Differential expression patterns of Toll-like receptor 4 at the maternal-fetal interface of pregnant Yorkshire and Meishan pigs

Liu Huazhen[1], Zhang Gaoying[1], Peng Kemei[1], Liu Yinxue[1], Yu Mei[2]
(1. College of Animal Science and Veterinary Medicine, Huazhong (Central China) Agricultural University, WuHan 430070;
2. College of Animal Science and Veterinary Medicine, Key Lab of Agricultural Animal Genetics, Breeding and Reproduction of Ministry of Education, Huazhong (Central China) Agricultural University, WuHan 430070)

Abstract: Toll-like receptor 4 (TLR4) has been suggested to play a very important role in modulation of immunological tolerance in the human female reproductive tract. To better understanding of functions of TLR4 in establishment and maintenance of pregnancy in pigs, the study was performed to compare the expression patterns of TLR4 at maternal-fetal interface of pregnant Yorkshire and Meishan pigs. The uteri from Yorkshire and Meishan gilts on days 26 and 50 of gestation were obtained respectively. Immunohistochemical analysis indicated that TLR4 was detected in uterine epithelium and trophoblast of these two types of pigs on days 26 and 50 of gestation. In Yorkshire gilts, the expression of TLR4 was higher in uterine epithelium than that in trophoblast on day 26 of gestation, while it was lower in uterine epithelium than that in trophoblast on day 50 of gestation. In Meishan pigs, the expression of TLR4 in trophoblast was higher than that in uterine epithelium on either day 26 or day 50 of gestation and TLR4 was found to be mainly present in the cells located at the bottom of trophoblast on day 50 of gestation. Compared with Meishan pigs, TLR4 was abundant in uterine epithelium of Yorkshire pigs on days 26 and 50 of gestation, yet it was decreased in trophoblast of Yorkshire pigs on day 50 of gestation. The results indicated that TLR4 at the maternal-fetal interface is expressed in differential patterns between Yorkshire and Meishan pigs and provided novel information about the functions of TLR4 in pig pregnancy.

Keywords: basic veterinary medicine; pig; pregnancy; maternal-fetal interface; toll-like receptor 4

0 Introduction

High prenatal mortality (recessive abortion) in early and mid gestation results in great economic loss in pig production. The commercial pork breeds ovulate approximately 16-18 ova per estrus and have high fertilization rate exceeding 95%, yet the average size of a litter is 10.5 piglets (Anderson et al., 1993; Youngs et al., 1994; Geisert and Schmitt, 2002; Wessels et al., 2007). That is to say, only 60-70% can develop to a mature fetus. The Meishan pig is one of the famous Chinese indigenous prolific species. They farrow 4-5 more piglets per litter, although they have similar ovulation rates as other commercial pork breeds (Youngs et al., 1994; Biensen et al., 1999; Tayade et al., 2006). Previous work has indicated the differences between Meishan pig and commercial pork breeds, which are that in Meishan pig conceptuses develop more slowly and uniformly, and that the placentas are smaller and densely vascularized (Youngs et al., 1993; Wilson et al., 1999; Biensen et al., 1999). However, selection for improved placental efficiency has not improved litter size in swine significantly (Wilson et al., 1999).

Previous studies have revealed a strong immunological presence at the maternal-fetal interface during pregnancy (Weetman 1999; Mor and Abrahams, 2002; Blois et al., 2008; Nagamatsu and Schust, 2010). Clinical studies have indicated that some pregnancy complications are thought to be associated with intrauterine infections (Goncalves et al., 2002; Romero et al.,

Foundations: National Natural Science Foundation of China (30800808 and 30771537) and New Teacher Foundation of Ministry of Education of China (200805041031)
Brief author introduction:刘华珍，（1976-），女，副教授，主要研究方向：动物组织胚胎学。
Correspondance author: 余梅，（1968-），女，教授，主要研究方向：动物遗传育种与繁殖。 E-mail: yumei@mail.hzau.edu.cn

