Department of Production Animal Medicine
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Challenges of hyper-prolificacy in the pig: colostrum and gut microbiota

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DOCTORAL DISSERTATION

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To Kothon, Kabbo and Golpo

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List of original publications

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III. Hasan, S., Saha, S., Junnikkala, S., Orro, T., Peltoniemi, O., Oliviero, C. (2018). Late gestation diet supplementation of resin acid-enriched composition increases sow colostrum immunoglobulin G content, piglet colostrum intake and improve sow gut microbiota. Animal, 13, 1599-1606.

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The publications are referred to in the text by their Roman numerals.

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Abstract

In modern pig production there has been a steady increase in the litter size during recent decades. Large litters represent a major challenge for the sow, increase the farrowing duration and compromise sow welfare by prolonging this stressful process. Moreover, the continuous increase in litter size is a major cause of pre-weaning piglet mortality by increasing the proportion of low birth weight piglets, which are less vital and have reduced colostrum intake. Approximately 30% of hyper-prolific sows produce insufficient colostrum for their piglets. Colostrum plays an essential role in the health, survival and growth of piglets by providing energy, immunoglobulins, growth factors and many other bioactive components. Both colostrum yield and its composition are highly variable among sows, yet mechanisms and factors that regulate colostrogenesis are not fully understood.

The aim of this study was to evaluate sow colostrum IgG concentration on farm using a Brix refractometer, to thus improve the management of neonatal piglets immediately after initiation of farrowing. We established colostrum evaluation criteria, to be used at herd level, by comparing the Brix results with those from ELISA. We aimed to investigate sow physiology around farrowing, acute phase protein (APP) response and their association with colostrum yield (CY), colostrum composition and piglet colostrum intake (CI). The impact of sow CY, colostrum composition and quality on piglet performance were also investigated. We also aimed to determine the effects of yeast hydrolysate (YD) and resin acid-enriched composition (RAC) inclusion in sows' gestation and lactation diets on CY, colostrum immunoglobulins, nutritional composition and subsequent litter performance. We also sought to determine the influence of these two feed additives on the taxonomic profile of the hindgut microbiota of sows. Additionally we aimed to determine whether changing the gut microbiota of sows influences the microbial colonization of piglets after birth.

There was a correlation between Brix refractometer measurement of colostrum and the corresponding IgG concentration measurements of ELISA (r = 0.63, P < 0.001). A classification of colostrum quality was suggested; low levels of IgG (14.5 ± 1.8 mg/ml) were recorded for colostrum samples with Brix readings below 20%. Borderline colostrum IgG content (43.8 ± 2.3 mg/ml) had Brix readings of 20% to 24%, adequate colostrum IgG content (50.7 ± 2.1 mg/ml) had Brix readings of 25% to 29% and very good IgG colostrum content (78.6 ± 8.4 mg/ml) had Brix readings >30%. Sow CY was positively correlated with plasma haptoglobin (Hp) (P = 0.029), number of live-born piglets (P < 0.01) and negatively correlated with farrowing duration (P = 0.01). Piglet CI was positively associated with piglet weight at birth (P < 0.001) and negatively associated with the number of live-born piglets in the litter (P < 0.001). Both piglet CI and birth weight were positively associated with piglet average daily gain (ADG) (P < 0.001). Risk for piglet death, or a piglet being treated with an antibiotic before weaning, increase with a decrease in sow back fat thickness at farrowing (P = 0.04). Similarly, we found that piglets of litters with low BW_B and low CI had a higher risk of death before weaning (P < 0.001). Piglets born from sows having lower levels of colostrum IgA and serum amyloid A (SAA) and high plasma progesterone at the end of farrowing had higher risk of neonatal diarrhea (P = 0.04; P = 0.05; P = 0.04). Piglets born from sows having higher back fat thickness at weaning had higher risk of developing weaning diarrhea (P = 0.02).

There was a significant increase in CY in sows fed with YD during gestation (P = 0.04) and a higher level of fat in their colostrum (P = 0.01). In RAC fed sows there was a significant increase in colostrum IgG content. Piglets weaning weights of RAC fed sows were higher in two trial herds. Inclusion of YD and RAC in gestation and lactation diet increased the abundance of beneficial and fermentative fecal bacteria (*Roseburia*, *Paraprevotella*, *Eubacterium*, *Romboutsia* and *Clostridium sensu stricto*) significantly (P < 0.01) while, opportunistic pathogens, especially Proteobacteria, were suppressed. In addition, piglets from the sows fed YD had more beneficial microbial populations with higher diversity and fewer opportunistic pathogens at one week of age. However, feeding YD,

higher CY, colostrum composition and piglet birth weight were all correlated with specific sow gut microbiota.

In conclusion, Brix measurement of a sow's fresh colostrum is an inexpensive, rapid and sufficiently accurate method of estimating IgG concentration, providing indication of differentiation between good and poor IgG content of colostrum. Although colostrum is vital for piglet survival, both CY and composition are highly variable among sows. Sow body condition and physiological status around farrowing affect CY and colostrum immunoglobulin contents. Piglet survival and risk of death before weaning also depend on CI. Therefore, to support CY and CI, measures should be taken to ease the process of farrowing, increase piglet vitality and improve colostrum availability for piglets. Functional feed ingredients such as YD and RAC may increase colostrum availability, improve colostrum IgG and its energy content for neonate piglets, and also promote beneficial maternal microbial sources for neonates.

Yhteenveto

Viimeisten vuosikymmenten aikana pahnuekoko on kasvanut tasaisesti modernissa sianlihantuotannossa. Iso pahnuekoko on iso haaste emakolle, se hidastaa synnytystä joka aiheuttaa pitkittynyttä kipua heikentäen emakon hyvinvointia. Lisäksi jatkuva pahnuekoon kasvu pienentää syntyneiden porsaiden syntymäpainoa, mikä lisää vastasyntyneiden porsaiden kuolleisuutta. Pienet porsaat saavat myös vähemmän ternimaitoa ja niiden elinvoima on heikompi. Noin 30% korkeatuottoisista emakoista ei tuota riittävästi ternimaitoa porsailleen. Ternimaito on tärkeässä roolissa porsaan terveyden, eloon jäämisen ja kasvun kannalta, sillä se tuottaa energiaa, immunoglobuliineja, kasvutekijöitä ja monia täkritä biologisesti aktiivisia yhdisteitä. Sekä ternimaidon tuotanto ja sen koostumus vaihtelevat suuresti emakoiden välillä. Tästä huolimatta mekanismeja ja tekijöitä, jotka säätelevät ternimaidon synteesiä ei täysin tiedetä ja ymmärretä.

Tämän tutkimuksen tavoitteena oli arvioida ternimaidon laatua tilatasolla käyttäen Brix testiä, jotta vastasyntyneen porsaan ternimaitoon liittyvää hoitoa saataisiin parannettua välittömästi synnytyksen jälkeen. Me loimme ternimaidon laadun mittaamiseen tilatasolla käytettävät kriteerit vertaamalla Brix testien tuloksia laboratoriossa vakiintuneessa käytössä olleen ELISA – menetelmän tuloksiin. Tavoitteenamme oli myös tutkia emakon fysiologiaa synnytykseen liittyvää fysiologiaa, akuutin faasin reaktiota ja näiden yhteyttä ternimaidon laatuun, määrään ja saantiin. Emakon tuottaman ternimaidon määrän, koostumuksen ja laadun vaikutus porsaiden kasvuun oli myös keskeisiä tutkimustavoitteita. Lisäksi tavoitteenamme oli tutkia hiiva-hydrosulaatilla (YD) ja resiinihapolla (RAC) rikastettujen emakoiden tiineys- ja imetysrehujen vaikutusta ternimaidon määrään, immunoglobuliini - pitoisuuteen, ravitsemukselliseen koostumukseen ja pahnueen imetyksen aikaiseen kasvuun. Me myös tavoittelimme näiden kahden rehu – lisäaineen vaikutusta paksusuolen mikrobipopulaatioiden koostumukseen. Lisäksi tavoitteenamme oli selvittää miten emakon suoliston bakteeri-

populaatioiden muutokset heijastuvat porsaiden suoliston kolonisaatioon syntymän jälkeen.

Osoitimme yhteyden emakon ternimaidon Brix – testitulosten ja vastaavien vakiintuneella ELISA – menetelmällä tehtyjen IgG – pitoisuuksien välillä ($r = 0.63$, $P < 0.001$). Mittaustulostemme perusteella ehdotimme ternimaidon koostumukselle seuraavaa laatu – luokitusta: matala IgG – tasoa (alle 14.5 ± 1.8 mg/ml) vastasi Brix testin lukemia alle 20%. Kohtalaiseksi laatu luokiteltiin matalan IgG tason ylittävillä lukemilla (43.8 ± 2.3 mg/ml), mikä vastasi Brix – testin leukemia välillä 20 – 24 %. Hyväksi ternimaidon IgG – tasoksi määriteltiin 50.7 ± 2.1 mg/ml, mikä vastasi Brix – testin leukemia 25 – 29%. Erinomaiseksi luokiteltiin IgG – pitoisuus tasolla 78.6 ± 8.4 mg/ml, mikä vastasi Brix – testin leukemia päälle 30%. Emakoiden ternimaidon määrä korreloi positiivisesti plasman haptoglobiini – pitoisuuteen (HP, $P= 0.029$), syntyneiden porsaiden määrään ($P<0.01$) ja negatiivisesti synnytyksen kestoon ($P=0.01$). Porsaiden ternimaidon saannilla ja syntymäpainolla oli positiivinen yhteys ($P<0.001$), kun taas ternimaidon saannilla ja pahnuekoolla oli negatiivinen yhteys ($P<0.001$). Sekä ternimaidon saanti että syntymäpaino olivat positiivisessa yhteydessä porsaiden päiväkasvuun ($P<0.001$). Sekä porsaan ennen vieroitusta tapahtuvan kuoleman että antibioottihoidon riskin todennäköisyys kasvavat emakon synnytyksen yhteydessä mitatun selän rasvakerroksen paksuuden pienentyessä ($P=0.04$). Samoin havaitsimme, että syntymäpainoltaan alhaisten pahnueiden porsaat, jotka saivat vain vähän ternimaitoa, olivat alttiita kuolemaan ennen vieroitusta ($P<0.001$). Porsaat, jotka kuuluivat emakoille, joilla oli alhainen ternimaidon IgA – pitoisuus ja seerumin amyloidi A (SAA) sekä korkea progesteronipitoisuus synnytyksen lopussa, olivat alttiimpia saamaan porsasripulin ($P=0.04$; $P=0.05$; $P=0.04$). Lisäksi havaitsimme, että porsaat, joiden emällä selän rasvakerros oli paksu vieroituksen yhteydessä, olivat alttiimpia saamaan vieroitusripulin ($P=0.02$).

Havaitsimme myös, että tiineyden aikana hiiva-hydrosulaatilla (YD) rikastetuilla rehuilla ruokitut emakot tuottivat enemmän ternimaitoa (P=0.04), jossa todettiin myös olevan enemmän rasvaa (P=0.01). Emakoilla, jotka ruokittiin rikastetulla resiinihapolla (RAC) todettiin korkeammat IgG – pitoisuudet. Resiinihapon lisääminen emakon rehuun lisäsi myös porsaiden vieroituspainoja kahdessa koeasetelmassamme. Sekä hiiva – hyrosulaatin että resiinihapon lisääminen tiineyden ja imetyksen aikaiseen emakon rehuun lisäsi suotuisten ja fermentatiivisten bakteerikantojen suhteellista osuutta bakteeri – populaatioissa merkittävästi (Roseburia, Paraprevotella, Eubacterium, Romboutsia and Clostridium sensu stricto; $P < 0.01$). Toisaalta taas opportunistien patogeenisten ja etenkin Proteobakteeri – lajin osuus laski. Lisäksi hiiva – hydosulaatin lisääminen emakon rehuun lisäsi imevien porsaiden suoliston suotuisten bakteeri – populaatioiden osuutta, joiden monimuotoisuus oli suurempi sekä vähensi opportunistien patogeenisten bakteeri – populaatioiden osuutta yhden viikon iässä. Hiiva – hydrosulaatin lisääminen, korkea ternimaidon määrä, ternimaidon koostumus ja porsaan syntymäpaino kuitenkin korreloivat tiettyihin emakon suoliston bakteeri – populaatioihin.

