RELATIONSHIPS AMONG MATERNAL BACKFAT DEPTH, PLASMA ADIPOKINES AND THE BIRTHWEIGHT OF PIGLETS

Animal: An International Journal of Animal Bioscience

RELATIONSHIP AMONG MATERNAL BACKFAT DEPTH, PLASMA ADIPOKINES AND BIRTHWEIGHT OF PIGLETS

--Manuscript Draft--

Manuscript Number:	
Full Title:	RELATIONSHIP AMONG MATERNAL BACKFAT DEPTH, PLASMA ADIPOKINES AND BIRTHWEIGHT OF PIGLETS
Short Title:	Maternal backfat depth and birthweight of piglets
Article Type:	Research Article
Section/Category:	3. Physiology and Functional Biology
Keywords:	pregnant sows; backfat depth; adipokines; piglets; birth weight
Corresponding Author:	Alberto Sabbioni, Prof. University of Parma Parma, ITALY
First Author:	Paola Superchi, Prof.
Order of Authors:	Paola Superchi, Prof.
	Roberta Saleri, DVM, PhD
	Sven Mencik, Prof.
	Silvia Dander, Dr.
	Michela Ablondi, Dr.
	Valeria Cavalli, Dr.
	Chiara Izzi, Dr.
	Alberto Sabbioni, Prof.
Manuscript Region of Origin:	ITALY
Abstract:	A potentially important role into the mechanisms controlling intrauterine growth is provided by adipose tissue. The adipose tissue acts as a dynamic organ, with differentiated adipocytes functioning in an endocrine manner to secrete adipokines, as leptin and adiponectin, involved in modulating energy homeostasis. With the aim of assessing the relationships among maternal adiposity, leptin and adiponectin-pregnancy trend and foetal growth, 48 sows Large White x Landrace were recruited. On basis of backfat (BF) depth at the end of lactation phase, a Low Fat (LF, 11.60 mm; n=24) and a High Fat (HF, 18.20 mm; n=24) groups were formed. During the study, both groups received the same feeding level. At mating and at days 28, 85 and 113 of gestation, the BF was recorded and blood samples were collected to assess the leptin and adiponectin concentrations. At farrowing (BW0) and after 24 h (BW24), piglets were weighed and temperature was recorded. Body mass index (BMI) and ponderal index (PI) were calculated. Before suckling colostrum, blood samples were collected and leptin, adiponectin and IGF-I plasma levels were analysed. The BF depth change during pregnancy was the same in both groups ($P > 0.05$); the BF depth differences between LF and HF groups observed at mating persist during pregnancy as well ($P < 0.05$). A decrease in adiponectin and an increase in leptin plasma levels occur in both groups. Plasma adiponectin was lower in HF group compared to LF group ($P \leq 0.05$), while plasma leptin was not different between groups ($P > 0.05$). Consequently, the adiponectin-leptin ratio resulted lower in HF than in LF group ($P < 0.05$). Compared to HF group, LF sows give birth to lighter piglets ($P < 0.05$). In addition, 14% of the piglets in the LF group and 7% in the HF group reveal a weight that falls in the 25th percentile (≤ 1 kg) ($P < 0.05$). Piglet's anthropometric parameters and thermoregulatory ability were unaffected by maternal adiposity ($P > 0.05$). Piglet's mortality at 24 h from birth was 13% and 3%, in LF and HF groups, respectively ($P < 0.05$). Haematological differences were found only in the case of IGF-I level, which was lower in piglets born from LF than in those from HF sows ($P < 0.05$). Our findings suggest that differences in

	maternal adiposity, due to individual factors and not to feeding levels, influence the offspring weight by acting on the secretion of adipokines.
Suggested Reviewers:	Dominiek Maes Ghent University dominiek.maes@ugent.be He is experienced in studies about relationships between sow fatness and reproductive efficiency
	Christian Fink Hansen, Dr. University of Copenhagen cfh@sund.ku.dk Expert in pig neonatology
	Emma Baxter, Dr. Scotland's Rural College emma.baxter@sruc.ac.uk Author with experience in neonatal survival in pigs
Opposed Reviewers:	

RELATIONSHIP AMONG MATERNAL BACKFAT DEPTH, PLASMA ADIPOKINES AND BIRTHWEIGHT OF PIGLETS

P. Superchi[1], R. Saleri[1], S. Menčik[2], S. Dander[1], M. Ablondi[1], V. Cavalli[1], C. Izzi[1], A. Sabbioni[1,a]

[1] *Department of Veterinary Science, University of Parma, Via del Taglio 10, 43126 Parma, Italy.*

