

## Rumen-Protected Glucose Stimulates the Insulin-Like Growth Factor System and mTOR/AKT Pathway in the Endometrium of Early Postpartum Dairy Cows

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**Abstract:** This study aimed to elucidate the effects of a dietary rumen-protected glucose (RPG) addition on uterine involution through the analysis of an insulin-like growth factor (IGF) system and associated pathways in the post-natal endometrium. Twelve Holstein cows were assigned equally to two groups: a control group (CT) and an RPG group (200 g of RPG per cow per day). The plasma content of insulin-like growth factor 1 (IGF1) was determined by using the ELISA method. Expressions of IGF members, the matrix metalloproteinase, protein kinase B (AKT)/mechanistic target of rapamycin complex1 (mTOR) signaling pathway, and cell proliferation factors (proliferating cell nuclear antigen (PCNA) and Ki67) were detected using real-time polymerase chain reaction, Western blot, immunohistochemistry, and immunofluorescence, respectively. The results showed that the positive cells of PCNA and Ki67 were increased in the endometrium of RPG versus CT cows. The RPG addition significantly increased the plasma IGF1 level 14 d after delivery. The mRNA expressions of the IGF family members (IGF1, IGF2, type 1 IGF receptor (IGF1R) and IGF-binding proteins (IGFBP1, IGFBP2, IGFBP4 and IGFBP5)) were upregulated, and mRNA expressions of matrix metalloproteinase MMP3 and MMP9 were downregulated in cows from the RPG group compared with the CT group. Meanwhile, the protein expressions of IGF1, IGF2, IGF1R, IGFBP1 and IGFBP4 were upregulated in cows from the RPG group compared with the CT group. Immunohistochemical analysis identified a positive response for IGF1R and IGF2R in the endometrium of RPG versus CT cows. Furthermore, the RPG supplementation increased the protein expressions of phosphorylated (p)-AKT to total AKT and p-mTOR to total mTOR ratio in the endometrium. The current results indicated that the RPG supplementation promoted the proliferation of endometrial cells by stimulating the IGFs and mTOR/AKT pathway in the early post-natal endometrium of dairy cows.

**Keywords:** cow; endometrium; involution; rumen-protected glucose