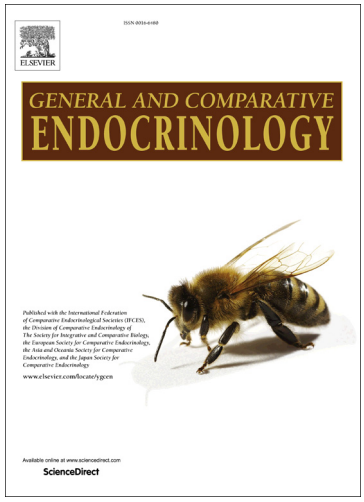

The basic route of the nuclear translocation porcine growth hormone (GH)-growth hormone receptor (GHR) complex (pGH/GHR) in porcine hepatocytes

Lan Hainan, Liu Huilin, Mahamad khan, Zheng Xin, Yang YuJiang, Zhang Hui, Yao Naiquan

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The basic route of the nuclear translocation porcine growth hormone (GH)-growth hormone receptor (GHR) complex (pGH/GHR) in porcine hepatocytes

Lan Hainan[a#1] Liu Huilin[b#], Mahamad khan, Zheng Xin[a], Yang YuJiang[a], Zhang Hui[a], Yao Naiquan

[a] College of Animal Science and Technology, Jilin Agricultural University, Changchun 130118, PR China

[b] College of life sciences, Jilin University, Changchun 130118, PR China

Abstract：Traditional views suggest that growth hormone and the growth hormone receptor (GH/GHR complex) exert their functions only on the plasma membrane. This paradigm, however, has been challenged by recent new findings that the GH/GHR complex could translocate into cell nuclei where they could still exhibit important physiological functions. We also reported the nuclear localization of porcine GH/GHR and their potential functions in porcine hepatocytes. However, the basic path of pGH/GHR's nuclear translocation remains unclear. Combining previous research results and our current findings, we proposed two basic routes of pGH/GHR's nuclear transportation as follows: 1) after pGH binding to GHR, pGH/GHR enters into the cytoplasm though clathrin- or caveolin-mediated endocytosis, then the pGH/GHR complex enters into early endosomes (Rab5-positive), and the endosome carries the GH/GHR complex to the endoplasmic reticulum (ER). After endosome docking on the ER, the endosome starts fission, and the pGH/GHR complex enters into the ER lumen. Then the pGH/GHR complex transports into the cytoplasm, possibly by the ERAD pathway. Subsequently, the pGH/GHR complex interacts with IMPα/β, which, in turn, mediates GH/GHR nuclear localization; 2) pGH binds with the GHR on the cell membrane and, subsequently, pGH/GHR internalizes into the cell and enters into the

[1] Corresponding Author:Hai-Nan Lan Tel: +86-0431-84517235, Fax: +86-0431-84517235, E-mail: tougao@jlau.edu.cn; zhengtougao@163.com