[2] *Department of Animal Husbandry, Faculty of Veterinary Medicine, University of Zagreb, Vjekoslava Heinzela 55, 10000 Zagreb, Croatia.*

[a] Corresponding author: Alberto Sabbioni. E-mail: alberto.sabbioni@unipr.it

Short title: Maternal backfat depth and birthweight of piglets

Abstract A potentially important role into the mechanisms controlling intrauterine growth is provided by adipose tissue. The adipose tissue acts as a dynamic organ, with differentiated adipocytes functioning in an endocrine manner to secrete adipokines, as leptin and adiponectin, involved in modulating energy homeostasis. With the aim of assessing the relationships among maternal adiposity, leptin and adiponectin-pregnancy trend and foetal growth, 48 sows Large White x Landrace were recruited. On basis of backfat (**BF**) depth at the end of lactation phase, a Low Fat (**LF**, 11.60 mm; n=24) and a High Fat (**HF**, 18.20 mm; n=24) groups were formed. During the study, both groups received the same feeding level. At mating and at days 28, 85 and 113 of gestation, the BF was recorded and blood samples were collected to assess the leptin and adiponectin concentrations. At farrowing (**BW0**) and after 24 h (**BW24**), piglets were weighed and temperature was recorded. Body mass index (**BMI**) and

ponderal index (**PI**) were calculated. Before suckling colostrum, blood samples were collected and leptin, adiponectin and IGF-I plasma levels were analysed. The BF depth change during pregnancy was the same in both groups (P >0.05); the BF depth differences between LF and HF groups observed at mating persist during pregnancy as well (P <0.05). A decrease in adiponectin and an increase in leptin plasma levels occur in both groups. Plasma adiponectin was lower in HF group compared to LF group (P ≤0.05), while plasma leptin was not different between groups (P >0.05). Consequently, the adiponectin-leptin ratio resulted lower in HF than in LF group (P <0.05). Compared to HF group, LF sows give birth to lighter piglets (P <0.05). In addition, 14% of the piglets in the LF group and 7% in the HF group reveal a weight that falls in the 25th percentile (≤ 1 kg) (P <0.05). Piglet's anthropometric parameters and thermoregulatory ability were unaffected by maternal adiposity (P >0.05). Piglet's mortality at 24 h from birth was 13% and 3%, in LF and HF groups, respectively (P <0.05). Haematological differences were found only in the case of IGF-I level, which was lower in piglets born from LF than in those from HF sows (P <0.05). Our findings suggest that differences in maternal adiposity, due to individual factors and not to feeding levels, influence the offspring weight by acting on the secretion of adipokines.

Keywords: pregnant sows**;** backfat depth**;** adipokines; piglets; birth weight

Implications. Birthweight represents a challenge in the pig industry. The adipose tissue, by secreting leptin and adiponectin, which are important in modulating glucose and lipid homeostasis, is a potentially regulator of the mechanisms that link maternal adiposity and intrauterine growth. It is likely, that leptin's role in foetal growth, untied by maternal fatness, is only permissive. Its increase during pregnancy may be the

signal to enhance the mobilization of maternal fat storage and the transplacental transfer of lipids to the foetus. Conversely, reduced levels of adiponectin may represent a mechanism by which a high maternal fat mass leads to an increased foetal weight.

Introduction

Birthweight is considered to be a critical indicator of postnatal performance. Growth and development of the foetus are the result of a balance between the foetal demand and the maternal substrate availability (Jansson and Powell, 2006). To ensure nutrients to foetus, the sow undergoes to an alteration in the regulation of glucose metabolism leading to a state of relative insulin resistance, attributed to the effect of placental hormones, as pregnancy progresses (Père *et al.*, 2000). The development of an insulin-resistant state, increasing hepatic gluconeogenesis and reducing glucose uptake in maternal skeletal muscle and adipose tissue, promotes lipolysis in adipose tissue, thereby making glucose and lipids available to the foetus. This complex system is monitored by a multitude of factors, including the body condition of the mother, the utero-placental blood flow and the expression and function of trophoblast nutrient transporters (Aye *et al.*, 2013). Maternal adiposity, as reflection of its nutritional status, is one of the main extrinsic factors programming nutrient partitioning and growth, development and function of the major foetal organ systems (Redmer *et al.*, 2004; Amdi *et al.*, 2014). Adipose tissue is a specialised endocrine and paracrine organ that modulates energy metabolism via secretion of circulating adipokines (such as leptin and adiponectin), which are involved in the regulation of body fatness and energy expenditure (Ahlsson *et al.*, 2013). Adiponectin and leptin are key modulators of insulin action and glucose metabolism; thus, they can be considered potential candidates for regulation of intrauterine foetal development. During pregnancy, leptin and adiponectin

