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Zinc Influences on Gene Expression and Protein Profiles Related to Atherogenesis : cDNA Microarray and Proteomic Approach

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Zinc deficiency has been shown to increase harmful effect on atherogenesis-related factors and can be a risk for cariovascular disease. The objective of the study is to identify the genes and proteins of relevance to the pathogenesis of atherosclerosis which are modulated by zinc. We applied two high throughout screening techniques, cDNA microarray and proteomic approach, to identify the differentially expressed genes and proteins *in vivo* and *in vitro* models. In study 1, we determined the zinc-regulated gene expressions in EA.hy926 cells under high and low homocysteine(Hcy) level using cDNA microarray. EA.hy926 cells were cultured either in Zn-deficient media(Zn-, 0 μM Zn) or in Zn-adequate media (Zn+, 12 μM Zn as $ZnCl_2$) within each high homocysteine (Hcy+, 10 mM) or low homocysteine (Hcy-, 0 mM) level, respectively. Profiling of human(1K, Clontech) microarray slides showed that in Zn+ compared to Zn- under Hcy+, mostly intracellular modulators-related 6 genes were upregulated and 1 gene for transcription proteins was downregulated ($p<0.05$). In Zn+ compared to Zn- under Hcy-, 5 genes for transcription related protein and cytokines were upregulated, and 6 genes for apoptosis-associated proteins and cytokines were downregulated ($p<0.05$). In study 2, rats were fed with one of experimental diet (Zn-adequate, 35 mg/kg diet; Zn-pair fed, 35 mg/kg diet; Zn-deficient, 0 mg/kg diet) for 5 wks. The aorta then was collected and the differentially expressed proteins were analyzed by proteomic technique using 3 different buffer systems (Bio-Rad III, isopropanol, vercoe). Isopropanol produced the best gel resolution. Software processing (PDQuest, Bio-Rad) showed that 18 proteins are present on the Zn-adequate and absent on the Zn-deficient gel. Also, 16 protein spots increased or decreased significantly ($p<0.05$) by more than 1.5 folds in the Zn-deficient gel. The obtained profiling of the genes and proteins would be useful to understand the cell signalling events related to atherogenesis.