

# Lower Synthesis and Higher Catabolism of Liver and Muscle Protein Compensate for Amino Acid Deficiency in Severely Protein-Restricted Growing Rat

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### Lower Synthesis and Higher Catabolism of Liver and Muscle Protein Compensate for Amino Acid Deficiency in Severely Protein-Restricted Growing Rat

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**Objectives:** Severely low-protein (LP) diets induce a decrease in body weight and an increase in relative food intake (FI) in rat. In the liver, changes in anabolic and catabolic protein pathways could transiently participate to compensate for amino acid (AA) deficiency. The present study investigated these liver and muscle protein metabolic pathways on LP diet fed growing rats.

**Methods:** Growing rats were fed for three weeks different diets containing 3–5–8–12–15 or 20% energy from milk protein. Body weight and FI were measured daily. At the end of the experiment, rats were injected with <sup>13</sup>C valine and tissues and biological fluids were collected for gene expression measurement, blood AA UPLC analysis and protein

synthesis rate determination in liver and muscle. Statistical analysis was done by 1- or 2-factor ANOVA, when data were repeated.

**Results:** P3, P5 and P8% diets resulted in significant growth retardation and significant decrease in lean mass. Severe protein deficiency induced a decrease in the rate of protein synthesis in the liver and muscle. In addition, the results showed activation of the GCN2 pathway, via ATF4-CHOP-TRB3 both in the liver and in the muscle, which suggests the inhibition of the initiation of translation at the level of the binding of the RNAt-Met. Liver proteolytic pathways were up-regulated including the ubiquitin-proteasome, the caspase system and the autophagy. In muscle, both the ubiquitin-proteasome pathway, and autophagy were increased as well as the calpain system. The GCN2 pathway, via ATF4-CHOP-TRB3 was activated in both liver and muscle, confirming the activation of protein degradation by the ubiquitin-proteasome pathways, and autophagy. In portal vein, indispensable AA were lower in severe protein deficient diet whereas in vena cava no difference was observed.

**Conclusions:** Severe protein restriction lowered protein synthesis and activated protein catabolism in both liver and muscle whereas no effect was observed for moderate protein restriction. These results confirm that the liver and muscle play a major role in supplying the body with indispensable AA in response to severe protein restriction.

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