Yhteenvetona Brix – mittaukset tuoreesta emakon ternimaidosta on halpa, nopea ja riittävän tarkka menetelmä IgG – pitoisuuden määrittämiseksi, mikä auttaa erottamaan hyvälaatuisen ternimaidon huonolaatuisesta. Vaikka ternimaidon saanti on elintärkeää vastasyntyneen porsaan selviytymiselle, sekä ternimaidon määrä että laatu vaihtelevat suuresti emakoiden välillä. Sekä emakon kuntoluokka että fysiologinen tila synnytyksen yhteydessä vaikuttavat ternimaidon laatuun. Vastasyntyneen porsaan riski kuolla on vahvasti sidoksissa ternimaidon saantiin. Siksi on tärkeää tukea sekä emakon tuottaman ternimaidon määrää että porsaan ternimaidon saantia hoidollisin keinoin. Hoidollisin keinoin pitäisi myös synnytysprosessia, parantaa porsaiden elinvoimaa ja ternimaidon saatavuutta. Funktionaaliset rehun lisäaineet, kuten hiiva – hydrosulaatti ja resiinihappo, saattavat lisätä ternimaidon riittoisuutta, parantaa ternimaidon laatua (IgG) ja

energiasisältöä vastasyntyneille porsaille. Lisäksi nämä rehun lisäaineet tukevat suotuisten bakteeri - populaatioiden siirtymistä imeville porsaille.

1. Introduction and Review of Literature

1.1 General introduction

During recent decades there has been a steady increase in litter size in commercial pig production. This has resulted in the hyper-prolific sow being able to wean up to 31.3 pigs/year (Lavery et al., 2019). However, the increasing number of piglets in a litter represents a major challenge for sow physiology during pregnancy, at parturition and during lactation. Increase in litter size can lengthen the farrowing duration, increase duration of this painful process, inflame the uterus and increase the risk for retained placentas (Björkman et al., 2017; Ison et al., 2018; Kaiser et al., 2018). Large litters also have a direct impact on piglets at birth. The higher the number of piglets born in a litter, the lower the piglet birth weight and the higher the variation in piglet birth weight within the litter (Quesnel et al., 2008; Akdag et al., 2009; Beaulieu et al., 2010; Matheson et al., 2018). The greater the number of piglets born than there are available teats on the sow's udder, the lower the birth weight and the greater the birth weight variation, all of which increase the piglets' competition for colostrum intake (Declerck et al., 2017). Similarly, a lower birth weight and a long farrowing duration are associated with lower piglet vitality at birth, which can delay access to the udder (Hoy et al., 1994; Islas-Fabila et al., 2018). Unlike for milk production, the ability of the sow to produce colostrum does not improve with an increase in litter size (Le Dividich et al., 2005; Devillers et al., 2007; Foisnet et al., 2010; Quesnel et al., 2012). Therefore, regardless of the final causation factors (crushing, diarrhea), early piglet death is mainly due to the low consumption of colostrum (Le Dividich et al., 2005; Decaluwé et al., 2014). Colostrum has different essential roles for newborn piglets, providing a source of energy necessary for body thermoregulation and growth (Le Dividich et al., 2005; Herpin et al., 2005), passive immunity for protection against pathogens (Rooke and Bland, 2002), and growth factors that stimulate intestinal growth and maturation (Xu et al., 2002). Colostrum yield (CY) is

highly variable among sows and can be affected by factors such as feeding, genetics, management, environmental traits, sow health, the process of farrowing and litter characteristics (Quesnel et al., 2012). Studies suggested that approximately 30% of the sows produce insufficient colostrum for their litters (Foisnet et al., 2010; Quesnel et al., 2012; Decaluwé et al., 2013). With continuous increase in litter size, insufficient CY can be considered to be one of the major causes of neonatal piglet mortality in commercial pig production. Therefore, increasing the CY and ensuring sufficient colostrum intake by the piglets represent major challenges in modern pig production.

1.2 Colostrum yield (CY) in sows

Colostrum is the first secretion of the mammary gland, which is synthesized during parturition and can be obtained already a few hours before parturition. It is characterized by a high concentration of immunoglobulins (Ig), and contains lower concentrations of lactose and lipids than milk (Quesnel et al., 2015). Considering variations over time in colostrum composition, colostrum production ends between 12 and 24 h post-partum in most sows and beyond 24 h in some sows (Quesnel et al., 2012). Colostrum is freely available for 12 h, and then suckling behavior progressively evolves towards a cyclic suckling pattern (Quesnel et al., 2012). After 24-36 h post-partum colostrum is gradually replaced by the milk (Klobasa et al., 1987). A strong decrease in the immunoglobulin (Ig) content and an increase in lactose and fat are the main indicators of the switch from colostrum to milk (Quesnel et al., 2012). The CY is highly variable among sows (Quesnel et al., 2012). Colostrum yield ranges between 0.8 and 4.8 kg, with an average between 3.3 and 3.7 kg (Devillers et al., 2007, Foisnet et al., 2010, Quesnel, 2011). However, colostrum yield estimated by Theil et al. (2014a) ranged from 2.8 to 8.5 kg, with an average of 6.0 kg. It is challenging to measure the CY in sows, limiting studies related to the piglet colostrum intake (CI) and CY in sows, despite the importance of colostrum in modern pig production.

1.2.1 Colostrum yield measurement methods

Different measurement methods were developed to estimate piglet colostrum intake. One of the most frequently used methods is the prediction equation developed by Devillers et al. (2004), estimating the weight of all the piglets at birth and 24 h after birth of the first-born piglet. This prediction equation was established using a model with bottle-fed piglets, and it can underestimate the actual colostrum intake due to bottle-fed piglets likely being less physically active. The deuterium oxide dilution (DO) technique is considered to be the gold standard to estimate more accurately colostrum intake by piglets (Theil et al., 2014a; Theil et al., 2014b). This method quantifies the water intake from colostrum, converting it into colostrum intake by accounting for the colostrum's chemical composition. However, the technique is relatively expensive and requires considerable labor. Recently, Theil at al. (2014a) developed a prediction equation for colostrum yield based on measured piglet colostrum intake by the DO technique. The equation predicts colostrum intake using piglet birth weight, 24 h weight gain and duration of colostrum intake. According to Theil et al. (2014a), colostrum intake calculated using the Devillers et al. (2004) formula underestimates colostrum intake by 30%. However, when comparing studies using the same method of calculation, the total yield of colostrum appears to be highly variable among sows. In the following paragraphs, we describe some factors and measures considered to be responsible for high variability and to improve colostrum yield in the sow.

1.2.2 Sow characteristics

Colostrum yield in sows is highly variable. The gestation length of a sow has been shown to affect the colostrum yield (Devillers et al., 2007; Decaluwé et al., 2013; Declerck et al., 2015). Gestation length was positively correlated with colostrum yield (Decaluwé et al., 2013), suggesting that piglets born earlier are less vital (Devillers et al., 2007, Decaluwé et al., 2013). On the other hand, Declerck et al. (2015) found that sows with a gestation length of 113 days produced more colostrum than sows with a gestation

length of 114-115 days. However, other studies did not report a relationship between gestation length and colostrum yield (Quesnel, 2011; Vadmand et al., 2015).

The influence of parity on colostrum yield in sows has also been reported. Devillers et al. (2007) established a tendency of higher colostrum yield in second and third parity sows, supported by the results of Decaluwé et al. (2013). In both studies, younger sows (first to third parity) produced significantly higher colostrum yields than the older sows. In contrast, Ferrari et al. (2014) reported that colostrum yield was lower in primiparous than in multiparous sows. However, other studies reported no parity effect on colostrum yield (Le Dividich et al., 2005; Quesnel, 2011; Declerck et al., 2015). Despite some discrepancies regarding sows of parity one or three, it seems that older sows (at least beyond parity four) consistently produce less colostrum than younger sows (Quesnel et al., 2015).

The thickness of back fat and sow body weight has not been shown to affect sow colostrum yield (Devillers et al., 2004; Quesnel, 2011). However, changes in the back fat thickness during 85-109 days of gestation were negatively associated with sow colostrum yield. An extra loss of one mm of back fat during this period of gestation was associated with an increase in colostrum yield of 113 g (Decaluwé et al., 2013). In Decaluwé et al. (2013), most of the sows were in a catabolic state during the gestation, therefore sow body protein use before farrowing had a negative effect on the colostrum yield. However, anabolic sows were positively associated with colostrum yield (Loisel et al., 2014). These discrepancies between the two studies may originate from the metabolic status of the sows during the pre-partum period. Furthermore, there was also no association between colostrum yield and number of functional teats in sows (Quesnel, 2011).

1.2.3 Litter characteristics

Unlike for milk production, most studies on colostrum yield in sows indicate it to be independent of litter size (Devillers et al., 2007; Foisnet et al., 2010; Quesnel, 2011; Decaluwé et al., 2013; Declerck et al., 2015). Litter weight was also not associated with sow colostrum yield (Le Dividich et al., 2005; Foisnet et al., 2010; Quesnel, 2011), except in the study by Devillers et al. (2007) where colostrum yield was positively correlated with mean piglet birth weight. On the other hand, in a recent study, it was reported that litter weight and litter size at birth were positively correlated with sow colostrum yield (Vadmand et al., 2015; Craig et al., 2017). However, the discrepancy might be due to the use of different prediction models to quantify the piglet colostrum intake. Colostrum yield can also be influenced litter vitality, by shortening the interval between birth and first suckling of the litter (Declerck et al., 2015). Colostrum yield can also be negatively correlated with within litter heterogeneity of birth weight (Devillers et al., 2007; Quesnel, 2011).

1.2.4 Farrowing and management

Induction of farrowing at 114 days of gestation had no influence on colostrum yield of sows (Otto et al., 2017). Foisnet et al. (2011) also recorded similar findings, with farrowing induction at 113 days not affecting colostrum yield. On the other hand, Devillers et al. (2007) found that sows with induced parturition produced lower colostrum yields than the naturally farrowing sows. This negative association can be due to the incomplete gestation length, as too early an induction might increase the birth of low weight and less vital piglets (Devillers et al., 2007). Previous studies did not report any influence of farrowing duration on colostrum yield (Devillers et al., 2007, Foisnet at al., 2010; Quesnel, 2011). However, in recent years litter size has increased considerably from that reported in previous studies. Therefore, studies including the more recent larger litter size may reveal different results. Quesnel (2011) established that the

number of stillbirth piglets was negatively associated with colostrum yield, and explained that alterations of endocrine status of sows in late pregnancy might have a detrimental effect on colostrum production.

1.2.5 Hormonal factors

In pigs, as in other species, lactogenesis is hormonally controlled. Several hormones regulate the onset and the progress of farrowing (Algers and Uvnäs-Morberg, 2007). It is initiated by the pre-partum peak of prolactin, which is induced by the drop in progesterone. The latter remains at a high concentration throughout the entire pregnancy, and should decrease markedly with the approach of parturition (Foisnet et al., 2010). Prolactin stimulates mammary growth and lacteal nutrient synthesis in swine (Algers and Uvnäs-Morberg, 2007). Progesterone, on the other hand, inhibits prolactin secretion, and down-regulates the expression of the prolactin receptors in the mammary gland. Foisnet et al. (2010) found that sows with a low yield of colostrum had greater concentration of plasma progesterone around farrowing than sows with high colostrum yield (**Figure 1**).