participate in the process of insulin resistance with antagonistic actions: leptin increases insulin resistance whereas adiponectin increases insulin sensitivity. Serum leptin concentrations have been demonstrated to be positively correlated with backfat depth in sows (De Rensis *et al.*, 2005). High leptin levels from the end of mid pregnancy to farrowing are reported in breeding sows where gestational hyperphagia is managed through dietary strategies (Saleri *et al.*, 2015). The increase of maternal leptin levels during pregnancy may also be a consequence of placental production. The expression of the short leptin receptor form in the sows' placental tissue at farrowing has been observed (Saleri *et al.*, 2015).

Inverse correlations between adiponectin and fat mass and between adiponectin and body mass index have been reported (Skvarca *et al.*, 2013). It has been shown that in pregnant women longitudinal changes in serum adiponectin concentrations occurs; lowest levels were seen in late pregnancy when insulin levels rise (Fuglsang *et al.*, 2006). An inverse correlation between levels of maternal adiponectin and insulin resistance as well as rates of endogenous glucose production has been observed (Ahlsson *et al.*, 2013).

The purpose of this study was to assess the trend of leptin and adiponectin plasma concentrations in pregnant sows with different backfat depth at mating-time. We hypothesised that the interaction between maternal backfat and adipokines constitutes one of the mechanisms behind the offspring growth.

Material and Methods

The study was carried out in compliance with Italian law (Lgs. D. 26/2014) on animal experiments and all animals were housed in accordance with EC Directive 2010/63/UE on animal husbandry.

Animals

Based on backfat **(BF)** depth at the end of lactation and parity order, 48 sows Large White x Landrace were recruited and Low Fat (**LF**, 11.60 ± 1.51 mm; n=24) and High Fat (**HF**, 18.20 ± 2.05 mm; n=24) groups were formed. Backfat depth was measured by a single operator on both left and right side on standing sows using an ultrasound scanner and the mean value was utilised (Lean-meater, Renco Corporation, Minneapolis, Minnesota, USA) (Maes *et al.*, 2004). Parity order was 4.0 ± 2.1 and 3.6 ± 1.2 for LF and HF groups, respectively. Sows were identified and moved in individual pens in the same gestation room. At onset of standing oestrus (4.75 ± 0.95 days after the end of lactation), they were artificially inseminated two times, at day 0 of gestation and again 24 h later using, in both cases, semen pooled from five Large White x Duroc boars. During gestation and transition period (from day 110 of gestation to day 3 after farrowing) all sows received the same standard diets offered twice a day at 0800 h and 1600 h (Table 1). From 0 to day 10 after mating sows were fed 1.5 kg per day of the gestation diet. The same diet was administered at a dose of 2 kg per day until day 28 when the sows were evaluated with ultrasound examination (Aloka SSD 500®, Hitachi Medical System SpA, Milano, Italy; linear probe 5.0 MHz). One of the sows belonging to the LF group was not pregnant and thus, it was removed from the study. From day 29 until day 109 of gestation, sows were housed in a group housing system and fed 2.5 kg/sow per day of the gestation diet. At day 110 of gestation, sows were moved to individual farrowing pens and fed 2.5 kg per day of the transition diet until three days after farrowing. Parturition was induced on day 113 of gestation by deep intramuscular injection of 0.7 ml per head of cloprostenol sodium (PGF VEYX ®, Veyx-Pharma GmbH, Söhreweg, Germany). The farrowing took place on day 114 of gestation for all

sows. Floor heating and an infrared lamp were used to create a microclimate for the piglets. After 24 h from birth, litter sizes were standardised to 12 ± 2 pigs by cross-fostering within groups. Access to water was always available on an *ad libitum* basis. Gestation took place in a temperature-controlled room with an average ambient temperature of 20°C. The day of farrowing and in the next 72 hours the ambient temperature was raised up to 23°C.

Measurements

The BF was evaluated at days 0, 28, 85 and 113 of gestation. In the same time-points, blood samples from sows were collected using jugular venepuncture in 10-ml vacutainer tubes with lithium heparin before the morning meal. Samples were immediately centrifuged (1327 × **g** for 10 min) and plasma was collected and stored at −20°C until analysis.