2003). Therefore, unexplained spontaneous losses could be caused by dysregulated immune mechanisms. The innate immunity, acting as the first line of defense against invading pathogens, is able to distinguish between what is infectious non-self and non-infectious self through the evolutionary conserved pattern recognition receptors recently attributed to the family of Toll-like receptors (TLRs) (Medzhitov and Janeway, 2002; Janeway and Medzhitov, 2002). Originally identified in *Drosophila*, up to date, 13 TLRs have been confirmed in mammals with their expressions varying among species (Beutler et al., 2006). They can recognize and bind to highly conserved sequences known as pathogen associated molecular patterns (PAMPs), which are shared by large groups of microorganisms (Medzhitov and Janeway, 2002; Uematsu and Akira, 2006; Kim et al., 2008). TLR4 was the first identified one in human and subsequently was found to be the specific receptor for recognition of lipopolysaccharide (LPS) (Medzhitov et al., 1997; Hoshino et al., 1999). Previous work suggests that *Escherichia coli* are the most commonly isolated pathogenic bacteria in clinical uterine disease in cattle, and there are high concentrations of the main pathogenic ligand of *E.coli,* LPS in the uterine lumen (Williams et al., 2005). TLR4 mRNA and protein have been detected in bovine endometrial stromal and epithelial cells by RT-PCR and flow cytometry (Herath et al., 2006). It has been reported the existence of ten TLRs at the mRNA level including TLR4 in the female reproductive tract in human and pig (Pioli et al., 2004; Schaefer et al., 2005; Aflatoonian et al., 2007; Linton et al., 2008). Another study using immunohistochemistry techniques indicated that TLR4 was only present in the endocervix, endometrium and uterine tubes and absent in vagina and ectocervix. In addition, a secretory form of TLR4 seems to be produced by the endocervical glands (Fazeli et al., 2005). Quantitative analysis showed that TLR4 expression declined progressively along the tract, with the highest expression in the upper tissues (fallopian tubes and endometrium), followed by cervix and ectocervix (Pioli et al., 2004). TLR4 has been found to be expressed in term placenta at the protein level in human (Holmlund et al., 2002; Kumazaki et al., 2004). Accordingly, we can say pregnancy of mammals is closely related to uterine TLR4 levels. Therefore, we are interested in the functions of TLR4 in pig pregnancy. However, little is known about the functions of TLR4 during pregnancy. So the present study was performed to compare the expression pattern of TLR4 protein at the maternal-fetal interface between Yorkshire and Meishan pigs to explore its potential role in pig pregnancy.

1 Materials and Methods

Pure-bred Yorkshire gilts (n=6) and Meishan gilts (n= 6) were obtained from Pig Breeding Farm of Huazhong Agricultural University, and they were housed under conventional conditions and vaccinated according to the schedule of the breeding farm. When they were on days 26 and 50 of gestation, the pigs were slaughtered respectively. The uteri were removed rapidly and transported in an ice-box to the laboratory. Then they were opened longitudinally along the antimesometrial side. Three healthy implantation sites were sampled per gilt. The samples were fixed immediately in 4% paraformaldehyde-0.1M phosphate for 24 h. All samples were routinely dehydrated in an ethanol series, and subsequently embedded in paraffin. Then they were dissected into serial sections of 6 μm thickness and mounted on poly-l-lysine-coated glass slides. All the slides were dried overnight at 37℃.

Streptavidin-biotin-peroxidase complex (SABC) immunohistochemical method was used to study the expression of TLR4 in the placenta. Slides were de-waxed in xylene and rehydrated through graded alcohols to distilled water. To block endogenous peroxidase, the sections were treated with 3% hydrogen peroxide (H_2O_2) diluted with distilled water at room temperature for 10

min. Then the sections in pH 6 citrate buffer were placed in a microwave oven until the water boiled to expose antigen fully. The sections were pre-incubated with 5% normal goat serum for 30 min, and then incubated with rabbit anti-TLR4 primary antibody (BA1717; Boster Corporation, China) overnight at 4℃ and then incubated with biotinylated sheep anti-rabbit secondary antibody. Subsequently, SABC was added to promote coloration. Then, the sections were stained with diaminobenzidine and counterstained with Harris haematoxylin. Control sections were prepared using the same method, omitting the primary antibody (Zhang et al., 2009; Liu et al., 2008).

For quantitative analysis, the expression level of TLR4 was studied using a computer-assisted image analysis system (HPIAS-2000, China). Quantification of TLR4 level for each sample was represented by the averaged optical density of 25 regions selected from 5 adjacent sections randomly (five regions per section). The significant difference was analyzed using SPSS v.11.5. Values of $P<0.05$ were considered statistically significant.

2 Results

Immunoreactivity for TLR4 protein was detected in all of the placentas examined, and the TLR4 expression patterns were dependent on gestational stage and breed type.