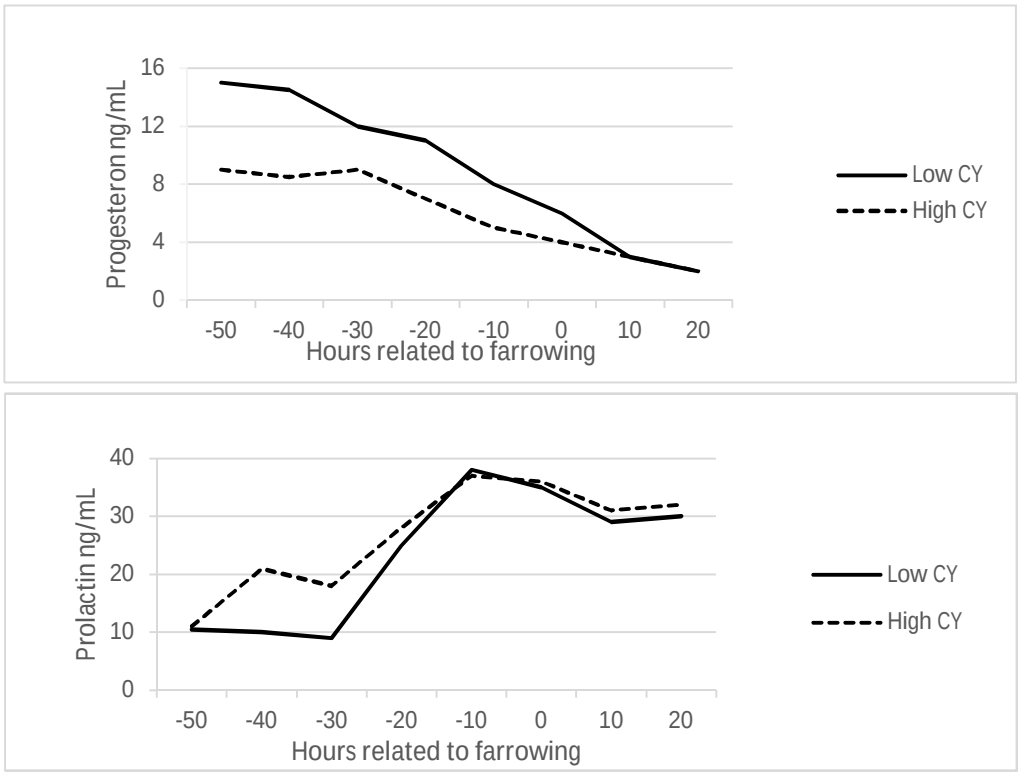

Figure 1: Plasma concentration of progesterone and serum concentration of prolactin around farrowing in sows producing a low (< 1.4 kg) or a high (> 2.8 kg) colostrum yield (CY) (adapted from Foisnet et al., 2010)

In the same study, the sows with lower colostrum yield had also a delayed prolactin increase. Loisel et al. (2015) investigated if the relative prepartum ratio of prolactin-to-progesterone could influence sow colostrum yield. They found that sows with a greater ratio produced more colostrum than sows with a lower ratio. This suggests that greater prolactin concentrations associated with lower progesterone concentrations before farrowing lead to greater colostrum yield (Loisel et al., 2015). In addition, colostrum production is affected by alterations in estrogen, relaxin, cortisol, and prostaglandin F2α

concentrations. These hormonal changes are also needed for adequate colostrum synthesis (DeHoff et al., 1986; Farmer and Quesnel, 2009).

1.2.6 Feeding, metabolic and nutritional factors

Overall, maternal nutrition plays a vital role in fetal development, early development of neonates, and lactation, and regulates the lifetime productivity of offspring (Zhang et al., 2019). Changes in dietary composition, specific feeding strategies or management of sows are common practices to improve sow colostrum yield (Theil et al., 2014a; Krogh et al., 2012). Inclusion of a late gestating diet with dietary fatty acid improved colostrum yield of sows and increased piglet survival. Dietary conjugated linoleic acid is known to affect the metabolism of mammary tissue and to increase milk yield in cows (Zheng et al., 2005). However, in sows, supplementation of conjugated linoleic acid in late gestation tended to decrease colostrum yield (Krogh et al., 2012). In addition, a diet high in fiber in late gestation increased sow colostrum yield (Theil et al., 2014a). Sows fed with sugar beet pulp or pectin residue produced more colostrum than those fed the low fiber diet during the end of gestation (Theil et al., 2014a). Other studies indicated that dietary supplementation of hydrolyzed yeast improved sow performance, significantly increasing colostrum yield, average daily gain of piglets and subsequent weaning weight (Le Dividich et al., 2009; Close and Taylor-Pickard, 2010).

1.3 Colostrum quality and composition

Colostrum is regarded as a high-density source of different components: macronutrients, micronutrients, and bioactive molecules such as immunoglobulins, growth factors and enzymes. All of these are essential for neonatal piglet survival and development (Theil et al., 2014b). Compared to milk, colostrum is characterized by a higher percentage of dry matter and proteins, but the concentrations of lactose and fat

are lower (Klobasa et al., 1987; Theil et al., 2014b). Therefore, in terms of composition, colostrum is distinguished between early (0 h), mid (12 h) and late (24 h) colostrum (Theil et al., 2014b; **Figure 2**). The lactose content increased steadily from 3.5% in early colostrum to 4% and 4.4% in mid and late colostrum respectively. The fat content was lowest in early and mid colostrum (5.1% to 5.3%), and highest in late colostrum (6.9%). In contrast with lactose and fat, the protein content decreased from 17.7% in early colostrum over mid and late colostrum decreased substantially to 12.2% and 8.6%, respectively (Theil et al., 2014b). These changes are similar to those reported by Klobasa et al. (1987).

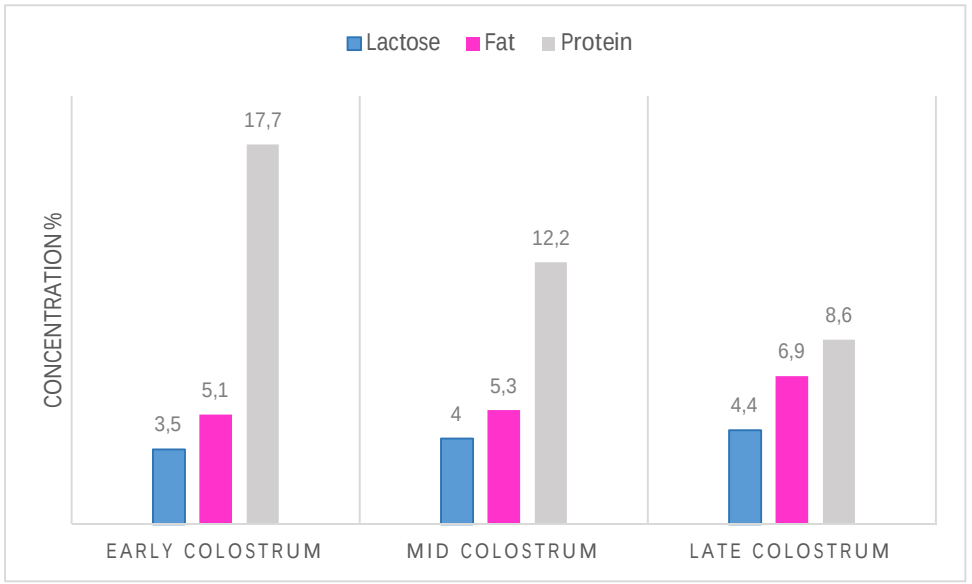

Figure 2. Average composition (%) of early (0 h), mid (12 h) and late (24 h) colostrum (adapted from Theil et al., 2014b).

Colostrum is characterized by a high concentration of IgG and a relatively low concentration of IgA and IgM (Klobasa and Butler, 1987; **Figure 3**). IgG is the most abundant isotype in the colostrum (81%) (Klobasa et al., 1987). The concentration of IgG in colostrum decreased markedly during farrowing and until 24 h after farrowing (Klobasa et al., 1987; Foisnet et al., 2010; Quesnel, 2011). The colostrum concentration

of IgG is highly variable and can be affected by many factors, such as parity, seasons, genotype, farrowing duration and teat location (Inoue et al., 1980; Klobasa and Butler, 1987; Rooke and Bland, 2002; Quesnel, 2011). All IgG in colostrum is derived directly from the plasma of the sow. The individual variation in IgG concentration in the serum of sows (Quesnel, 2011) causes considerable variation of IgG concentration in colostrum among sows (Klobasa and Butler, 1987). Supplementing sow gestation diet with immunomodulating and bioactive compounds has been found to increase colostrum IgG concentration. For example, conjugated linolenic acid (CLA) (Bontempo et al., 2004), non-specific immunostimulating products (Krakowski et al., 2002), shark liver oil (Mitre et al., 2005), fish oil (Leonard et al., 2010), a source of essential oils (Wang et al., 2008), fermented liquid feed (Demeckova et al., 2002), polyunsaturated fatty acid (PUFA) (Yao et al., 2012), seaweed extract (Leonard et al., 2010), and mannan oligosaccharides (O'Quinn et al., 2001) are commonly tested to increase sow colostrum immunoglobulin content.

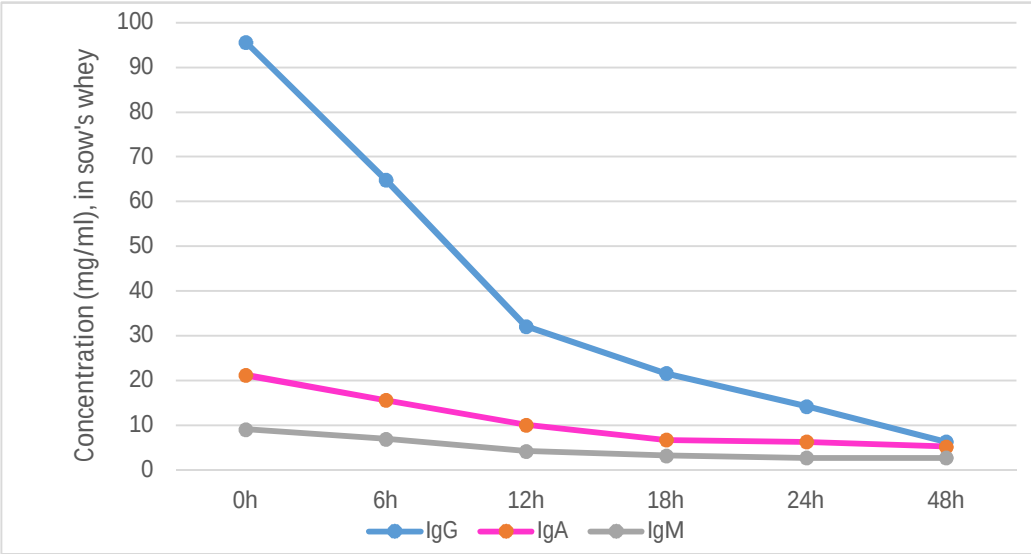

Figure 3. Concentration of IgG, IgM and IgA in sow whey during the first 2 days of lactation (adapted from Klobasa et al., 1987).

Colostrum is also a source of acute phase protein (APP), especially serum amyloid A (SAA). Age-dependent studies showed that SAA concentration was highest in neonate piglets (Moya et al., 2007) and calves (Orro et al., 2008). However, Larson et al. (2003) suggested that SAA in colostrum has local beneficial effects on the neonatal gut. Research has also found that colostrum-associated SAA peptide enhanced innate protection by stimulating intestinal epithelial cells and mucous production and thereby preventing binding of enteropathogenic bacteria (Larson et al., 2003).

1.4 Sow physiology and body condition around parturition, and their impact on piglets

At farrowing sows undergo not only hormonal changes, but also substantial metabolic and physiological changes occur during this very short period of time (Algers and Uväns-Morberg, 2007). Parturition in sows is a complex process, and several hormones regulate the onset and progress of farrowing and colostrum production, namely progesterone, prolactin and oxytocin. In a longer farrowing duration, due to stress and pain, increase in opioids might inhibit oxytocin and prolactin secretion (Jarvis et al., 1997), thereby reducing the colostrum yield. However, progesterone, which remains at a high concentration throughout the entire pregnancy, should decrease markedly with the approach of parturition (Liu et al., 1996). If sows had a delayed decrease in progesterone concentrations, and thereby a delayed increase in prolactin, they produced significantly less colostrum (Foisnet et al., 2010; Quesnel et al., 2012). A rise in plasma concentration of prolactin prior to farrowing is known to be one of the main factors initiating nest building behavior in prepartum sows (Algers and Uvnäs-Morberg, 2007). Yun et al. (2014) found that the onset of nest building, by providing abundant nesting materials and space, was accompanied by an increase in plasma oxytocin and prolactin concentrations in prepartum sows. Although modern farrowing crates constrain, and

sows hardly have access to nest building materials, studies of Yun et al. (2014) confirmed that a plentiful supply of nesting materials to a sow prior to parturition tended to increase piglet serum IgG and IgM concentration during early lactation.

Because piglets are born devoid of gammaglobulins, colostrum provides them immunological protection (Rooke and Bland, 2002). Beyond the neonatal period, the supply of maternal immunity and bioactive compounds by colostrum is relatively more important (Rooke and Bland, 2002; Le Dividich et al., 2005). Sow body condition at farrowing significantly influences CY, as Decaluwé et al. (2013) reported – the sow back fat changes at gestation are negatively correlated with sow CY. Studies also revealed a significant positive correlation between sow back fat during lactation and piglet survival and growth (Grandinson et al., 2005).