Number of total born, born alive, dead within the first 24 hours of life and gender were recorded. Piglets were individually weighed (electronic dynamometer; Wunder Sa. Bi. srl, Trezzo sull' Adda -MI, Italy) within the first 2 hours of life (**BW0**) and 24 h after birth of first born piglet (**BW24**). Body mass index (**BMI**) and ponderal index (**PI**) of all piglets were calculated from the crown-rump length and birthweight (Baxter *et al.*, 2008). Body temperature was assessed at birth and at 24 h using an infrared ear thermometer (accuracy 0.2°C) (GIMA, Gessate- MI, Italy). Before suckling colostrum, six piglets born alive per litter - three males and three females- were held in dorsal recumbency and 5 ml of blood from external jugular vein into vacutainer tubes with lithium heparin were taken. The blood samples were processed in the same way as above mentioned for sows.

Diets and blood analyses

Proximate analyses of diets were performed according to the Commission Regulation (EC) 152/2009 laying down the methods of sampling and analysis for the official control of feed (Annex III).

Adiponectin plasma concentration, was determined using a species specific commercial kit (Porcine Adiponectin ELISA, BioVendor, Brno, Czech Republic). The sensitivity of the method was 0.03 ng/ml and the variability coefficients within and among samples were 6.7% and 8.2%, respectively. Leptin plasma concentration was assessed using a commercial kit (Multispecies Leptin RIA- Linco Research, St. Louis, MO, USA). The sensitivity of the method was 100 pg/ml and the variability coefficients within and among samples were 4.7% and 9.1%, respectively. Plasma IGF-I content was evaluated using a multispecies IGF-I ELISA (Alpco Diagnostic, Salem NH, USA), according to manufacturer's instructions. The intra- and interassay coefficients of variation were 7.8% and 5.3 %, respectively. The minimal detection limit was 30 pg/ml.

Statistical analyses

Data on litter size were processed by ANOVA (SAS 9.4, SAS Inst. Inc., Cary, NC, 2013), according to a model including the group of sows (LF, HF) as a fixed factor and the parity order as a covariate. Data on piglets were processed by ANOVA, according to a model that included the fixed factors of the group of sows (LF, HF) and sex (M, F), and the random factor of sow within the group. The data recorded on sows were analysed according to a repeated measure model, including the group (LF, HF) as a fixed factor and, as a covariate, the parity order. Time was included as the repeated statement, and interaction between time and group was considered. Residual were checked for normality by means of PROC UNIVARIATE. When not normally

distributed, data were log transformed. Based on birthweight, piglets were divided in four percentiles classes (25^{th}, 50^{th}, 75^{th} and 95^{th}) by means of PROC UNIVARIATE. The chi square test was applied to the observed and expected frequencies of piglets, as categorised in percentiles weight classes, in relation to the adiposity of sows. Mortality per litter was evaluated applying the chi square test. The significance level was set at $P \leq 0.05$.

Results

Sows parameters

Data on maternal adiposity changes during gestation are reported in Table 2. The differences in backfat depth observed at mating between LF and HF groups persist for the entire pregnancy ($P < 0.05$). During pregnancy, no differences in backfat depth gain were observed between groups ($P > 0.05$). Adiponectin and leptin plasma concentrations and adiponectin-leptin ratio are summarised in Figure 1. Adiponectin concentration showed a decrease from 0 to 113 days of gestation ($P < 0.05$): at these point times, mean values (± SD) were 195.85 ± 21.5 and 61.67 ± 7.4 µg/ml for LF group and 98.19 ± 10.5 and 19.87 ± 2.4 µg/ml for HF group, respectively (Figure 1A). As compared to LF group, plasma adiponectin was lower in HF group at mating, at day 85 of gestation ($P < 0.05$) and at farrowing ($P = 0.05$) (Figure 1A). After the first month of gestation plasma leptin increased in both groups to reach the highest concentration at farrowing ($P < 0.05$). No differences between groups were observed in plasma leptin throughout the pregnancy ($P > 0.05$). At conception, 85 and 113 days of gestation, the adiponectin-leptin ratio was lower in HF than in LF group ($P < 0.05$) (Figure 1B).