2.1 TLR4 expression patterns on day 26 of gestation

Immunohistochemical analysis showed that the uterine epithelium, glandular epithelial cells, endothelium, and trophoblast of these two types of pigs on day 26 of gestation were TLR4 positive (Fig.1a-b). In Yorkshire pig, the expression level of TLR4 protein in uterine epithelium was significantly higher than that in trophoblast cells (table 1). Yet in Meishan pig, the expression level of TLR4 protein in trophoblast cells was significantly higher than that in uterine epithelium (table 1).

2.2 TLR4 expression patterns on day 50 of gestation

In this period, the uterine epithelium, glandular epithelial cells, endothelium, and trophoblast cells of these two types of pigs were also TLR4 positive (Fig.1c-f). In Yorkshire pigs, the TLR4 expression level in trophoblast cells was higher than that in uterine epithelium (table 1). In Meishan pigs, it was very interesting that TLR4 positive immunostaining was mainly restricted to the trophoblastic cells in their basolateral sides located at the bottom of the folds (fetal side) on day 50 of gestation (Fig.1e-f), and the expression of TLR4 protein in trophoblast was higher than that in uterine epithelium (table 1).

2.3 Comparison of TLR4 protein expression patterns between Yorkshire and Meishan pigs

Compared with Meishan pig, the level of TLR4 protein expression in uterine epithelium of Yorkshire pig was significantly higher on day 26 of gestation (table 1) and day 50 gestation (table 1), yet the level of TLR4 protein expression in trophoblast was higher on day 26 of gestation (table 1) and significantly lower on day 50 of gestation (table 1).