1.5 Sow alternative feeding and its influence on gut microbiota, colostrum yield and quality

Colostrum yield (CY) is associated with sow, piglets and environmental traits (Farmer and Quesnel, 2009). Feeding sows with alternative compounds, able to modulate their natural ability to improve CY, is an important topic. However, to date, studies related to supplementation of gestating sow diets with specific compounds, consequent gut microbiota modulation and their effect on sow and piglet performances are scarce. Sow feeding strategies include the use of fibers, prebiotics, probiotics, essential oils and organic acids at different stages of production (Gresse et al., 2017). The mode of action of these feed ingredients relies on their ability to modify favorably the microbiota of the gut, which is of importance for sow health and consequently piglet health. Beneficial bacteria can act as a barrier against pathogenic bacteria, having the ability to lower the pH of the gastrointestinal tract and produce anti-microbial compounds (Lallès et al., 2009). Microbiota fermenting indigestible carbohydrates produce short chain fatty acid

(SCFA) that are an important energy source for the sow. Butyrate, in particular, is a gut-health-promoting compound that acts as the main energy source for colonocytes and exerts anti-inflammatory properties (Sassone-Corsi and Raffatellu, 2015). It is thus of interest to modify favorably the microbiota towards fermentative butyrate-producing and anti-pathogenic bacteria. Studies show that the reduction in the number of pathogenic bacteria in response to dietary supplementation is associated with an increase in beneficial microbiota, which in turn may modify the substrate availability and physiological conditions of the gastrointestinal tract (e.g. fermentation products, luminal pH and bile acid concentration) (Liu et al., 2008). However, supplementing probiotics at farrowing maintained a genuine anabolism in sows, thus maintaining high feed intake, cutting weight losses during lactation and improving litter performances (Böhmer et al., 2006).

Among prebiotics, yeast hydrolysate can bind and inhibit pathogen bacteria-like *Salmonella* spp., *Clostridium* spp. and *Escherichia coli*, thereby promoting growth of beneficial gut bacteria, better utilization of feed nutrients and reduced spread of pathogens to piglets (Castillo et al., 2008; Liu et al., 2008; Burkey et al., 2004; White et al., 2002). Yeast hydrolysate has also been associated with positive immune stimulation by activation of an alternative complement pathway, release of lysosomal enzymes, binding to the specific receptor of macrophages and cytokines in different animal species (Yang et al., 2008; Ferket, 2002; Iji et al., 2001; Caine et al., 2002).

Resin acid-enriched composition (RAC) has been used in feed as a novel additive to improve performance in broilers (Vienola et al., 2018). RAC modulates the microbial population in the small intestine of broilers, changes the microbial digestion and improves the feed conversion ratio and gut microbiota (Kettunen et al., 2017; Vienola et al., 2018). RAC, a novel dietary product, typically comprises resin acids (RA) (~8%) and free fatty acids (~90%), and 2 to 3% neutral components (in trees naturally occurring compounds like alcohols or terpenic hydrocarbons such as squalene). RA of RAC has been used to enhance immunity and regulate inflammation and wound healing (Kang et

al., 2008; Park et al., 2017). Conjugated linolenic (CLA), pinolenic and oleic acids are characteristic fatty acid components of RAC and the effects of their supplementation in gestating and lactating diets have been well studied (Bontempo et al., 2004; Corino et al., 2009; Yao et al., 2012; Liu et al., 2018). Studies indicated dietary supplementation of these essential fatty acids improves sow colostrum immunoglobulins, and significantly increases average daily gain of piglets and subsequent weaning weight (Bontempo et al., 2004; Corino et al., 2009; Yao et al., 2012; Liu et al., 2018). However, the peculiar fatty acid composition of RAC, and its content of resin acids, suppress the pathogenic bacteria and influence the growth of beneficial microbiota (Dorman and Deans, 2000; Vienola et al., 2018). Moreover, feeding sows with konjak flour (Tan et al., 2015), resistance starch (Leblois et al., 2018), fermented feed (Demeckova et al., 2002, Wang et al., 2018) or essential oils (Ariza-Nieto et al., 2011) is a growing practice to modulate beneficial gut microbiota, thereby influencing sow and piglet performances.

1.6 Piglet colostrum intake (CI), growth, immunity and gut microbiota development.

It is well known that insufficient colostrum intake (CI) is a major cause of pre-weaning mortality and mortality ranges between 10-13% in the principal pig-breeding countries (Edwards, 2002; Kilbride et al., 2012; Hales et al., 2014; Decaluwé et al., 2014). This pre-weaning mortality usually occurs during the first 3 days after birth (Le Dividich et al., 2005). Inadequate CI by the piglet is a major cause of mortality during the first days after birth, mainly due to consequent hypothermia and hypoglycemia (Le Dividich et al., 2005; Theil et al., 2014b). Piglet pre-weaning mortality and weight gain depend on colostrum intake, especially in low birth weight piglets (Declerck et al., 2016; Decaluwé et al., 2014; Devillers et al., 2011; Quesnel et al., 2012). Devillers et al. (2011) reported that the rate of pre-weaning mortality was on average only 7.1% when piglets ingested more than

200 g of colostrum, whereas the rate was on average 43.4% when the CI was less than 200 g (**Figure 4**).

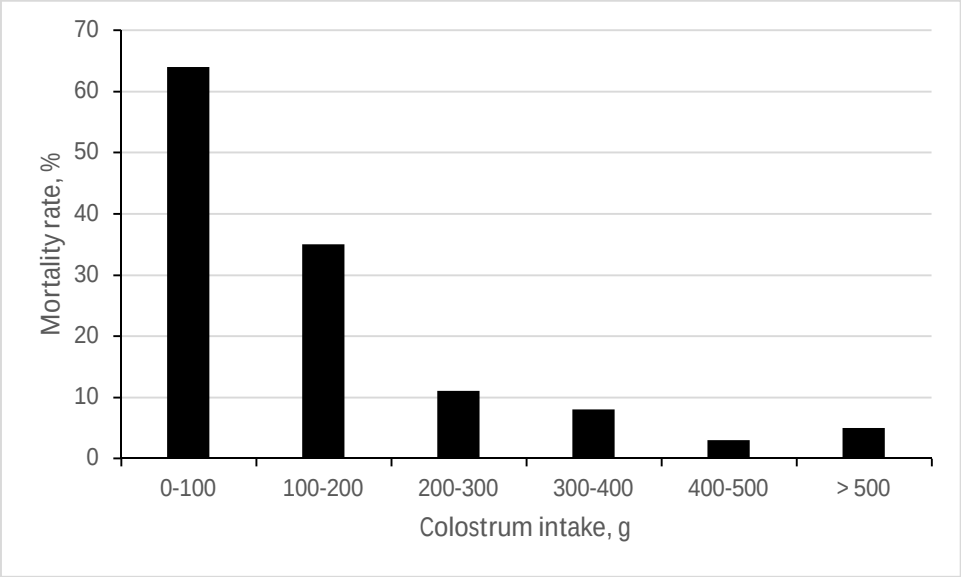

Figure 4. Influence of colostrum intake during the first 24 h after the onset of parturition on mortality of piglets until weaning (adapted from Devillers, 2004 and Quesnel et al., 2012).

Weaning weights of the piglets were dependent on colostrum intake (Devillers et al., 2011; Decaluwé et al., 2014; Ferrari et al., 2014; Vallet et al., 2015). However, Devillers et al. (2011) found that if piglets ingest more than 290 g of colostrum they reached, at 42 days of age, a bodyweight of 12.34 kg compared with 10.45 kg for piglets ingesting less than 290 g of colostrum (**Figure 5**).

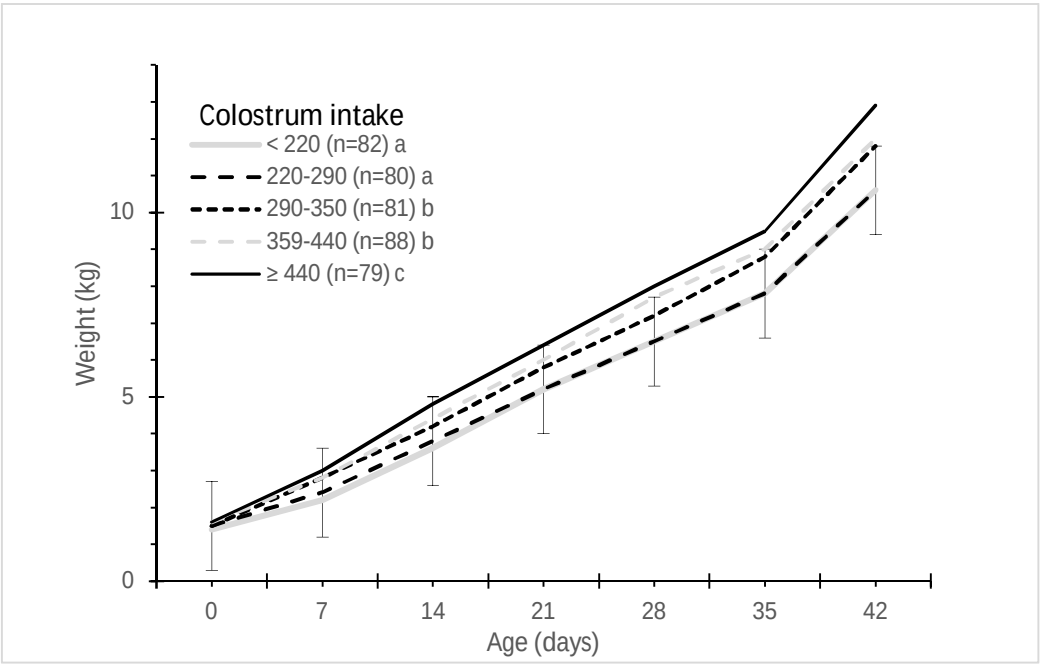

Figure 5. Influence of different levels of colostrum intake during the first 24 h after the onset of parturition, on piglet growth from one to 42 days of age (adapted from Devillers et al., 2011).

In piglets, plasma concentration of IgG at weaning was positively correlated to plasma IgG concentration at 24 h (**Figure 6**). Moreover, the total amount of piglet plasma IgG at 24 h was positively correlated with the amount ingested with the colostrum (Devillers et al., 2011). Piglets are born immunologically underdeveloped and their immunity in the first weeks of age therefore depends completely on maternal colostrum. In addition, insufficient intake of maternally derived immunoglobulins (Ig) has a negative effect on piglet health status, thus weight gain and survival, at later stages in life (Rooke and Bland, 2002; Le Dividich et al., 2005; Devillers et al., 2011; Quesnel et al., 2012; Decaluwé et al., 2014; Declerck et al., 2016). Regarding immunity, piglets with a high colostrum and milk intake might be more immunocompetent and better protected against infections. Furthermore, colostrum and milk contain various bioactive compounds that promote

gastrointestinal development and nutrient absorption in young growing piglets (Wang and Xu, 1996; Xu et al., 2002; Thymann et al., 2006).

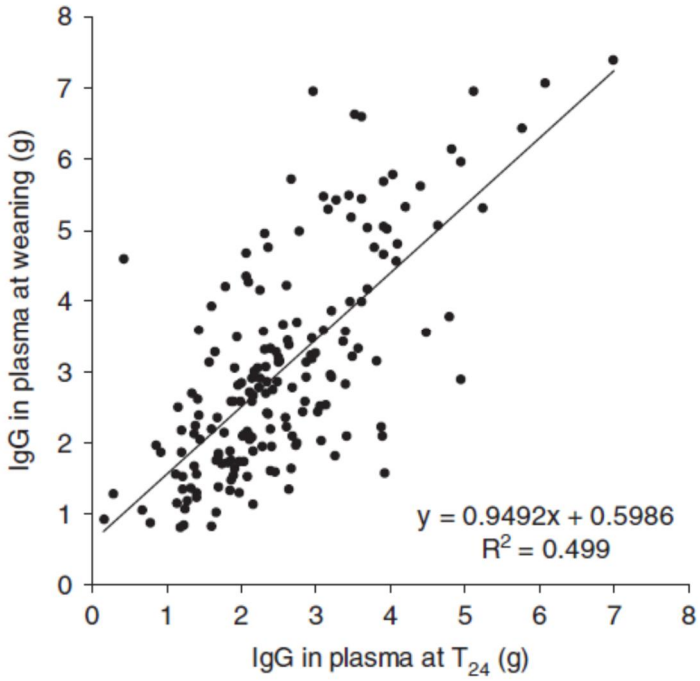

Figure 6. Relationship between total amount of IgG in piglet plasma at weaning and 24 h after the onset of farrowing (T_{24}) (adapted from Devillers et al., 2011)

There are reports that the suckling piglet has a unique microbiota, largely acquired from the mother (Tan et al., 2015; Li et al., 2017). The piglets acquire mainly fecal microbiota from the sow, but also microbial communities present in the birth canal, on the skin of the mother and from the ambient environment. Furthermore, the chemical and microbial composition of colostrum and milk might also influence the intestinal microbiota of the progeny (Mach et al., 2015).

