechanisms, including modulation of the immune response. The components responsible for these effects and the mechanism by which these components exert their immunological action are not completely understood. Thus, deciphering how these products as a whole, as well as their specific dairy and microbial bioactive components interact with human organisms is necessary for optimizing the health promoting potentials of fermented dairy products. The primary objective of this study is to define global patterns of gene expression in human blood cells that characterize the short-term response of healthy individuals to a single ingestion of milk and yogurt.

Materials and method

Nutritional intervention study



Six healthy male individuals. Normal controlled diet devoid of dairy products, fermented products, fresh vegetables, fresh fruits and juices.

Microarray and data analysis

Total RNA isolated from human blood samples collected at 0h,2h,4h and 6h. Cyanine 3 labeled antisense RNA was generated by linear amplification. Genome-wide gene expression profiles were obtained by hybridization to 4x44k whole human genome Agilent oligonucleotide microarrays.
Image analysis was carried out using Agilent feature extraction software. Rank difference analysis of microarray (RDAM) method was performed for data normalization and to find out differentially expressed genes. Kinetic clustering of genes was done by searching for dense regions detected by Gene DIVER in a multidimensional space where points with a shared variation profile across multiple comparisons are in the same neighborhood. Preliminary functional analysis was conducted with GENERATOR.

Results

1. ~900 genes differentially expressed with a false discovery rate of ≤10%.
2. Two distinct clusters of genes involved in protein biosynthesis and immune response emerged based on their kinetic profile.
3. Expression of pattern recognition receptors such as TLR2, CD14, CD69 and other immune cytokine receptor genes might indicate differential modulation of innate immune response upon yogurt and milk ingestion.
4. Casein kinase II and Vitamin D Receptor, a casein kinase II substrate are differentially expressed.

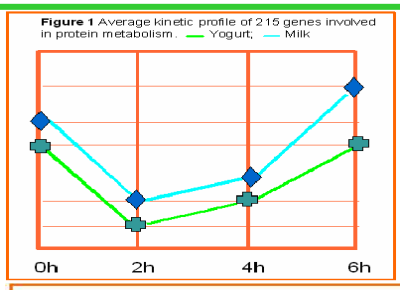


Figure 1 Average kinetic profile of 215 genes involved in protein metabolism. Yogurt; Milk

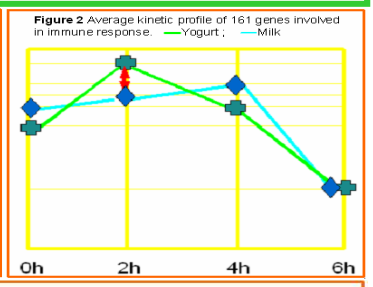


Figure 2 Average kinetic profile of 161 genes involved in immune response. Yogurt ; Milk

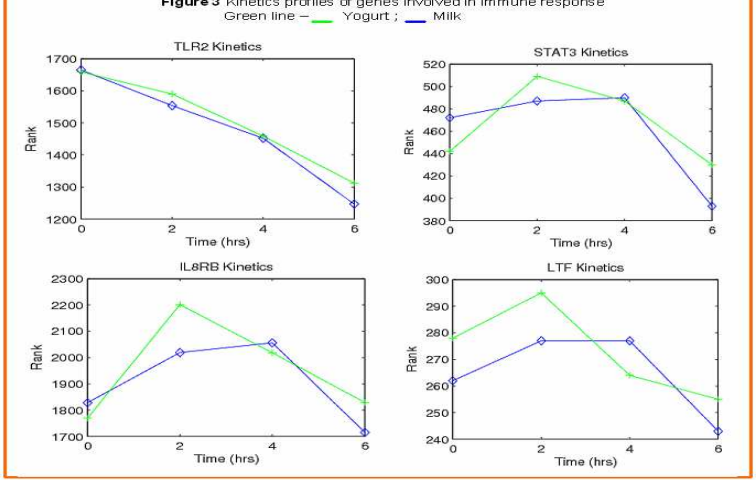


Figure 3 Kinetics profiles of genes involved in immune response
Green line – Yogurt ; Milk

Table 1 Differential expression of genes with a role in protein biosynthesis

Gene	Description
RPL31	Ribosomal Protein L31
RPL5	Ribosomal Protein L5
RPL3	Ribosomal Protein L3
RPL24	Ribosomal Protein L24
RPS15A	Ribosomal Protein S15 A
RPLP0	Ribosomal Protein, Large, P0
RPS18	Ribosomal Protein S18
RPL13	Ribosomal Protein L13
RPL30	Ribosomal Protein L30
RPS3A	Ribosomal Protein S3A
RPL9	Ribosomal Protein L9

Table 2 Differential expression of genes with a role in immune response

Gene	Description
STAT3	Signal transduction and activator of transcription 3 (acute-phase response factor)
TLR2	Toll like receptor 2
CD14	CD 14 antigen
L17F	Interleukin 17F
BCL2L1	B-cell CLL/lymphoma 2-like 1
CASP8	Caspase 8,apoptosis-related cysteine peptidase
CD69	CD 69 molecule
IL8RB	Interleukin 8 receptor, beta
IL23A	Interleukin 23,alpha subunit p19
FCER1A	Fc fragment of IgE, high affinity 1 receptor for alpha polypeptide
LTF	Lactotransferrin

Outlook : Further analysis of the different kinetic gene clusters and focusing on the set of genes involved in specific pathways might give more insight on health promoting aspects of dairy products.