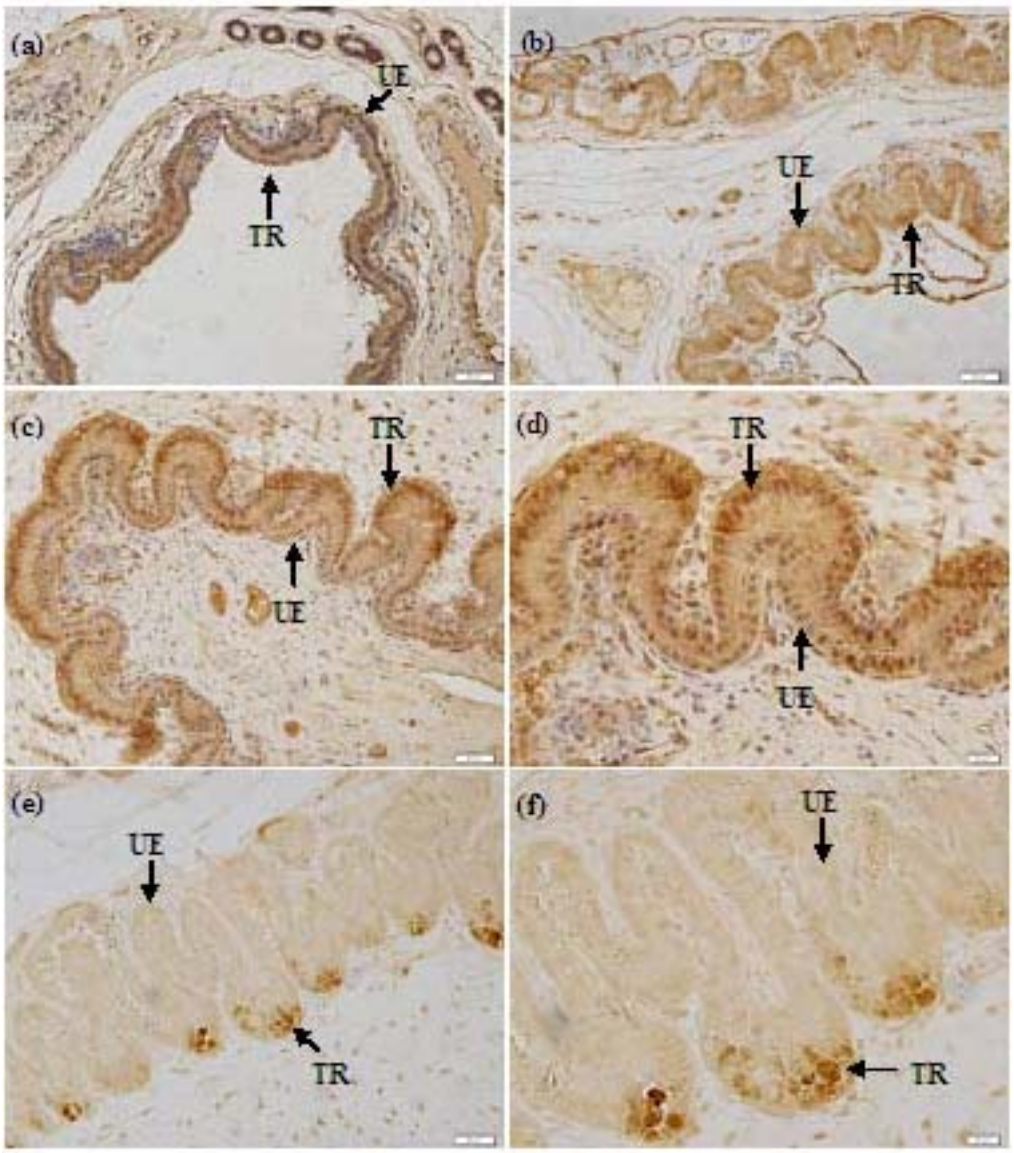

Fig.1 The expression patterns of TLR4 protein at the maternal-fetal interface of Yorkshire and Meishan pigs at different gestation period. (a) The expression of TLR4 protein in uterine epithelium (UE) of Yorkshire pig on day 26 of gestation was higher than that in trophoblast (TR). (b) The expression of TLR4 in TR of Meishan pig on day 26 of gestation was stronger than that in UE. (c and d) The expression of TLR4 in TR of Yorkshire pig on day 50 of gestation was stronger than that in UE. (e and f) The expression of TLR4 in TR of Meishan pig on day 50 of gestation was stronger than that in UE, and the TLR4 positive immunostaining was mainly restricted to the trophoblastic cells located at the bottom.

Table 1 TLR4 immunostaining intensity at the maternal-fetal interface on gd26 and gd50

breeds	TLR4 in uterine epithelium		TLR4 in trophoblast	
	gd26	gd50	gd26	gd50
Yorkshire	81.57 ± 2.50^{a}	63.49 ± 11.34^{b}	57.57 ± 6.52^{a}	94.86 ± 12.82^{b}
Meishan	37.55 ± 1.39^{c}	29.42 ± 6.73^{d}	55.19 ± 7.71^{a}	142.9 ± 15.55^{c}

Each value is mean ± SD (n = 25). The different letter in superscript means significant difference ($P < 0.01$).

3 Discussion

The maternal-fetal interface is a unique site with special requirements for the immune regulation, because it must accept and foster the immunologically distinct fetus on one hand, and on the other hand, it must deal with invading bacterial and viral pathogens to avoid infection. Therefore, the immune system at the maternal-fetal interface can affect the outcome of a

pregnancy (Linton et al., 2008). Growing evidence indicated that TLR4 is expressed by the epithelium of the female reproductive tract (Pioli et al., 2004; Schaefer et al., 2005; Herath et al., 2006; Aflatoonian et al., 2007), suggesting that TLR4 may play a very important role during pregnancy. Normal term and preterm human placentas have been shown to express TLR4 at the RNA and protein levels corroborating the hypothesis (Holmlund et al., 2002; Kumazaki et al., 2004). In the present study, the expression patterns of TLR4 at the maternal-fetal interface of pregnant Yorkshire and Meishan pigs were compared for the first time. It has been shown that the expression patterns of TLR4 were dependent on gestational stage and breed type. The tentative explanation is that the different expression pattern of TLR4 at the maternal-fetal interface of these two types of pigs reflects its special functions in pregnancy.

Pregnancy is a complex process involving a series of events, such as implantation, trophoblast proliferation, placental development and immune protection. It has three distinct immunological phases including pro-inflammatory, anti-inflammatory and pro-inflammatory in humans (Koga et al., 2009). According to the three distinct immunological phases in pregnancy, the whole process ordinarily can be divided into three separate periods: early, mid and late pregnancy. A special feature of early pregnancy of viviparous animals is the embryonic implantation, and the formation of placenta, which is responsible for physiological exchange between the developing fetus and its mother. There are different placenta types including epitheliochorial, syndesmochorial, endotheliochorial and hemochorial placentas. In invasive hemochorial placenta, its formation requires a strong inflammatory response, because the trophoblast has to break the epithelial lining of the uterus in order to adhere and invade into the endometrial tissue (Mor, 2007). Pigs are a species with non-invasive epitheliochorial placenta, which means in the early stage of implantation, the trophoblast does not have to break the epithelium lining of the uterus. It is likely that the immune system acts to weaken the local immune level to accept the fetus. In the present study, we found that in early pregnancy (gd26), the expression level of TLR4 in uterine epithelium in Yorkshire pigs was significantly higher than that in Meishan pigs. Thus, intense immune level possibly results in high prenatal mortality (25-35%) before gd30 in commercial swine.

