Abstract

Iron absorption, transport, and storage in the body is very strictly regulated mechanism by the reason of absence of a controlled pathway provided its excretion. Hence we are interested in transport mechanism of non-haem iron which is mediated by molecules DMT1 (divalent metal transporter 1, membrane iron importer), Dcytb (duodenal cytochrom b, membrane ferrireductase), ferroportin 1 (membrane iron exporter), hephaestin (membrane ferroxidase) and ceruloplasmin (cytoplasmatic ferroxidase) and enable iron uptake from food up to its binding to plasma transferrin.

Our project monitors the effect of iron availability to the expression of the molecules potentially involved in non-transferrin iron transport across cell membranes. We studied the influence of iron deficiency and iron overload to the regulation of iron uptake by these molecules in various functional types of human cells.

Cells were maintained in RPMI 1640 medium and supplemented with other additives. The expression was tested on mRNA level by quantitative real-time PCR with reverse transcription in *in vitro* study using human cell lines K562 and Caco-2. K562 cells (human erythroleukemia) represent cells with high utilization of no-transferrin iron and Caco-2 cells (human colorectal carcinoma) is a model of cells with different apical and basal membrane involved in iron absorption. The mRNA level was affected by changes of non-transferrin iron availability for 24 h. We tried to simulate iron deficiency and high iron level in organism to compare it with iron body levels during iron-metabolism related diseases.

Due to the iron deprivation in K562 cell line we observed statistically significant decrease of mRNA levels of transport molecules DMT1 and ferroportin 1 (40%) when comparing with control. In Caco-2 cell line, in contrast, were mRNA levels of all transport molecules except ceruloplasmin increased. On the other hand, the preincubation of K562 cells in medium with high iron level, when comparing with control, led to significantly increased mRNA level of ferroportin (70%) and in Caco-2 cells it led to statistical significant increased (40-60%) of the mRNA level of Dcytb, ferroportin and hephaestin.

We conclude that changes in non-transferrin iron availability in iron utilizing K562 cells affect the expression of tested proteins, i.e. proteins potentially involved in non-transferrin iron transport, in opposite directions with regard to iron deficiency or high level respectively. In Caco-2 cell line, used as enterocytes model, non-transferrin iron availability caused

increased mRNA levels of most tested molecules in the cases of iron deficiency as well as iron overload.

Keywords Non-transferrin iron transport; DMT1; Dcytb; ferroportin; hephaestin; ceruloplasmin