Newborn piglet's performance and hormone plasma levels

The effects of maternal BF depth on piglet's performance are reported in Table 3. No differences were observed in respect to total born and born alive number between groups (P >0.05). Conversely, maternal adiposity affected foetal growth; piglets born from HF sows showed a higher BW0 (+ 7%; P <0.014) and BW24 (+ 4%; P <0.001) than those from LF sows. In addition, significant differences in percentile weight grouping was observed (P <0.001). On total born per group, 14% of piglets in the LF and 7% in the HF group revealed a weight falling in the 25th percentile (≤ 1kg). Anthropometric parameters (BMI, PI) were not affected by maternal BF depth (P >0.05). In the first 24 h of life, the thermoregulatory ability was the same in both groups (P >0.05). Piglet's mortality from 0 to 24 h of life was 13% and 3% for LF and HF groups, respectively (P =0.035). Plasma adiponectin and leptin levels were not affected by maternal adiposity (P >0.05) (Table 4). Higher IGF-I plasma levels were recorded in piglets born from HF than LF sows (P <0.001).

Discussion

Pregnancy is a dynamic anabolic state during which nutritional needs increase due to the growing foetus and the development of associated maternal tissues. Pregnancy-induced changes in body weight and fat deposition are physiological events of maternal adaptation, linked to the hormonal pregnancy changes (i.e. progesterone, prolactin and cortisol) (Saleri *et al.*, 2015). A previous research reported that maternal backfat depth at mating had a greater influence on offspring growth, than feed level during gestation (Amdi *et al.*, 2014). In this study, we focused on the endocrine role of maternal adipose tissue during pregnancy, to investigate how a different adiposity at mating could influence the evolution of pregnancy both in terms of maternal hormone

levels and weight and size of the newborn piglets. Firstly, the increase in maternal fat stores during pregnancy was the same in both groups, but sows with the lower backfat depth at mating gave birth to lighter piglets. The percentage of piglets weighing less than 1 kg was double in LF than HF group. This result could suggest an intrauterine growth restriction in piglets born from LF sows, although the thermoregulatory capacity and anthropometric parameters were found to be adequate in all piglets (Amdi *et al.*, 2013). It is known that foetal glucose/insulin/insulin-like growth factor axis is the main driver of growth (Hellström *et al.*, 2016). In the foetus, growth is directly modulated by IGF system and it is not regulated by growth hormone. Insulin-like growth factor-I and -II are expressed in foetal tissue only until birth. Insulin-like growth factor-II expression is more extensive in foetal tissues than IGF-I from mid to late gestation in rodents and humans (Randhawa and Cohen, 2005). It has been shown that a poor maternal body condition at conception and in early pregnancy is signaled to the foetus which reacts by promoting peripheral glucose utilization, essential for brain and heart, and by reducing the demand for amino acids for growth, thereby to maintain energy supply at the expense of growth (Bloomfield *et al.*, 2013). After birth, GH stimulates IGF-I secretion with a quick increase of IGF-I blood levels. In our study, lower IGF-I values were observed in piglets born from LF compared to HF group. Energy balance is modulated also by adipose tissue hormones, i.e adipokines, which are acting to regulate insulin sensitivity, appetite and lipid metabolism (Ahlsson *et al.*, 2013). In both groups, the most abundant adipokines produced by adipose tissue, leptin and adiponectin, showed an inverse trend during pregnancy. Physiologically, decreased adiponectin and increased leptin concentrations are associated with insulin-resistant state (Ahlsson *et al.*, 2013). However, it is known that the regulation of maternal adiponectin and leptin during pregnancy becomes very complex. The high levels of

leptin in pregnancy are in agreement with a mechanism of resistance to central leptin action previously reported in swine (Saleri *et al.*, 2015), in humans and mice (Trujillo *et al.*, 2011). Production and regulation by non-adipose tissue, i.e placenta, contribute to this increase in pregnant sows. Probably, the increase in maternal leptin enhances the mobilization of maternal fat stores to increase the transplacental transfer of lipids to the foetus during the latter stages of pregnancy (Walsh *et al.*, 2014). In isolated rat adipocytes, leptin inhibits accumulation of lipids by increasing the turnover of triglycerides, inhibiting basal and insulin-stimulated *de novo* lipogenesis, but stimulating oxidation of glucose and free fatty acids (Harris, 2014). In humans, maternal leptin concentration was not associated with infant birthweight (Misra *et al.*, 2013). Similarly, in our study, leptin levels in sows and piglets do not differ between groups, even though differences in birthweight of piglets were observed. These results support that leptin may plays a permissive role in foetal growth. In addition, it has been shown that leptin deficiency in women is not associated with major abnormalities (Christou *et al.*, 2002). To clarify the leptin role, it is important to take into account also the adiponectin role. The strict link between adiponectin and leptin is underlined by the plasma adiponectin to leptin ratio (A/L ratio) which has been proposed as a better marker for insulin resistance in pregnancy than leptin or adiponectin alone (Skvarca *et al.*, 2013). Our data showed that the A/L ratio is lower in HF than LF group, as evidence that HF sows could have a better ability to provide adequate carbohydrate availability for the fast-growing foetus. The lower adiponectin levels detected in HF than LF group match the higher birthweight of offspring. Therefore, adiponectin may be an important player in the mechanism by which maternal energy is stored in fat mass leading the pattern of foetal growth (Zhang et al., 2016). Since we detected the same trend in the adiponectin release in both groups, we hypothesised that adiponectin in pregnant sows