Mid gestation is a period for rapid fetal growth and development and the predominant immunological feature in this period is an anti-inflammatory in humans (Koga et al., 2009). Many clinical studies have indicated a strong association between intrauterine infections and pregnancy losses, and up to 40% of preterm labor cases are close to infections (Goldenberg et al., 2000; Lamont, 2003). It has been reported that the uterine epithelium and the trophoblast communicate through molecular signals to protect the fetus from infection (Koga et al., 2009). The trophoblast can recognize the presence of viruses and bacteria through pattern recognition receptors (Mor et al., 2005; Costello et al., 2007). In human placenta, the main cell type expressing TLRs protein is the trophoblast with the expression patterns varying by gestation stage (Holmlund et al., 2002; Kumazaki et al., 2004). In this study, we found that the TLR4 expression level in trophoblast was higher than that in uterine epithelium in these two types of pigs on gd 50. The above results indicate that trophoblasts in the placenta are able to respond to the invading pathogens, and to a certain extent they compose a part of the innate immune system to participate in the physiological protection of the placenta. The higher TLR4 expression level in the trophoblast than that in Yorkshire suggests that elevated TLR4 and immune function may play a role in higher litter sizes in Meishan pig.

Furthermore, it is worth noting that the TLR4 positive immunostaining was observed mainly in the trophoblastic cells in their basolateral sides (fetal side) on day 50 of gestation in Meishan

pigs. The result is in line with the finding that the expression of TLR4 proteins was detected only on the basolateral side of mucosal epithelial cells of the intestinal tract (Zhang et al., 2009). Therefore, the immune responses can be initiated only when the bacteria invade the basolateral compartment from the apical side. The placenta serves as a highly specialized barrier, protecting the developing fetus from infection, and on the other hand, it must co-localize with commensal bacteria. These observations are helpful to explain how an immune response can be mounted against pathogenic, but not commensal bacteria (Abrahams and Mor, 2005).

In conclusion, differential expression patterns of TLR4 at the maternal-fetal interface in Yorkshire and Meishan pigs possibly affect pig pregnancy outcome, yet the mechanisms need further study.

