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Selenoprotein expression in the rat colon during Se deficiency. By V. PAGMANTIDIS¹, G. BERMANO², I. BROOM², J.R. ARTHUR³ and J.E. HESKETH¹, ¹*Department of Biological and Nutritional Sciences, University of Newcastle Upon Tyne NE1 7RU*, ²*University of Aberdeen* and ³*Rowett Research Institute, Bucksburn, Aberdeen AB21 9SB*

Selenium is an essential trace element, which is present in several proteins, called selenoproteins, that have various biological roles. In particular cytosolic glutathione peroxidase (GPX1), phospholipid hydroperoxide glutathione peroxidase (GPX4), and gastrointestinal glutathione peroxidase (GPX2) are involved in the cell's antioxidant system. Selenium is incorporated into these proteins as the amino acid selenocysteine (Se-cys), via recognition of the stop codon UGA as a codon for Se-cys. The incorporation of Se-cys at specific UGA codons requires a specific structure (SECIS) in the 3' untranslated region (3' UTR) of the mRNAs coding for selenoproteins. When selenium supply is limiting, the expression of the selenoproteins is decreased, which is also reflected in termination of translation due to the recognition of the UGA codon as a normal stop codon, increased mRNA instability and alteration of the mRNA levels. Colon cancer is a major cause of death in the UK. There is strong evidence linking diet to the development of colon cancer. Selenium has been suggested to protect against colon cancer, but relatively little is known of how Se deficiency affects the colon. The aim of this work was to investigate how Se deficiency affects expression of the glutathione peroxidases in the rat colon.

Previous studies have shown that in rats Se deficiency affects different selenoproteins to various extents and also that their regulation varies between tissues (Bermano *et al.* 1995). Particularly in the liver, GPX1 mRNA levels were greatly reduced under severe Se deficiency, whereas GPX4 mRNA levels showed little or no change. In the present study, rats were fed diets with different amounts of selenium from 402.8 ng/g (superoptimum), 110.8 ng/g (normal), 62.5 ng/g, 33.3 ng/g to 7.6 ng/g (severely deficient). Total RNA was extracted from the colon by a phenol-guanidinium-chloroform procedure and GPX1, GPX2 and GPX4 mRNA abundances were analysed by Northern hybridization. The results show that under severe Se deficiency the mRNA abundance for GPX1 decreased by about 80% ($P < 0.05$), GPX4 mRNA levels decreased by 25% ($P < 0.05$), whereas for GPX2 there was no significant change in the mRNA levels. Preliminary data from a cell culture experiment suggest that under Se depletion the GPX1 and GPX4 mRNA levels are reduced, whereas the mRNA abundance for GPX2 is not. The results imply that, in the colon as is also found in the liver, GPX4 is less sensitive than GPX1 to Se deficiency. However in the liver GPX4 mRNA abundance is unaffected by severe Se deficiency, whereas it is reduced in the colon. In the colon GPX2 expression appears highly conserved when Se supply is low; this has been found previously in studies with Caco-2 cells (Wingler *et al.* 1999), but has not been observed before *in vivo*. Overall the data show that the pattern of change in glutathione peroxidase gene expression in response to Se deficiency is different in the rat colon compared with the liver.

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Bermano G, Nicol F, Dyer JA, Sunde RA, Beckett GJ, Arthur JR & Hesketh JE (1995) *Biochemical Journal* **311**, 425–430.
Wingler K, Böcher M, Flohe L, Kollmus H & Brigelius-Flohe R (1999) *European Journal of Biochemistry* **259**, 149–157.