



Effect of HIF-1a/VEGF signaling pathway on plasma progesterone and ovarian prostaglandin F_{2a} secretion during luteal development of pseudopregnant rats

X.Y. Pan^{1,2}, Z.H. Zhang¹, L.X. Wu³ and Z.C. Wang¹

¹Provincial Key Laboratory for Developmental Biology and Neurobiology, College of Life Sciences, Fujian Normal University, Fuzhou, China

²Department of Histology and Embryology, Jilin Medical College, Jilin, China

³Department of Pathophysiology, Maternal and Child Health Hospital of Fujian Province, Fuzhou, China

Corresponding author: Z.C. Wang

E-mail: zcwang@fjnu.edu.cn

Genet. Mol. Res. 14 (3): 8796-8809 (2015)

Received November 5, 2014

Accepted April 28, 2015

Published August 3, 2015

DOI <http://dx.doi.org/10.4238/2015.August.3.3>

ABSTRACT. The corpus luteum is a temporary endocrine structure in mammals that plays an important role in the female reproductive cycle and is formed from a ruptured and ovulated follicle with rapid angiogenesis. Vascular endothelial growth factor (VEGF) is thought to be vital in normal and abnormal angiogenesis in the ovary, but the molecular regulation of luteal VEGF expression during corpus luteum development *in vivo* is still poorly understood at present. Therefore, we examined whether hypoxia-inducible factor-1a (HIF-1a) is induced and regulates VEGF expression and luteal function *in vivo* using a pseudopregnant rat model treated with a small-molecule inhibitor of HIF-1a, echinomycin. Corpus luteum development in the pseudopregnant rat ovary was determined after measuring plasma progesterone concentration and ovarian prostaglandin F_{2a} content to reflect changes

in HIF-1a and VEGF on different days of this developmental process. At day 7, the corpus luteum was formed and the expression of HIF-1a/VEGF reached a maximum, while a significant decrease in HIF-1a/VEGF expression was observed when luteolysis occurred at day 13. Additionally, echinomycin blocked luteal development by inhibiting VEGF expression mediated by HIF-1a and following luteal function by detecting the progesterone changes at day 7. These results demonstrated that HIF-1a-mediated VEGF expression might be an important mechanism regulating ovarian luteal development in mammals *in vivo*, which may provide new strategies for fertility control and for treating some types of ovarian dysfunction, such as polycystic ovarian syndrome, ovarian hyperstimulation syndrome, and ovarian neoplasia.

Key words: Corpus luteum; Hypoxia-inducible factor-1a; Echinomycin; Progesterone; Vascular endothelial growth factor