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Review

Regulation of protein metabolism by insulin: Value of different approaches and animal models

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Abstract

Insulin induces protein accretion by stimulating protein synthesis and inhibiting proteolysis. However, the mechanisms of regulation of protein metabolism by insulin are complex and still not completely understood. The use of approaches combining hyperinsulinemic clamp and isotopic methods, or measurement of the activation of intracellular kinases involved in insulin signaling, in addition to the use of different animal models in a comparative physiology process, provide better understanding of the potential regulation of protein metabolism by insulin. Studies using the clamp technique in lactating goats have shown a clear inhibitory effect of insulin on proteolysis, with an interaction between the effects of insulin and amino acids. Such studies revealed that the insulin-inhibited proteolysis is improved in lactating goats, this adaptative process limiting the mobilization of body protein under the conditions of amino acid deficit which occurs during early lactation. Insulin signaling studies in growing chickens have also provided some interesting features of insulin regulation compared to mammals. Refeeding or insulin injection leads to the activation of the early steps of insulin receptor signaling in the liver but not in the muscle. Muscle p70 S6 kinase, a kinase involved in the insulin

Abbreviations: 4E-BP1, eukaryotic initiation factor 4E binding protein; ERK1/2, extracellular signal-regulated protein kinase 1/2; FOXO, forkhead box-O transcription factor; IDE, insulin degrading enzyme; IRS-1, insulin receptor substrate 1; MAFbx, muscle atrophy F box; MAPKs, mitogen-activated protein kinases; mTOR, mammalian target of rapamycin; MurRF-1, muscle ring finger-1; P70S6K, 70 kDA ribosomal protein S6 kinase; PI3K, phosphatidylinositol-3′kinase; PKB/AKT, protein kinase B; PTEN, phosphatase and tensin homolog; S6, ribosomal protein S6; Shc, Src homology and collagen protein

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activation of protein synthesis, was found to be markedly activated in response to insulin and to refeeding, suggesting that other signaling pathways than those classically described in mammalian muscles may be involved in signal transduction. Finally, although the role of insulin has been doubtful and has long been considered to be minor in ruminants and in avian species, this hormone clearly regulates protein metabolism in both species.

Keywords: Protein metabolism; Insulin; Signaling; Goat; Chicken

Contents

1. Introduction

Tissue proteins are constantly synthesized and degraded, and the respective intensities of protein synthesis and proteolysis determine protein balance: there is protein accretion if protein synthesis is higher than proteolysis, and maintenance or loss if the opposite occurs. Protein synthesis and degradation are regulated by physiological, genetic and environmental factors, such as ambient temperature and nutritional factors, and hormones, among which insulin is recognized to be a key factor in such regulation.

In this review, our intention is firstly to give a brief overview of the general role of insulin in protein turnover based on data obtained in vitro or in monogastric mammals. We then review work undertaken with birds and ruminants which improves our understanding of the role and mechanisms of action of this hormone in vivo. We have chosen these two examples for the value of interspecies comparisons and the value of the approaches used. Differences between species enrich, enlarge and renew the understanding of physiological regulations. Birds and ruminants exhibit interesting features with regard to insulin regulation compared to monogastric mammals: for instance, insulin causes less pronounced hypoglycemia