is involved in the management of mother's energy resources, regardless their backfat depth. In the concept of energy balance, we can see a complex of mechanisms involving nutrient availability, growth and immunity. In this sense, adiponectin role is also connected to the success of pregnancy: a crucial aspect is the maternal immune tolerance of the foetus. Maternal immune responses regulate the early key events of pregnancy (i.e., implantation, angiogenesis, and vascular remodeling) and abnormalities in these early events are associated with foetuses' intrauterine growth restriction and survival (Morelli *et al.*, 2015). It is known that intrauterine growth restriction results in significant perinatal and long-term complications, including increased neonatal mortality and morbidity. We may hypothesise that also in sow, adiponectin might play an active role in this mechanism. In support of this hypothesis, recently the presence of adiponectin and its receptors was demonstrated in the porcine uteri, conceptuses, and trophoblasts during early pregnancy (Smolinska *et al.*, 2012). In *vitro* studies, it was showed that adiponectin arouses pro-inflammatory cytokine production in human trophoblasts (i.e., IL-1β and IL-8) and placenta (i.e., IL-1β, IL-6 and TNFα) and thus it may be detrimental to the initiation and progression of pregnancy (Lappas *et al.*, 2005; McDonald and Wolfe, 2011). In our study, the maternal immune responses did not influence the litter number. However, the different plasma levels of adiponectin observed between the groups of sows was associated with different weight of the piglets at birth. All together, these findings suggest a critical role of adipokines, i.e leptin and adiponectin, in modulating maternal energy balance in different stage of pregnancy. Keeping an eye on the new findings on the endocrine function of adipose tissue, we propose that the adiposity at mating time can be used as an effective indicator to optimise the reproduction efficiency of sow. Endocrinology of maternal

adipose tissue and its influence on the offspring request further studies to elucidate the pathways involved in foetus growth and its adaptation to intrauterine environment.

Acknowledgements

The authors would like to thank Dr P. Benaglia for technical assistance. The authors declare that there are no conflicts of interest.

References

Ahlsson F, Diderholm B, Ewald U, Jonsson B, Forslund A, Stridsberg M and Gustafsson J 2013. Adipokines and their relation to maternal energy substrate production, insulin resistance and fetal size. European Journal of Obstetrics & Gynecology and Reproductive Biology 168, 26-29.

Amdi C, Giblin L, Ryan T, Stickland NC and Lawlor PG 2014. Maternal backfat depth in gestating sows has a greater influence on offspring growth and carcass lean yield than maternal feed allocation during gestation. Animal 8, 236-244.

Amdi C, Krogh U, Flummer C, Oksbjerg N, Hansen CF and Theil PK 2013. Intrauterine growth restricted piglets defined by their head shape ingest insufficient amounts of colostrum. Journal of Animal Science 91, 5605-5613.

Aye IL, Powell TL and Jansson T 2013. Adiponectin – The missing Link between maternal adiposity, placental transport and fetal growth? Placenta 34, (suppl 34) S40-S45.

Baxter EM, Jarvis S, D'Eath RB, Ross DW, Robson SK, Farish M, Nevison IM, Lawrence AB and Edwards SA 2008. Investigating the behavioural and physiological indicators of neonatal survival in pigs. Theriogenology 69, 773-783.

Bloomfield FH, Spiroski A and Harding JE 2013. Fetal growth factors and fetal nutrition. Seminars in Fetal & Neonatal Medicine 18, 118-123.

Christou H, Serdy S and Mantzoros CS 2002. Leptin in relation to growth and developmental processes in the fetus. Seminars in Reproductive Medicine 20, 123-129.