2. Aims and hypotheses of the study

The aims of this thesis were to investigate the impact of colostrum yield, colostrum composition and quality on piglet performance. We also included here the feeding strategies and other relevant factors affecting sow physiology around farrowing, their effect on colostrum yield (CY), colostrum quality and gut microbiota of sows and piglets after birth. The specific aims and hypotheses of the studies are listed below.

1. The objective of this study was to evaluate a Brix refractometer as a tool to estimate IgG in sow colostrum on-farm, comparing it with an ELISA laboratory assessment, to determine the degree of agreement between the two methods. We aimed also to establish criteria to interpret Brix results at farm level and to describe the chemical composition of sow colostrum in the observed farms.

   We hypothesized that Brix measurements at farm level might help to identify sows with an impaired IgG concentration at early colostrogenesis.

2. We aimed to measure sow physiology parameters at farrowing, CY, colostrum composition, piglet colostrum intake (CI) and their possible prolonged effect on piglet growth and mortality until weaning. We studied the sow acute phase proteins (APPs) status, and its association with CY, colostrum composition and piglet growth.

   We hypothesized that disturbances in homeostasis due to inflammation, tissue injury during gestation and the longer farrowing process can induce a nonspecific acute phase response with an adverse effect on CY, Ig content, colostrum composition, piglet survival and piglet growth until weaning. We hypothesized that SAA level in colostrum can have beneficial effects on piglet growth and health.

3. We aimed to determine the effects of yeast derivate (YD) and resin acid-enriched composition (RAC) inclusion in sows' gestation and lactation diets on CY, colostrum immunoglobulins, colostrum nutritional composition and subsequent litter performance. Our aim was also to investigate the influence of YD and RAC on the taxonomic profile of the hindgut microbiota of sows and piglets by means of high-throughput sequencing analysis.

   We hypothesized that inclusion of these feed ingredients in gestation and lactation diets would modify the hindgut microbiota of the sow, and that the modifications could be associated with better colostrum yield and immunoglobulin content. We also hypothesized that piglets of the sows fed a YD diet would have better gut microbiota colonization, possibly contributing to better piglet performance.

3. Materials and Methods

The experimental protocol was approved by the National Animal Experiment Board in Finland (ESAVI, Regional State Administrative Agency for Southern Finland, permission ESAVI/333/04.10.03/2011). The experiments were carried out in five different commercial piggeries in Finland and one piggery in The Netherlands. This section of the thesis presented an overview of the material and methods for all the studies conducted (I-IV). The experiments were repeated for different batches of sows that farrowed during that time. A detailed description of all the studies can also be found in the original publications reproduced in the final section of this thesis.

3.1 Animals and experimental design

A summarized description of the animals, main herd characteristics, treatments and management are presented in Table 1. During pregnancy sows were loose housed and feed was served in individual feeding cages. One week before expected farrowing the sows were transferred to the farrowing department, where they were housed individually in farrowing crates, and in one herd group free farrowing with individual getaway farrowing pens. In each herd, sows were included in the experiments based on the start of farrowing on a first come first sampled principle. Sows farrowed spontaneously and a researcher sampled all sows upon availability at farrowing. No restriction on parity of the sows was imposed, but it was taken into account that parities were uniformly distributed across the different herds. Parturition was observed, with as little interference as possible in the farrowing process. The farrowing duration was calculated based on the birth of the first piglet to represent the beginning, and the expulsion of the last piglet the end. When a piglet was born, the back was dried with a paper towel, the birth rank number was marked on the back, with a thick permanent marker, and the birth weight (BW_B) was measured.

Table 1. Data summaries for four studies to investigate the impact of colostrum yield, colostrum composition and quality on piglet performance.

Study	No. of herd	No. of animals	Breeds	Housing	Parity	Diet
I	11	153	Yorkshire × Landrace	Crate	1-10	Standard lactation
II	1	19	Yorkshire × Landrace	Crate	1-8	Standard gestation and lactation
		18	Yorkshire × Landrace	Crate	1-8	Standard gestation and lactation supplemented with YD (Progut®)*
III	1	21	Yorkshire × Landrace	Crate	1-7	Standard lactation
		23	Yorkshire × Landrace	Crate	1-7	Standard lactation supplemented with RAC (Progres®)**
	2	23	Yorkshire × Landrace	Crate	1-7	Standard lactation
		24	Yorkshire × Landrace	Crate	1-7	Standard lactation supplemented with RAC (Progres®)**
	3	15	Topigs 20	Crate	1-6	Standard lactation
		15	Topigs 20	Crate	1-6	Standard lactation supplemented with RAC (Progres®)**
IV	1	44	Topigs TN70	Crate	1-7	Standard lactation
	2	47	Topigs TN70	Crate	1-7	Standard lactation
	3	39	DanAvl	Crate	1-8	Standard lactation
	4	20	DanAvl	Crate	1-7	Standard lactation
	5	60	Topigs 20	Crate and pen	1-6	Standard lactation
	6	20	Duroc × Landrace	Pen, group farrowing	1-7	Standard lactation

**Progut® (hydrolyzed yeast), Hankkija Oy, Finland **Progres® (resin acid with a fatty acid carrier derived from coniferous trees), Hankkija Oy, Finland.*

During the first 24 h from the start of birth, piglets were allowed to consume only maternal colostrum. Only after they had been weighed for colostrum intake calculation (24 h after the start of farrowing) were piglets allowed to be provided with a milk supplement. Six piglets from each litter were selected and ear-tagged based on their

body weight at birth (BWB) in a block of three categories, 2 piglets weight <1 kg, 2 piglets 1.4-1.8 kg and 2 piglets >1.8 kg, representing small, normal and large piglets, respectively. Cross-fostering was allowed only after the 24 h weighing, but not for the six selected piglets, which stayed with their original mothers till weaning. Litters were balanced according to the number of functional teats, as is usually done on commercial farms. All the six ear-tagged piglets were followed until 3-4 weeks of age.

3.2 Observed parameters and colostrum yield calculation (II, III, IV)

Individual piglet colostrum intake (CI) within a litter was summed to calculate a sow's CY. Colostrum intake was estimated by the regression equation as described by Devillers et al. (2004), based on the variables: BW_B (kg), weight at 17 to 24 h of age (BW_{24}, kg), duration of CI (t in min and 17 h ≤ t ≤ 25 h), and time between birth and first suckling (t_{FS}, min). The equation is as follows: $CI = -217.4 + 0.217 \times t + 1861019 \times BW24/t + BWB \times (54.80\text{-}1861019/t) \times (0.9985 – 3.7 \times 10\text{-}4 \times t_{FS} + 6.1 \times 10\text{-}7 \times t^2_{FS})$. The t_{FS} was estimated to be 35 min, which was based on our observations (Study 1, Hasan et al., 2016). A 6 g/kg BWB miscalculation of CI for piglets or less than 2% error with an error of 15 minutes in t_{FS} generates a 6 g/kg BWB miscalculation of CI for piglets or less than 2% error (Devillers et al., 2004). Sow back fat was measured at the level of last rib, 6 to 7 cm from one side of the backbone using a digital back-fat indicator (Renco lean-meater®, Renco Corporation, Mineapolis, MN, USA) at farrowing (BF_F) and at weaning (BF_W). Observed sow parameters were: parity, gestation length, farrowing duration (time start from birth of the first piglets to last piglets), back fat thickness at farrowing and weaning, and numbers of live born and stillborn piglets. Gestation length was calculated based on the day of first insemination (start) and the day of parturition. Observed piglet parameters were CI, birth interval, pre-weaning mortality, BW_B, BW_{24}, body weight at weaning, and average daily gain (ADG) from birth (BW_B) to weaning.

3.3 Sample collection

3.3.1 Colostrum sample (I, II, III, IV)

Twenty milliliters (ml) of colostrum were collected from each sow within 0-3 h after birth of the first piglet. Colostrum samples were collected from the first three teats of same side of the anterior udder. Samples were subdivided into different aliquots and stored at -20°C until further analysis.

3.3.2 Blood sample (II, III, IV)

Sow blood samples were collected from the vena *saphena* at the beginning and at the end of farrowing using lithium heparin tubes, and centrifuged at 1000 × g for 10 minutes, the plasma being separated, divided in different aliquots and stored at -20°C for further analysis. No blood samples were collected from herd 6.

3.3.2 Sow (II, III) and piglet (II) fecal sample

Fresh fecal samples were individually collected from the rectum of sows using sterile 50 ml tubes. Piglet fecal samples were collected at 1 week and 4 weeks of age using sterile swabs and 5 ml Eppendorf tubes. After collection, samples were kept in an icebox and transported immediately to the laboratory and stored at -80°C before total genomic DNA extraction.

3.4 Brix measurement of colostrum sample

A 0.3 ml of freshly drawn colostrum sample was used for the on-farm measurement of Brix percentages shortly after collection. A commercial digital refractometer (digital hand-held pocket refractometer; Atago, Tokyo, Japan) was used with a range of 0 to 53% Brix.

3.5 Colostrum and blood sample analysis

3.5.1 Analysis of colostrum immunoglobulins and chemical composition (I, II, III, IV)

Concentration of immunoglobulins (Ig) was quantified using swine IgG, IgA and IgM ELISA quantification kits (Bethyl Laboratories, Montgomery, Texas, USA). The intra- and inter-assay coefficients of variation were 4.8%, 3.3%, 1.3% and 6.7%, 5.3%, 6.8% for IgG, IgA and IgM, respectively. The colostrum total solid (TS), fat, protein and lactose contents were analyzed using MilkoScanTM FT+ (Foss, Hillerød, Denmark), according to the method described by Decaluwe et al. (2013).

3.5.2 Analysis of colostrum and plasma SAA and Hp (III, IV)

Colostrum and plasma serum amyloid A (SAA) were analyzed with commercial multispecies indirect ELISA (PhaseTM SAA Assay, Tridelta Development Ltd., Kildare, Ireland) according to the manufacturer's instructions for swine. The intra- and inter-assay coefficients of variation were 12% and 12% respectively. Colostrum and plasma haptoglobin (Hp) concentrations were analyzed with a hemoglobin-binding assay developed for cows (Makimura and Suzuki, 1982) with modifications, in which tetramethylbenzidine was used as a substrate and 5 µl of sample volume. Pooled and lyophilized aliquots of porcine acute phase serum were used as standards. The assay was calibrated using a porcine serum sample of known Hp concentration provided by the European Commission Concerted Action Project (number QLK5-CT-1999-0153). The intra- and inter-assay coefficients of variation were 8% and 11% respectively.

3.5.3 Analysis of plasma progesterone (II, IV)

Blood plasma progesterone was analyzed using a commercially available 125I radioimmunoassay coated tube kit (RIA) (Progesterone ImmuChem, ICN Pharmaceuticals, USA). A 50 µl plasma sample was added to the coated tubes. After

vortex mixing, the tubes were incubated at room temperature for two hours. The supernatant was decanted, and the tubes were left standing inverted for five minutes. Each tube was counted for one minute in a y-counter (Wallac®, LKB-Wallac, Turku, Finland). The detection limit of the assay was 0.3 ng/ml, and the intra- and inter-assay coefficients of variation were 6.83% and 3.33% respectively.

