

Regulation of intestinal metal transporter expression by erythropoietin

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Iron deficiency anaemia (IDA) leads to local tissue hypoxia and increased levels of the hormone erythropoietin (Epo)⁽¹⁾. In IDA, intestinal Fe absorption is up-regulated reflecting the increased erythroid Fe demand⁽²⁾. Interestingly, the uptake of Cu is also increased in models of Fe deficiency⁽³⁾. We have shown recently that Epo directly regulates the intestinal Fe transporter expression⁽⁴⁾ and here we have investigated whether Epo might also regulate the expression of the Cu transporter genes hCTR1, ATP7a and ATP7b.

Experiments used human intestinal Caco-2 cells. Cells were exposed to Epo (1 unit/ml) for 24 h. Fe and Cu transporter mRNA expression was measured by Q-PCR. Statistical analysis was performed using Student's unpaired *t* test, significant at *P* < 0.05.

Table 1. Effect of Epo treatment on Cu and Fe transporter mRNA expression. n 6–12 in each group; NS, non-significant

Cu transporters	Epo-treated mRNA			Fe transporters	Epo-treated mRNA		
	(% control)	SEM	<i>P</i> -value		(% control)	SEM	<i>P</i> -value
hCTR1	+ 88.5	15.3	0.01	DMT1	+ 43.4	7.7	0.01
ATP7a	+ 21.1	14.0	NS	Dcytb	- 6.3	11.7	NS
ATP7b	+ 55.5	10.7	0.03	FPN	+ 39.0	8.7	0.02
				Hephaestin	+ 65.9	22.1	0.04

Following Epo treatment, the expression of DMT1, FPN and hephaestin, as well as the Cu transporters hCTR1 and ATP7b, were increased significantly (Table 1). These data suggest that Epo acts directly on intestinal epithelial cells to increase the expression of both the Fe–Cu transport pathways. The ferrioxidase activity of hephaestin is essential for Fe efflux from enterocytes. Hephaestin is a Cu-dependent enzyme and it is possible that increased Cu transporter expression following Epo may be important in providing Cu to maintain hephaestin activity.

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