De Rensis F, Superchi P and Kirkwood RN 2005. Relationships between backfat depth and plasma leptin during lactation and sow reproductive performance after weaning. Animal Reproduction Science 90, 95-100.

Fuglsang J, Skjaerbaek C, Frystyk J, Flyvbjerg A and Ovesen P 2006. A longitudinal study of serum adiponectin during normal pregnancy. British Journal of Obstetrics and Gynaecology 113, 110-113.

Harris RBS 2014. Direct and indirect effects of leptin on adipocyte metabolism. Biochimica et Biophysica Acta 1842, 414-423.

Hellström A, Ley D, Hansen-Pupp I, Hallberg B, Löfqvist C, van Marter L, van Weissenbruch M, Ramenghi LA, Beardsall K, Dunger D, Hård AL and Smith LEI 2016. Insulin-like growth factor 1 has multisystem effects on foetal and preterm infant development. Acta Pædiatrica 105, 576-586.

Jansson T and Powell TL 2006. Human placental transport in altered fetal growth: does the placenta function as a nutrient sensor? Placenta 27, (suppl.A) S91-S97.

Lappas M, Permezel M and Rice GE 2005. Leptin and adiponectin stimulate the release of proinflammatory cytokines and prostaglandins from human placenta and maternal adipose tissue via nuclear factor-κB, peroxisomal proliferator-activated receptor-y and extracellularly regulated kinase ½. Endocrinology 146, 3334-3342.

Maes DGD, Janssens GPJ, Delputte P, Lammertyn A and de Kruif A 2004. Back fat measurements in sows from three commercial pig herds: relationship with reproductive efficiency and correlation with visual body condition scores. Livestock Production Science 91, 57-67.

McDonald EA and Wolfe MW 2011. The proinflammatory role of adiponectin at the maternal-fetal interface. American Journal of Reproductive Immunology 66, 128-136.

Misra VK, Straughen JK and Trudeau S 2013. Maternal serum leptin during pregnancy and infant birth weight: the influence of maternal overweight and obesity. Obesity 21, 1064-1069.

353 Morelli S, Mandal M, Goldsmith LT, Kashani BN and Ponzio NM 2015. The maternal immune
354 system during pregnancy and its influence on fetal development. Research and
355 Reports in Biology 6, 171-189.
356 Noblet J and Perez JM 1993. Prediction of digestibility of nutrients and energy values of pig
357 diets from chemical analysis. Journal of Animal Science 71, 3389–3398.
358 Père MC, Etienne M and Dourmad JY 2000. Adaptations of glucose metabolism in multiparous
359 sows: Effects of pregnancy and feeding level. Journal of Animal Science 78, 2933-
360 2941.
361 Randhawa R and Cohen P 2005. The role of the insulin-like growth factor system in prenatal
362 growth. Molecular Genetics and Metabolism 86, 84-90.
363 Redmer DA, Wallace JM and Reynolds LP 2004. Effect of nutrient intake during pregnancy on
364 fetal and placental growth and vascular development. Domestic Animal Endocrinology
365 27, 199-217.
366 Saleri R, Sabbioni A, Cavalli V and Superchi P 2015. Monitoring blood plasma leptin and
367 lactogenic hormones in pregnant sows. Animal 9, 629-634.
368 Skvarca A, Tomazic M, Blagus R, Krhin B and Janez A 2013. Adiponectin/leptin ratio and
369 insulin resistance in pregnancy. Journal of International Medical Research 41, 123-128.
370 Smolinska N, Maleszka A, Dobrzyn K, Kiezun M, Szeszko C and Kaminski T 2012. Expression
371 of adiponectin and adiponectin receptors 1 and 2 in the porcine uterus, conceptus, and
372 trophoblast during early pregnancy. Theriogenology 82, 951-965.
373 Trujillo ML, Spuch C, Carro E and Señarís R 2011. Hyperphagia and central mechanisms for
374 leptin resistance during pregnancy. Endocrinology 152, 1355-1365.
375 Walsh JM, Byrne J, Mahony RM, Foley ME and McAuliffe FM 2014. Leptin, fetal growth and
376 insulin resistance in non-diabetic pregnancies. Early Human Development 90, 271-274.
377 Zhang Z, Lu Q, Huang J, Jiao C, Huang S and Mao L 2016. Maternal and cord blood
378 adiponectin levels in relation to post-natal body size in infants in the first year of life: a
379 prospective study. BMC Pregnancy and Childbirth 16,189-195.