3.6 Microbial composition and bioinformatics analysis (II, III)

DNA was extracted from sow feces (250 mg) using a QIAamp DNA Stool DNA kit (Quagen, ct. no. 51504), following the manufacturer's instructions. The quality and concentration of DNA were assessed using a Nanodrop 2000 (Thermo Fisher Scientific). DNA was stored at -20°C until sequencing. The 16s hypervariable region V3-V4 and mixed primers 341F_1-4 (CCTACGGGNGGCWGCAG) and 785R_1-4 (GACTACHVGGGTATCTAATCC) were amplified with partial Illumina TruSeq adapter sequences added to the 5' ends (F_1; ATCTACACTCTTTCCCTACACGACGCTCTTCCGATCT, F_2; ATCTACACTCTTTCCCTACACGACGCTCTTCCGATCTgt, F_3; ATCTACACTCTTTCCCTACACGACGCTCTTCCGATCTagag, F_4; ATCTACACTCTTTCCCTACACGACGCTCTTCCGATCTtagtgt, R_1; GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTGACT, R_2; GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTa, R_3; GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTtct, R_4; GTGACTGGAGTTCAGACGTGTGCTCTTCCGATCTctgagtg). The DNA sequencing was done by the DNA Sequencing and Genomics Laboratory, Institute of Biotechnology, University of Helsinki, Finland, according to Pereira et al. (2017). The software package MOTHUR (v 1.39.5) was used to process the 16S rRNA gene amplicons (Schloss et al., 2009). Sequences were assigned to ≥97% ID OTUs by similarity with chimera filtering using the USEARCH algorithm (Edgar, 2013). The annotation of the representative OTU and taxonomic information for each OTU was obtained from the Ribosomal Database Project

(RDP) classifier (Cole et al., 2013). Data visualization and further analyses were done using Calypso (Zakrzewski et al., 2016).

3.7 Statistical analysis

Statistical analyses were performed using SPSS 22.0, 24.0 (IBM Company Headquarters, Chicago, IL) and Stata 14.0 (StataCorp, TX). Data are expressed as LSmean ± SEM unless otherwise indicated. Significance is reported at a *P* value of < 0.05, and tended to significance for *P* < 0.1.

3.7.1 Analysis of variance (ANOVA)

The overtime change of the colostrum IgG composition in the profile analysis T_0 to T_{24} was subjected to ANOVA using a repeated measurement GLM in study I.

3.7.2 Univariate analysis and model building

All the models are based on univariate analysis and tested the association of CY (II, III, IV) and IgG (I, II, III, IV) (dependent variables) with other explanatory variables. Models generated from univariate analysis were included in the final models if *P* < 0.25, and biologically meaningful interactions were considered.

In study I, Linear regression was used to determine which variables were associated with colostrum IgG content and composition. The dependent variable was colostrum IgG content (IgG 0 to 3 h mg/ml) and composition (% fat, % protein, % lactose, % TS) and independent variables were herd and parity for each model.

In study II, Sow data were subjected to linear regression with treatment (YD and CON) as a fixed factor, and farrowing duration, total piglets born, live born piglets, level of progesterone at the beginning of farrowing and litter birth weight as covariates.

In study III, treatment (RAC and CON) as a fixed factor and herd as a random factor, and parity and farrowing duration as covariates were used for analyzing sow level data. For piglet data, all the colostrum Ig and compositions were tested with univariate analysis with ADG as the dependent variable.

3.7.3 Mixed model analysis

In study IV, hierarchical mixed linear regression models were built to study variables associated with sow level continuous outcome variables (farrowing duration, number of total born piglets, colostrum yield, colostrum IgG, IgA and IgM concentrations). Square root transformation (for colostrum IgA and IgM) and logarithmical transformation (for colostrum IgG and farrowing duration) were used to achieve normal distribution of outcome variables. Farm and trial batch within the farm were included as random factors in all models. Similar mixed logit models were used to study associations of explanatory variables (back fat at farrowing, progesterone at the end of farrowing) with dichotomous outcome variables (antibiotic treatment of piglets – yes/no and litter diarrhea at 24 hour post-partum – yes/no) in this sow level dataset. Farm and trial batch inside the farm were included as random factors. Final models were built similarly to the linear mixed models described above. For initial analysis of the piglet level dataset four level hierarchical mixed models were used for continuous outcomes (colostrum uptake and average daily gain at 3-4 weeks of age). Piglet within sow, sow within trial batch, trial batch within farm, and farm were all included as random factors, and piglet colostrum uptake and average daily gain at 3-4 weeks of age were covariates. Similar four level mixed logit models were used for piglet level dichotomous outcome variables (death before weaning, diarrhea at 7 days of age – yes/no and diarrhea at weaning – yes/no). All the same model building strategies were used as for sow level mixed linear and logistic models.

In study III, a mixed model was performed with ADG, where feed was a fixed factor and herd was a random factor, lactose and CI covariates, and sows a random factor nested within herd.

4. Results

This section summarizes the result of studies I-IV, which are presented in the last section of this thesis as published or submitted papers.

4.1 Validation of Brix refractometer (I)

We established a good correlation between the digital Brix refractometer values and the log transformed ELISA IgG measurements of colostrum samples at 0-3 h from farrowing. The Brix ELISA correlation analysis (r = 0.63, $P < 0.001$) is examined graphically and presented in Figure 7. A proposed classification of the Brix values into four categories for assessment of IgG content using a Brix refractometer is presented in Table 2.

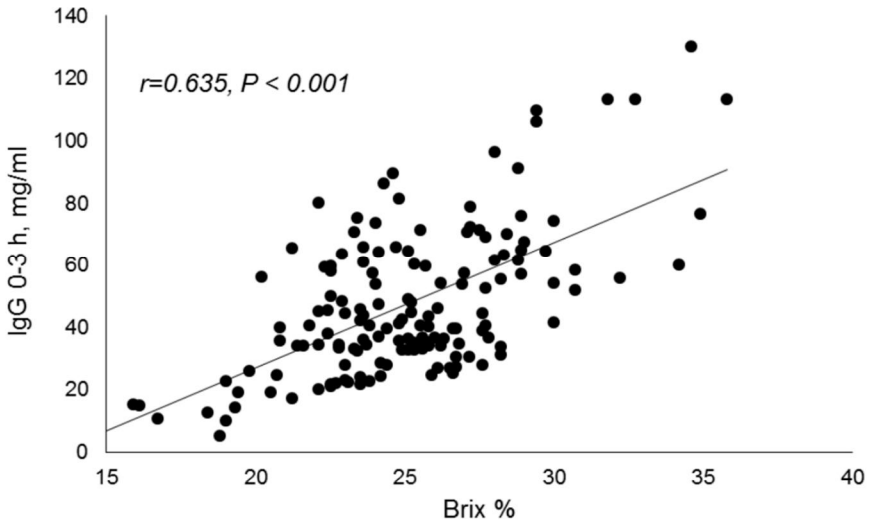

Figure 7. Relationship between Brix refractometer values (%) and IgG measurement using ELISA for 0-3 h colostrum sample.

Table 2. Colostrum immunoglobulin G (IgG) content based on two methods of evaluation, and categories of estimation.

Brix %	ELISA IgG 0-3, mg/ml (average ± SEM)	IgG estimation categories
< 20	14.5 ± 1.8	Poor
20-24	43.8 ± 2.3	Borderline
25-29	50.7 ± 2.1	Adequate
≥ 30	78.6 ± 8.4	Very good

The concentration of IgG decreased on average by 50% during the first day of lactation. Statistical analysis of the time effect showed that a major drop (43%) in colostrum IgG concentration occurred within 10 h of farrowing and concentration decreased on average by 80 ± 15.9% in 70% of sows within 24 of farrowing. The reduction trend in Brix measurement was similar to that for ELISA measurement.

4.2 Factors affecting sow colostrum yield (II, III, IV)

Average CY by sows in different studies is summarized in Table 3.

The factors associated with sow CY were plasma Hp, farrowing duration and live-born piglets. An additional individual live-born piglet increased CY by 93.6 g ($P < 0.01$). This amount was much higher in study II, numbers of piglets born alive (per piglet) and live born litter birth weight (per gram) were associated with an increase in CY of 199.2 and 4.5 g respectively. Sow plasma Hp at farrowing was also positively correlated with sow CY ($P < 0.05$).

An additional minute of farrowing duration reduced CY by 2.2 g (P = 0.01). However, in study II, we noted previously that a sow having a farrowing duration of 350 min or longer produced 451 g less colostrum compared with a sow with a farrowing duration shorter than 350 min.

Table 3. Summaries for different studies to investigate the impact of colostrum yield, colostrum composition and quality on piglet performance.

	Study I	Study II	Study III	Study IV	Total average
CY, g	-	4132	4468	4346.1	4315.3
CI, g	-	344	326	308.9	326.3
IgG, mg/ml	52.0	63.8	88.4	80.0	71.0
IgA, mg/ml	-	9.4	10.7	10.3	10.1
IgM, mg/ml	-	4.6	4.5	4.9	4.6
Protein %	17.1	16.9	16.5	16.6	16.7
Fat %	5.2	4.6	4.5	4.5	4.7
Lactose %	5.8	5.5	4.3	4.5	5.0
DM %	30.0	28.5	27.2	27.4	28.2
Colostrum SAA, mg/L	-	-	424.9	385.2	405.0
Colostrum HP, mg/L	-	-	1293.0	1325.0	1309.0
Plasma SAA, mg/L	-	-	18.0	20.0	19.0
Plasma HP, mg/L	-	-	1831.0	1883.0	1857.0

In study IV, the average progesterone level in each herd is described in Figure 8. Sow average plasma progesterone level at the start of farrowing was 3.8 ± 0.2 ng/ml and at the end 3.2 ± 0.2 ng/ml.

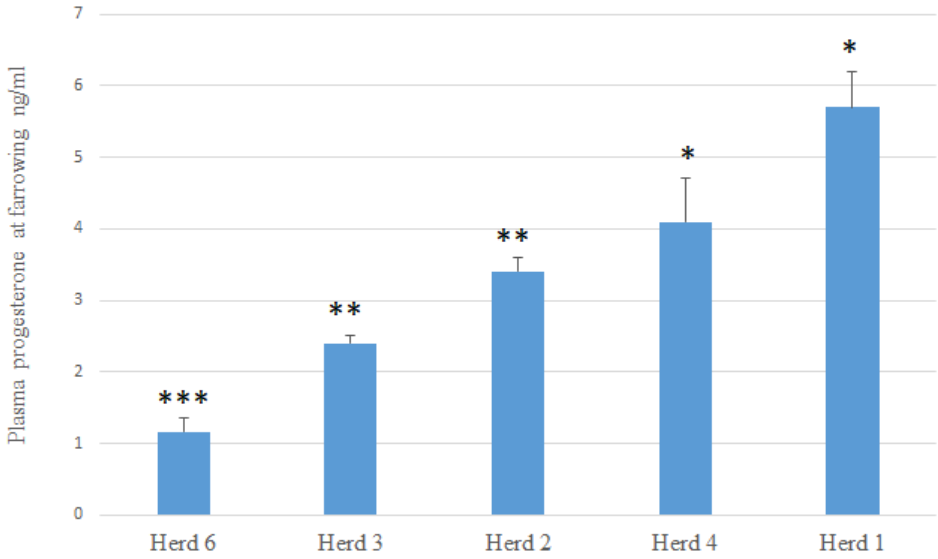

*Figure 8. Mean and SEM plasma progesterone in five herds at the beginning of farrowing. No blood samples from herd 5 were taken.******* Abundant nesting materials in getaway farrowing pen (entire pen floor with 15-20 cm of straw); ****** Limited amount of nesting material in farrowing crate (2-4 liters of saw dust and/or straw); ***** No nesting material in farrowing crate*

However, 15% of the sows had 50% higher plasma progesterone than the average level at the beginning of farrowing. Moreover, at the end of the farrowing some of the sows (n = 24) still had 50% higher than average progesterone level in plasma at that stage. However, we did not establish a significant relationship between CY with progesterone level around farrowing in the multivariable regression analysis, including herd as a random factor. Although, in study II, sows with a blood progesterone level of 4.5 ng/ml

or higher produced 1571 g less colostrum compared with sows with normal (<4.5 ng/ml) blood progesterone levels during the start of farrowing ($P < 0.05$).

4.3 Factors affecting sow colostrum quality and composition (I, II, III, IV)

Summaries of colostrum composition from all the studies are presented in Table 3. Concentration of immunoglobulins (especially IgG) varied among studies and between herds.