References

[1] Abrahams, V. M., Mor, G., 2005: Toll-like Receptors and their Role in the Trophoblast.Placenta. 26, 540-547.
[2] Aflatoonian, R., Tuckerman, E., Elliott, S.L., Bruce, C., Aflatoonian, A., Li, T.C., Fazeli, A., 2007: Menstrual cycle-dependent changes of Toll-like receptors in endometrium. Hum. Reprod. 22, 586-593.
[3] Anderson, L.H., Christenson, L.K., Christenson, R.K., Ford, S.P., 1993: Investigations into the control of litter size in swine. II. Comparisons of morphological and functional embryonic diversity between Chinese and American breeds. J. Anim. Sci. 71, 1566-1571.
[4] Beutler, B., Jiang, Z.F., Georgel, P., Crozat, K., Croker, B., Rutschmann, S., Du, X., Hoebe, K., 2006: Genetic analysis of host resistance: Toll-like receptor signaling and immunity at large. Annu. Rev. Immunol. 24, 353-389.
[5] Biensen N.J., Wilson M.E., Ford S.P., 1999: The impacts of uterine environment and fetal genotype on conceptus size and placental vascularity during late gestation in pigs. J. Anim. Sci. 77, 954-959.
[6] Blois, S.M., Barrientos, G., Garcia, M.G., Orsal, A.S., Tometten, M., Cordo-Russo, R.I., Klapp, B.F., Santoni, A., Fernandez, N., Terness, P., Arck, P.C., 2008: Interaction between dendritic cells and natural killer cells during pregnancy in mice. J. Mol. Med. 86, 837-852.
[7] Costello, M.J., Joyce, S.K., Abrahams, V.M., 2007: NOD protein expression and function in first trimester trophoblast cells. Am. J. Reprod. Immunol. 57, 67-80.
[8] Fazeli, A., Bruce, C., Anumba, D.O., 2005: Characterization of Toll-like receptors in the female reproductive tract in humans. Hum. Reprod. 20, 1372-1378.
[9] Geisert R.D., Schmitt RAM, 2002: Early embryonic survival in the pig: can it be improved? J. Anim. Sci. 80(E. Suppl. 1), E54-E65.
[10] Goldenberg, R.L., Hauth, J.C., Andrews, W.W., 2000: Intrauterine infection and preterm delivery. N. Engl. J. Med. 342,1500-1507.
[11] Goncalves, L.F., Chaiworapongsa, T., Romero, R., 2002: Intrauterine infection and prematurity. Ment. Retard. Dev. Disabil. Res. Rev. 8, 3-13.
[12] Herath, S., Fischer, D.P., Werling, D., Williams, E.J., Lilly, S.T., Dobson, H., Bryant, C.E., Sheldon, I.M., 2006: Expression and function of Toll-like receptor 4 in the endometrial cells of the uterus. Endocrinology. 147, 562-570.
[13] Holmlund, U., Cebers, G., Dahlfors, A.R., Sandstedt, B., Bremme, K., Ekstrom, E.S., Scheynius, A., 2002: Expression and regulation of the pattern recognition receptors Toll-like receptor-2 and Toll-like receptor-4 in the human placenta. Immunology.107, 145-151.
[14] Hoshino, K., Takeuchi, O., Kawai, T., Sanjo, H., Ogawa, T., Takeda, Y., Takeda, K., Akira, S., 1999: Cutting edge: Toll-like receptor 4 (TLR4)-deficient mice are hyporesponsive to lipopolysaccharide: evidence for TLR4 as the Lps gene product. J. Immunol., 162, 3749-3752.
[15] Janeway, C.A.Jr., Medzhitov, R.,2002: Innate immune recognition. Annu. Rev. Immunol. 20,197-216.
[16] Kim, C.H., Park, F.W., Ha, N.C., Kang, H.J., Lee, B.L.,2008: Innate immune response in insects: recognition of bacterial peptidoglycan and amplification of its recognition signal. BMB. Rep. 41, 93-101.
[17] Koga, K., Aldo, P.B., Mor, G., 2009: Toll-like receptors and pregnancy: Trophoblast as modulators of the immune response. J. Obstet. Gynaecol. Res. 35, 191-202.
[18] Kumazaki, K., Nakayama, M., Yanagihara, I., Suehara, N., Wada, Y., 2004: Immunohistochemical distribution of Toll-like receptor 4 in term and preterm human placentas from normal and complicated pregnancy including chorioamnionitis. Hum. Pathol. 35, 47-54.
[19] Lamont, R.F., 2003: The role of infection in preterm labour and birth. Hosp. Med. 64, 644- 647.
[20] Linton, N.F., Wessels, J.M., Cnossen, S.A., Croy, B.A., Tayade, C., 2008: Immunological mechanisms affecting angiogenesis and their relation to porcine pregnancy success. Immunol. Invest. 37, 611-629.
[21] Liu, H.Z., Li, X.Y., Tong, J.J., Qiu, Z.Y., Zhan, H.C., Sha, J.N., Peng, K.M., 2008: Duck cerebellum participates in regulation of food intake via the neurotransmitters serotonin and neuropeptide Y. Nutr. Neurosci. 11, 200-206.
[22] Medzhitov, R., Preston-Hurlburt, P., Janeway, CA. Jr., 1997: A human homologue of the Drosophila Toll protein signals activation of adaptive immunity. Nature. 388, 394-397.