380 **Table 1** *Ingredients and chemical analysis of diets (on air dry basis g/kg as fed)*

	Gestation diet (g/kg)	Transition diet (g/kg)
Ingredients:		
Wheat bran	240	--
Barley	230	267
Corn	180	310
Unmolassed sugar-beet pulp	147	150
Sunflower meal	137	--
Soybean meal	--	135
Fish meal	--	46
Soybean protein	--	10
Soybean oil	15	20
Dextrose	--	40
Rapeseed meal	20	--
Ground limestone	15	--
Dicalcium phosphate	10	15
Sodium chloride	4	4
Lysine HCl	0.5	1
Vitamins and minerals[1]	1.5	2.0
Chemical analysis:		
Dry matter (g/kg)	878	872
CP (g/kg)	141.2	153.6
Crude fibre (g/kg)	82.2	58.4
Crude fat (g/kg)	38.2	42.1
Digestible energy (MJ/kg)[2]	12.9	13.5

381 [1] Supplied per for kg of diet : Cu: 40 mg, Zn: 80 mg Fe: 150 mg, Se: 0.2 mg, I: 0.6 mg, Mn: 50 mg,
382 vitamin A: 12,000 IU, vitamin D3: 1,000 IU, vitamin E: 100 IU, vitamin K: 20 mg, vitamin B12: 55 µg,
383 vitamin B1: 2 mg, vitamin B2: 5 mg, vitamin B6: 1.5 mg, nicotinic acid: 12 mg, pantothenic acid: 10 mg,
384 folic acid: 5 mg, choline chloride: 500 mg, biotin: 200 µg.

385 [2] According to the equation proposed by Noblet and Perez (1993).

386

Table 2 *Pregnancy changes in backfat depth in sows with Low Fat or High Fat at the end of the previous lactation (Least squares mean values ± SEM).*

	Groups			
	LF	HF	SEM	*P* - value
BF depth (mm)				
day of mating	11.9	17.1	1.69	<0.001
day 28 of gestation	12.4	17.3	1.77	0.003
day 85 of gestation	13.9	18.9	1.47	0.013
day 113 of gestation	14.6	19.7	1.47	<0.001
Δ BF (mating – day 113 of gestation) (mm)	2.7	2.5	0.48	0.358

LF (Low Fat; 11.6 ± 1.5 mm) and HF (High Fat; 18.2 ± 2.0 mm); BF= backfat

Table 3 *Effects of maternal backfat depth on anthropometric parameters and growth performance of piglets (Least squares mean values ± SEM).*

	Groups			
	LF	HF	SEM	*P* – value
Total born (n.)	17.2	15.7	3.16	0.327
Born alive (n.)	15.1	14.1	1.94	0.182
BW0 (g)	1244	1334	278	0.014
BW24 (g)	1310	1360	85	<0.001
BMI (kg/m^2)	20.87	20.63	2.091	0.384
PI (kg/m^3)	83.98	84.44	6.739	0.599
Body temperature (°C)				
at birth	37.92	37.78	0.947	0.267
at 24 h	38.75	38.71	0.495	0.608

LF (low fat: 11.6 ± 1.5 mm) and HF (high fat: 18.2 ± 2.0 mm) are referred to backfat depth recorded by sows at the end of the previous lactation; BW0= Birthweight; BW24= Body weight at 24 h of life; BMI= body mass index; PI= ponderal index

Table 4 *Plasma adiponectin, leptin and IGF-I in newborn piglets in relation to backfat depth of sows (Least squares mean values ± SEM).*

	Groups			
	LF	HF	SEM	*P* – value
Adiponectin (µg/ml)	14.3	14.9	1.66	0.339
Leptin (ng/ml)	3.0	3.3	0.57	0.096
IGF-I (pg/ml)	4.4	5.6	1.00	< 0.001

LF (low fat: 11.6 ± 1.5 mm) and HF (high fat: 18.2 ± 2.0 mm) are referred to backfat depth recorded by sows at the end of the previous lactation

Figure caption

Figure 1 Trend of adiponectin and leptin (A) and adiponectin/leptin ratio (B) during gestation, in relation to backfat depth of sows. Blood sampling period started at the day of mating (0) and ended at the day 113 of gestation. Error bars indicate standard deviation. Differences between groups within sampling time are labelled * ($P<0.05$). Differences among sampling time within groups are labelled a,b,c, ($P<0.05$).

Figure 1

Click here to download Figure Figura 1 gennaio TIF.tif