The study IV analysis was performed to learn more about these factors. We found that sow colostrum quality (IgG, IgA and IgM content) was significantly influenced by sow parity, with older sows having a higher immunoglobulin content, except for IgM. Parities over five had a negative influence on colostrum IgM. In addition, sow back fat at farrowing was positively correlated with colostrum IgA level ($P < 0.01$). We did not get similar parity effects in other studies. However, in study III, we found a significant effect of herd and dietary supplementation on colostrum IgG concentration.

4.4 Importance of colostrum for piglets' survival and weight gain (IV)

Both piglet colostrum intake and birth weight were positively associated with piglet ADG (birth to weaning), a colostrum intake of 1 g was associated with an increase in the ADG of 0.13 g till weaning ($P < 0.001$). Similarly, low litter BW_B and low litter colostrum intake during the first 24 h of life also increased the risk of a piglet dying before weaning (OR = 0.998; Confidence Interval = 0.998-0.999 and OR = 0.994; Confidence Interval = 0.992 – 0.997; $P < 0.001$ respectively). However, if piglets died before weaning or survived until weaning, colostrum uptake was, on average, 203.6 ± 11.6 g and 339.5 ± 3.5 g respectively (Figure 9). Weight at weaning and ADG of the piglets were correlated with CI independently of BW_B ($P = 0.001$). If a piglet consumed ≤ 200 g of colostrum and

managed to survive, its growth was on average the lowest, while proportionally higher CI correlated with higher weaning weight (Figure 10).

We found that the lower the sow back fat thickness at farrowing, the higher was the risk for piglets to die and/or for piglets to be treated with an antibiotic before weaning (OR = 0.923; Confidence Interval = 0.854 – 0.997; *P* = 0.04 and OR = 0.782; Confidence Interval = 0.630 – 0.970; *P* = 0.02 respectively). We also found that lower colostrum level of IgA increases the risk of piglet diarrhea during their first week of life (OR = 0.771; CI = 0.598 – 0.993; *P* = 0.04), and lower level of colostrum SAA tended to increase the risk of piglet litter diarrhea in first day of their life (OR = 0.998; CI = 0.995 – 1.0; *P* = 0.05). However, a high level of sow plasma progesterone at the end of farrowing (> 4.9 ng/ml) also increased the risk of litter diarrhea in the first day of their life (OR = 3.71; CI = 1.04 – 13.23; *P* = 0.04).

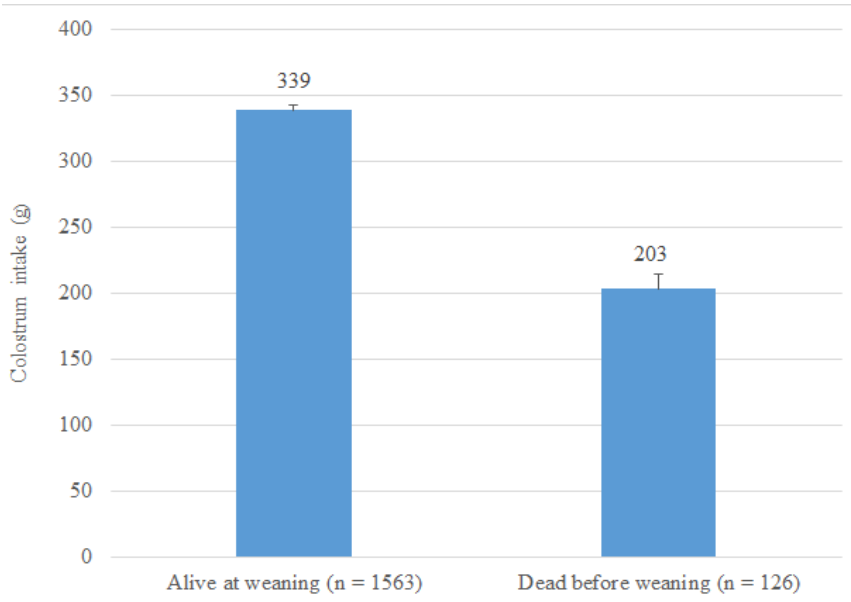

Figure 9. Piglet colostrum intake and survivability until weaning. Mean ± SEM

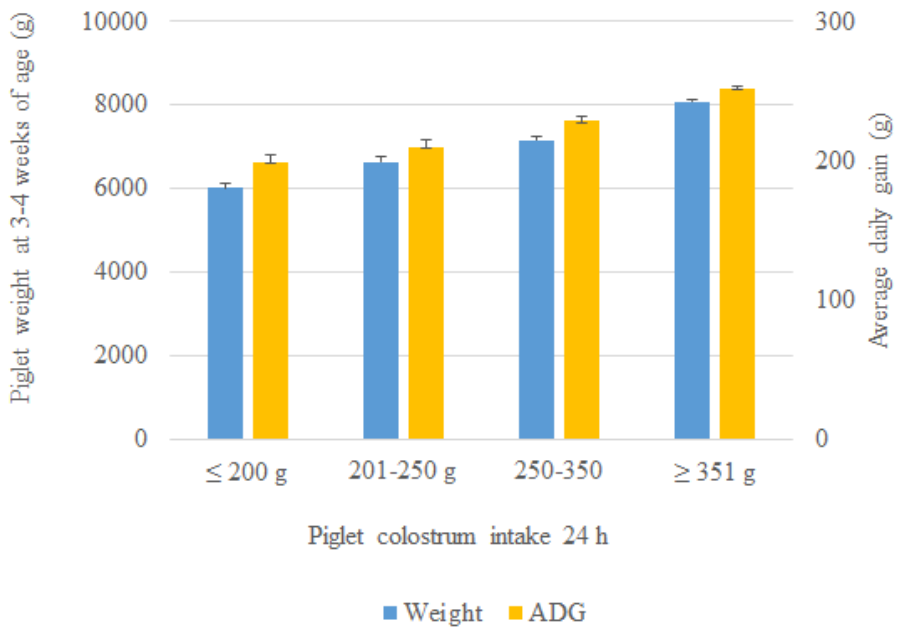

Figure 10. Correlation between average daily gain (ADG) and different colostrum intake categories (formulated according to Quesnel et al. (2012), with respective indicative average weight at 3-4 weeks found in this study piglet population. Mean ± SEM

4.5 Dietary supplementation with yeast derivatives during gestation and lactation (II, III)

4.5.1 Effect of dietary supplementation on sow performance

In study II, feeding sows a yeast derivative (YD) diet during gestation significantly reduced farrowing duration, birth interval and blood progesterone level around the start of farrowing. The average number of piglets born in total and live born piglets were increased for the YD fed sows. Similarly, dietary supplementation of gestating and

lactating diet with YD significantly ($P < 0.01$) increased sow CY and fat percentage of colostrum, but there were no significant changes in colostrum IgG, IgA, IgM, and protein, lactose and dry matter percentages.

In study III, late gestation dietary supplementation of sow feed with RAC resulted in significantly higher colostrum IgG levels ($P = 0.007$) in all three herds, although the treatment did not influence colostrum IgA and IgM concentration. However, the RAC supplementation of sow diets increased CY in two trials out of three. In addition, colostrum dry matter, lactose and protein percentages were unaffected by the dietary treatment. The RAC-supplemented sows tended to have increased colostrum SAA ($P < 0.10$) in all three trials.

4.5.2 Effect of dietary supplementation on gut microbiota of sow (II, III) and piglet (II) after birth

In study II, supplementing the sow diet with YD profoundly decreased the abundance of Proteobacteria species in their gut microbiota. In contrast, the species abundance of *Roseburia*, *Paraprevotella*, *Falsiporphyromonas*, *Eubacterium* and *Alkalitalea* significantly increased in sows fed with YD. However, the YD supplemented sows supported significant decreases in abundance of *Turicibacter*, *Papillibacter*, *Helicobacter*, *Escherichia/Shigella* and *Desulfovibrio* species in their gut microbiota.

In study III, feeding sows during the late gestation with RAC significantly increased Firmicutes ($P = 0.01$), and conversely Bacteroidetes and Proteobacteria were significantly less abundant ($P = 0.01$). RAC treatment resulted in significant increases in the abundances of *Romboutsia* and *Clostridium sensu stricto* ($P = 0.045$; $P = 0.011$ respectively) and significant decreases in the abundances of *Barnesiella*, *Sporobacter*, *Intestinimonas* and *Campylobacter* ($P = 0.016$; $P = 0.048$; $P = 0.009$; $P = 0.007$ respectively).

In study II, piglets at one week of age, raised with the sows fed with YD, exhibited significantly increased abundance of Firmicutes and decreased abundance of Bacteroidetes compared with the control. One-week old piglets raised with the YD sows also had a significantly greater proportion of the genera *Oscillibacter*, *Clostridium IV*, *Blautia*, *Gemmiger*, *Anaerobacterium*, *Anaerovibrio* and *Paraprevotella.*

4.5.3 Effect of gut microbiota on sow and piglet performance (II)

Pearson's correlation analysis revealed that high colostrum yield, high colostrum proteins, high colostrum IgG, low blood progesterone level and lower farrowing duration were positively correlated with the abundance of the bacterial families *Lacotobacillaceae*, *Ruminococcaceae*, *Acidaminococcaceae*, *Planctomycetaceae*, *Marinilabiliaceae*, *Veillonellaceae* and *Prevotellaceae*. Piglets growing faster and larger in size at four weeks of age had higher relative abundances of *Lactobacillus*, *Flavonifractor*, *Barnesiella*, *Gemmiger*, *Faecalibacterium*, *Roseburia* and *Anaerophaga* at one week of age. On the other hand, piglets growing more slowly and with poor ADG had more *Desulfovibrio*, *Acidaminobacter*, *Dethiosulfatibacter*, *Fastiduisipila*, *Ruminnococcus* and *Anaerotruncus* at one week of age (P <0.01).

5. Discussion

According to our hypothesis, the current study demonstrated that Brix measurement of a sow's fresh colostrum is an inexpensive, rapid and satisfactorily accurate method for estimating IgG concentration, providing an indication of differentiation between good and poor IgG content of colostrum. The study also showed that sow CY, piglet CI and colostrum composition are highly variable. A prolonged duration of farrowing and low Hp in sow plasma decreased sow CY, in agreement with our hypothesis. Sow parity had effects on colostrum Ig content and older sows (parity over 5) had more IgG and IgA in their colostrum than younger sows. Sows with thicker back fat at farrowing had higher colostrum IgA. In addition, piglet CI was correlated with ADG and survivability until weaning. The CY of a sow can also be improved by gestation feeding of YD. Feeding RAC in late gestation significantly increases colostrum IgG and therefore our hypothesis regarding this point was accepted. Feeding such functional ingredients to gestating sows increases the abundance of beneficial and fermentative bacteria (*Roseburia*, *Paraprevotella*, *Eubacterium*) while, some opportunistic pathogens, including Proteobacteria, especially the genera *Desulfovibrio*, *Escherichia/Shigella* and *Helicobacter*, were suppressed. These beneficial gut microbiota of the sow therefore improve the litter performance by promoting early beneficial gut microbiota colonization in neonatal piglets.

5.1 Brix refractometer measurement of colostrum quality and implication at farm level

We validated the Brix refractometer as an acceptable method for on-farm assessment of colostrum IgG content during the initial hours of parturition, when IgG is expected to peak. When the Brix refractometer in the early hours of colostrogenesis (0 to 3 h) returns values <20%, which were correlated with ELISA average colostrum IgG of 14.5 mg/ml, it indicates an unexpectedly low level of IgG for this period of time ("Poor" category). Our

intermediate category, “Borderline”, is more indicative of average values of colostrum IgG, which are slightly under expected averages. Categories “Adequate” and “Very good” express values that are around the expected averages or exceed them. Our category “Borderline” should be interpreted more carefully, and should not be considered to estimate an inadequate IgG content at early colostrogenesis, especially if the established Brix values are in the highest range of this category (23% to 24%). In contrast, levels falling into the lowest range of this category (20% to 21%) might be considered more critical. Our suggestion, for Borderline results with Brix, would be to take another sample after a maximum 1 to 2 h, to investigate if the development of the estimated IgG content is stable, increasing or decreasing from the initial value. Our choice of a cut-off point of 50 mg/ml of IgG in colostrum, as adequate at early colostrogenesis (0 to 3 h), is based on the lowest range of IgG found, at this specific stage, in 12 studies summarized by Hurley (2015).