[23] Medzhitov, R., Janeway, C.A. Jr., 2002: Decoding the patterns of self and nonself by the innate immune system. Sci. 296, 298-300.
[24] Mor, G., Abrahams, V.M., 2002: Immunology of implantation. Immunol. Allergy. Clin. N .Am. 22, 545-565.
[25] Mor, G., Romero, R., Aldo, P.B., Abrahams, V.M., 2005: Is the trophoblast an immune regulator? The role of toll-like receptors during pregnancy. Crit. Rev. Immunol. 25, 375-388.
[26] Mor, G., 2007: Pregnancy reconceived. Natural History. 116, 36-41.
[27] Nagamatsu, T., Schust, D.J., 2010: The immunomodulatory roles of macrophages at the maternal- fetal interface. Reprod. Sci. 17, 209-218.
[28] Pioli, P.A., Amiel, E., Schaefer, T.M., Connolly, J.E., Wira, C.R., Guyre, P.M., 2004: Differential expression of Toll-like receptors 2 and 4 in tissues of the human female reproductive tract. Infect. Immun. 72, 5799-5806.
[29] Romero, R., Chaiworapongsa, T., Espinoza, J., 2003: Micronutrients and intrauterine infection, preterm birth and the fetal inflammatory response syndrome. J. Nutr. 133, 1668S-1673S.
[30] Schaefer, T.M., Fahey, J.V., Wright, J.A., Wira, C.R., 2005: Innate immunity in the human female reproductive tract: antiviral response of uterine epithelial cells to the TLR3 agonist poly(I:C). J. Immunol. 174, 992-1002.
[31] Tayade, C., Black, G.P., Fang, Y., Croy, B.A., 2006: Differential gene expression in endometrium, endometrial lymphocytes, and trophoblasts during successful and abortive embryo implantation. J. Immunol. 176, 148-156.
[32] Uematsu, S., Akira, S., 2006: Innate immune recognition of viral infection. Uirusu. 56, 1-8.
[33] Weetman, A.P., 1999: The immunology of pregnancy. Thyroid. 9, 643-646.
[34] Wessels J.M., Linton N.F., Croy B.A., Tayade C., 2007: A review of molecular contrasts between arresting and viable porcine attachment sites. Am. J. Reprod. Immunol. 58, 470-80.
[35] Williams E.J., Fischer D.P., Pfeiffer D.U., England G.C., Noakes D.E., Dobson H., Sheldon I.M., 2005: Clinical evaluation of postpartum vaginal mucus reflects uterine bacterial infection and the immune response in cattle. Theriogenology. 63, 102-117.
[36] Wilson M.E., Biensen N.J., Ford S.P., 1999: Novel insight into the control of litter size in pigs, using placental efficiency as a selection tool. J. Anim. Sci. 77, 1654-1658.
[37] Youngs C.R., Ford S.P., McGinnis L.K., Anderson L.H., 1993: Investigations into the control of litter size in swine: I. Comparative studies on in vitro development of Meishan and Yorkshire preimplantation embryos. J. Anim. Sci. 71, 1561-1565.
[38] Youngs, C.R., Christenson, L.K., Ford, S.P., 1994: Investigations into the control of litter size in swine. III. A reciprocal embryo transfer study of early conceptus development. J. Anim. Sci. 72, 725-731.
[39] Zhang, G.Y., Wang, Y., Peng, K.M., Wang, C., Tian, G., Liu, H.Z., 2009: Strategic localization of toll-like receptor 4 in the digestive tract of blunt snout bream (Megalobrama amblycephala). Anat. Histol. Embryol. 38, 401-405.

妊娠大白猪和梅山猪母胎界面 TLR4 的表达模式比较研究

刘华珍[1]，张高英[1]，彭克美[1]，刘银雪[1]，余梅[2]
（1. 华中农业大学动物科技学院动物医学院，武汉 430070；
2. 华中农业大学动物科技学院动物医学院教育部农业动物遗传育种与繁殖重点实验室，武汉 430070）

摘要：研究发现 TLR4 在人类雌性生殖道免疫耐受中发挥重要的调节作用。为了更好地理解 TLR4 在猪妊娠维持中的作用，本研究比较了 TLR4 在妊娠 26 天和 50 天大白猪和梅山猪母胎界面的表达模式。研究结果显示，TLR4 在子宫内膜上皮及滋养层中均有分布，但呈现不同的表达模式。在大白猪中，妊娠 26 天时，子宫内膜上皮中 TLR4 的表达量比滋养层中高，而妊娠 50 天时，滋养层中的表达量比子宫内膜上皮中高；在梅山猪中，妊娠 26 天和 50 天时，滋养层中的表达量比子宫内膜上皮中的高，并且妊娠 50 天时 TLR4 主要位于滋养层细胞的基底端。大白猪与梅山猪相比，子宫内膜上皮中 TLR4 的表达量较高。以上研究结果表明，妊娠大白猪和梅山猪母胎界面 TLR4 存在不同的表达模式，为探明 TLR4 在猪妊娠中的作用提供新的资料。

关键词：基础兽医学；猪；妊娠；母胎界面；TLR4
中图分类号：S852.1