

**EXPRESSION OF THE H-SUBUNIT AND L-  
SUBUNIT OF FERRITIN IN BONE  
MARROW MACROPHAGES AND CELLS OF  
THE ERYTHRON DURING CHRONIC  
IMMUNE STIMULATION**

**Volume 1**

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## ABSTRACT

Ferritin is the major protein responsible for the sequestration, storage and release of intracellular iron. The ferritin protein shell exists as heteropolymers of various combinations of two types of subunits, the H-subunit and L-subunit, a phenomenon that gives rise to the existence of isoferritins. As the roles of the H-subunit and L-subunit differ in the mineralization process, the subunit composition of ferritin will influence the metabolic properties of the assembled ferritin molecules.

The primary aim of the present study was to quantitatively measure the expression of the H-subunit and L-subunit of ferritin in bone marrow macrophages and cells of the erythron in patients with chronic T-helper cell type-1 immune stimulation. A second aim was to investigate the possible role that the expression of the H-subunit and L-subunit of ferritin may have in the establishment and maintenance of an iron transfer block.

The study subjects included 48 patients with chronic diseases from the Department of Internal Medicine, Kalafong Hospital and 10 patients with osteoarthritis, scheduled for hip replacement at the Department of Orthopaedics, Pretoria Academic Hospital. Bone marrow and blood samples were collected from each patient. The expression of the H-subunit and L-subunit of ferritin in bone marrow macrophages and cells of the erythron was quantitatively evaluated by post-embedding immunolocalisation with immunogold transmission electron microscopy.

The patients were subdivided into groups with a predominantly T-helper cell type-1 immune reaction (pro-inflammatory) and normal immune status on the basis of C-reactive protein, neopterin and cytokines (INF- $\gamma$ , TNF- $\alpha$ , Il-1 $\beta$ , Il-6, Il-12, Il-2, Il-8, GM-CSF, Il-4, Il-5, TGF- $\beta$  and Il-10).

The study showed

- up-regulation of the H-subunit of ferritin in the bone marrow macrophage in patients with chronic T-helper cell type-1 immune stimulation
- no effects for chronic T-helper cell type-1 immune stimulation on the expression of the L-subunit of ferritin in the bone marrow macrophage
- no effects for chronic T-helper cell type-1 immune stimulation on the expression of either the H-subunit or L-subunit of ferritin in cells of the bone marrow erythron
- a 70% prevalence of iron transfer block in patients with chronic T-helper cell type-1 immune stimulation
- up-regulation of the H-subunit of ferritin in the bone marrow macrophage in osteoarthritis patients who had normal T-helper cell type-1 immune activity, but significantly increased TGF- $\beta$  levels
- up-regulation of the H-subunit of ferritin in the patients with iron transfer block
- iron availability loses its primary role in the establishment of the circulating red blood profile in conditions with chronic pro-inflammatory activity
- indications that the H-subunit and L-subunit of ferritin may play a role in the iron availability for red blood cell haemoglobin production
- various correlations in the osteoarthritis patients between the H-subunit and L-subunit of ferritin and different cytokines

## Key words

ferritin, isoferritins, H-subunit, L-subunit, iron, chronic immune stimulation

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