

Induction of Autophagy by Akt/mTOR Pathway in the Bone Marrow due to Protein Malnutrition

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INTRODUCTION Protein malnutrition alters the extracellular matrix and production of hematopoietic stem cells, contributing to marrow hypoplasia no evidence of apoptosis. Nutritional imbalances as malnutrition or nutrient deprivation can activate autophagy, catabolic process regulated by signaling pathway Akt/mTOR

OBJECTIVES Whereas the protein malnutrition leads to impaired hematopoiesis and bone marrow hypoplasia, we propose in this study to evaluate the autophagic signaling in total bone marrow cells in a murine model of protein malnutrition

MATERIAL AND METHODS Mice C57BL/6J received normal protein diet 12% protein (C) or low protein 2% protein (M) for 5 weeks. Proteins of signalling autophagic: Bcl-2, Beclin-1, LC3, total and phosphorylated Akt/mTOR, complex mTOR (Raptor, Rictor and Gβ1) of total bone marrow cells were quantified by Western blotting and the mRNA by RT-PCR. Autophagosomes were assessed by transmission electronic microscopy. The aminogram of both groups was evaluated

RESULTS AND DISCUSSIONS The M group showed a reduction of protein concentrations and serum albumin and amino acids Isoleucine, Lysine, Methionine, Valine, and Taurine. Group M presented leukopenia with neutropenia and lymphopenia and reduction in erythrocyte and reticulopenia parameters, featuring an anemia not regenerativa with reduced bone cellularity. The amount of p-Akt/mTOR p-ser2448/2481, Rictor and Gβ1 was significantly lower in group M. Since the total mTOR, Raptor, Beclin and LC3 were significantly increased. Bcl-2 and total Akt showed no significant differences. The expression of Akt mRNA was lower in the cells of malnourished, since the expression of GβL, BCL-2 and Beclin was

increased. Group M were found presence of autophagosomes by transmission electron microscopy **CONCLUSIONS** This study demonstrated the existence of autophagy in bone marrow with decreased p-Akt/mTOR in malnourished animals. These data may partly justify the marrow hypoplasia these animals with impairment of the production of blood cells and indicate the importance of proper diet and nutritional intervention in the treatment of hospitalized patients, who often are malnourished frame.

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Keywords: Malnutrition, Akt/mTOR, autophagy