The major practical point in assessing colostrum IgG content at the farm level might be to identify those sows with a low level of colostrum IgG content. Those sows represent a risk for successful acquisition of passive immunity for the piglets. The concentration of IgG in sow colostrum significantly affects the level of acquired IgG in piglet plasma (Kielland et al., 2015). According to our study I and those conducted by Devillers et al. (2011) and Quesnel (2011), within 10 to 12 h after farrowing the level of IgG dropped by half (35 to 40 mg/ml) and after 24 h there was a >70% drop in colostrum IgG content (10 to 16 mg/ml), which no longer represents an adequate level. Consequently, estimation, using the Brix refractometer, might be of help for effective on-farm colostrum management. This is of great importance, especially with large litters, when cross-fostering and split suckling are common management practices employed to maximize colostrum intake. In large litters the average amount of colostrum available is less for each piglet. Therefore, if the estimated colostrum IgG content appears not to be good, a farmer knowing it in advance can pay more attention to those management practices. Furthermore, as we know, the concentration of IgG in colostrum is highly

variable and there was to date no easy method to predict the level on-farm. Therefore, the Brix refractometer represents an inexpensive and satisfactory method for IgG estimation of sow colostrum at farm level.

5.2 Sow colostrum yield, factors and practical implications

The CY of sows in our studies was calculated according to the formula provided by Devillers et al. (2004). Therefore, studies conducted with the formula by Theil et al. (2014a) are not fully comparable with our studies. Theil's formula predicts almost 43% more colostrum yield than Devillers' formula (Devillers et al., 2004). The aims of our studies were to establish the factors that might impair sow colostrum production around farrowing. To overcome this, the farmer may try to minimize the negative factors, and maximize the positive ones to allow sows to improve their capacity regarding colostrum yield. Therefore, the studies were conducted in commercial piggeries, to ensure realistic conditions prevailed.

We found significantly lower sow CY if farrowing duration was relatively longer. This could be partly explained by hormonal changes because the duration of farrowing is mainly regulated by hormones, and therefore sow physiology should also be influenced (Algers and Uväns-Morberg, 2007). Several hormones regulate the onset and the progress of farrowing, namely progesterone, prolactin and oxytocin. In a longer farrowing duration, opioids (due to a pre-existing stress condition, like housing constriction) might be attributed to inhibition of oxytocin and prolactin secretion (Jarvis et al., 1997), thereby reducing the colostrum yield. However, progesterone, which remains at a high concentration throughout the entire pregnancy, should decrease markedly with the approach of parturition, to allow uterine contractions and lactogenesis (Liu et al., 1996). In the case that sows experience a delayed decrease in progesterone concentrations at farrowing, and thereby a delayed increase in prolactin, this might explain lower colostrum yield (Foisnet et al., 2010; Quesnel et al., 2012). In our studies, sow farrowing duration was relatively longer than that reported in earlier

studies (Devillers et al., 2007; Declerck et al., 2015). This was probably due to the larger litter size in our studies because farrowing duration is significantly influenced by litter size and number of stillborn piglets (Oliviero et al., 2010). After excessive prolonged farrowing sows are exhausted (Oliviero et al., 2010) and a slower recovery may interfere with the sow CY. In addition, in prolonged farrowing, piglets may suffer from hypoxia, and therefore reduced vitality, reduced suckling stimulus and reduced oxytocin level of the sow (Herpin et al., 1996).

In our study IV, we found that colostrum yield was significantly increased with increase in number of live-born piglets. This observation is not in accordance with previous findings (Devillers et al., 2007; Quesnel, 2011). This is probably because in recent years litter size has been continuously increasing and those reference studies are several years old and involved smaller litter sizes than our current studies. Therefore, our findings might be due to a numerically higher stimulation of the udder by the piglets. At the same time, the increase in CY for each additional piglet born is less than half of the recommended minimum requirement per piglet. Therefore, it does not justify further increase of litter size to improve the CY.

We found that CY was positively associated with sow plasma Hp (IV). At farrowing, sows undergo not only hormonal changes, but also substantial metabolic and physiological changes during this very short period of time (Algers and Uväns-Morberg, 2007). The acute phase response in sows can appear as nonspecific to disturbances in homeostasis due to inflammation, tissue injury during gestation and farrowing (Sorrells et al., 2007). The positive association of CY and Hp may not be directly related to the inflammation process, but it is more a reflection of Hp function as a hemoglobin binding protein (Eaton et al., 1982). Tissue damage (and hemolysis) can initially cause a decrease in serum Hp concentrations before the inflammatory stimulus initiates the Hp production in the liver. Studies with calves showed initially decreased Hp concentrations in the case of low-grade Eimeria infection (Seppä-Lassila et al., 2015) and during transportation

(Arthington et al., 2003). Thus in our study, the lower plasma Hp at farrowing associated with sows having lower CY may be connected with initiation of an inflammatory process, for example due to longer farrowing causing more tissue damage, hemolysis and depletion of circulating Hp. Inflammatory markers indicate that farrowing *per se* induces a systemic inflammatory response (Kaiser et al., 2018). The response may be greater in prolonged farrowing.

We found that high colostrum SAA tended to be linked to reduced neonatal piglet diarrhea incidence during the first day of life. Age-dependent studies showed that SAA plasma concentration is highest in neonate piglets (Moya et al., 2007) and calves (Orro et al., 2008). Higher colostrum SAA concentrations were associated with higher serum SAA concentrations of lambs at 1-5 days of age (Peetsalu et al., 2019). The function of SAA abundance in colostrum was suggested by Larson et al. (2003) to have a local beneficial effect on the neonatal gut. They found that colostrum-associated SAA peptide enhanced innate protection by stimulating intestinal epithelial cells and mucous production, thereby preventing binding of enteropathogenic bacteria. This could explain our findings between high SAA in colostrum and reduced piglet diarrhea. Interestingly, in study III we found that supplementing the sow diet with resin-acid-enriched composition (RAC) tended to increase the sow colostrum SAA. On the basis of the results of study III, higher SAA content in colostrum could be seen as a positive feature for improving piglet survival.

Sow body condition at farrowing has significant influence on CY. Decaluwé et al. (2013) reported that the sow back fat reduction at the end of gestation was negatively associated with sow CY. Our studies (IV) revealed that sow back fat thickness at farrowing was positively correlated with colostrum IgA, underlining the importance of fit sows at the start of lactation, avoiding excessive leanness. Another study also revealed a significant correlation between sow back fat during lactation and piglet survival and growth (Grandinson et al., 2005). Our findings (IV) on back fat thickness and

colostrum IgA content confirm this previous study where sufficiently high levels of sow body reserves were considered important at the start of lactation for piglet growth and survivability (Grandinson et al., 2005). This also strengthens our finding (IV) that piglet antibiotic treatment and survival until weaning were negatively associated with back fat thickness of the sow at farrowing.

Sufficient intake of colostrum is essential for neonate survival and it considerably decreases the piglet mortality until weaning. An uptake of 200 g of colostrum per piglet is crucial to keep the pre-weaning mortality as low as 7.1%. This rate can be up to 43.4% if the colostrum intake goes below 200 g per piglet (Devillers et al., 2011). We noted in our study IV that 36% of the piglets got less than 250 g of colostrum, and 23% of piglets got less than 200 g of colostrum during the first 24 h of their life. We confirmed (Figure 9) that insufficient CI could lead to a significant increase in piglet mortality until weaning, which was suggested by Decaluwé et al. (2014). Decaluwé et al. (2014) also mentioned that weaning weights of the piglets depended on CI. Our findings support the suggestion of Quesnel et al. (2012) that a minimum average of 250 g colostrum intake is recommended for each piglet to achieve good growth and body weight before weaning, as shown in Figure 10.

5.3 Sow farrowing environment, hormonal changes and colostrum yield

Although it was not the primary purpose of the study IV to investigate housing conditions at farrowing, it is notable that the average progesterone levels were lowest in the herds where sows had unlimited access to nest building materials and where sows were loosely group housed in getaway farrowing pens (herd 6). Meanwhile, the average progesterone level was higher in those herds in crate housing and in which sows had limited access to or no nesting material (Figure 8). A decrease in plasma progesterone and a rise in plasma concentration of prolactin prior to farrowing are known to initiate nest building behavior in prepartum sows (Algers and Uväns-Morberg, 2007). Yun et al.

(2014) demonstrated that onset nest building by providing abundant nesting materials and space was accompanied by an increase in plasma oxytocin concentration in prepartum sows. Moreover, the same study also confirmed that for sows in a non-crated system a plentiful supply of nesting materials prior to parturition tended to increase piglet serum IgG and IgM concentrations during early lactation. Our findings in study IV are in line with those of Yun et al. (2014) and Farmer (2016), suggesting that nesting materials and space for the movement of the sow may be beneficial for improving colostrum production, successful CI by piglets and ensure better quality colostrum. That we could not establish an association between progesterone level and CY could be due to the average progesterone level at farrowing being higher in this study than previously reported (Foisnet et al., 2010). In study IV, the higher plasma progesterone at the end of farrowing also increased the risk of neonatal piglet diarrhea during first day of life. This is probably because at each single herd level the higher than average progesterone level and reduced use of nesting material were associated with a detrimental effect on sow colostrum quality, as found previously (Foisnet et al., 2010; Yun et al., 2014). Piglets are born agamma-globulinemic and colostrum provides the immunological protection for the first 2-3 weeks (Rooke and Bland, 2002). Therefore, we can assume that litters of sows with higher plasma progesterone suffered from neonatal diarrhea because of lower immunoglobulin intake. This is supported by our findings that higher colostrum IgA content reduced the incidence of piglet diarrhea during the first week of their life.

5.4 Dietary supplementation of sow gestation diet

We found a significant improvement in CY of sows fed with yeast derivatives (YD) during pregnancy. Sows fed YD produced 23% more colostrum, which would be sufficient to feed three extra piglets in a litter, and had a 21% increase in colostrum fat content. Moreover, supplementing YD in gestating sows significantly reduced farrowing duration, birth interval, and plasma progesterone at farrowing and increased the number of live

born piglets. Our findings are in line with those of Le Dividich et al. (2009), reporting that sows fed with a YD during gestation and lactation produced 15% more colostrum and therefore the colostrum intake of piglets was 12% higher. The development of specific strategies to improve colostrum production and composition through sow gestation feeding has not been explored extensively. This is most likely because of the difficulty and laboriousness in measuring colostrum yield. Quesnel et al. (2012) suggested that feeding strategies able to favor the decline of progesterone and increase concentration of prolactin at lactogenesis II would be expected to improve colostrum yield. The effect of high fiber diet on CY of sows was tested in several studies (Loisel et al., 2013; Krogh et al., 2015; Feyera et al., 2018), but the results were not significant. Theil et al. (2014b) mentioned that the beneficial effect of fiber depends on the fiber source, and colostrum intake of the piglets was significantly greater when sows were fed with pectin residue, potato pulp or sugar beet pulp for a longer period during pregnancy.

The improvement in CY and other farrowing characteristics with YD supplementation might be due to the changes in the gut microbiota of the sows. The dietary supplementation with YD might have also been associated with positive immune stimulation (Bass et al., 2019), which may have improved the colostrum components. Many studies have demonstrated that certain microorganisms can exert beneficial effects on the sow and thus boost the production performance of the litter (Halas et al., 2012; Mach et al., 2015; Bass et al., 2019). We found that feeding YD to sows during pregnancy increased abundances of *Paraprevotella*, *Roseburia*, *Eubacterium* and *Alkalitalea*. Among these, *Paraprevotella* and *Roseburia* are the intestinal microbes that are able to degrade cellulose and hemicellulose (Chassard et al., 2007; Morotomi et al., 2009). Moreover, *Roseburia* and *Eubacterium* produce butyric acid, the main energy source for the colonocytes and protection from inflammation (Pryde et al., 2002; Ogwa et al., 2004; Canani et al., 2011). Thus, it can be speculated that in response to YD in feed, the gut microbiota switch to a population that may favor the host metabolism,

hydrolyze the feed and promote nutrition absorption. These factors could have led to the increased CY and better colostrum functional components established in our study.

In our study III we found that supplementing a sow late gestating diet with novel feed ingredients RAC consistently increased IgG in three different trials. This is the first study investigating the effects of this component in the swine diet. In recent years, many studies have looked at the impact of dietary supplementation that presumably has immunomodulation effects (e.g. fish oil, fermented liquid feed, mannan oligosaccharides) on colostrum immunoglobulin contents and immune status of piglets (Bontempo et al., 2004; Yao et al., 2012). Immunoglobulin G in the colostrum derives exclusively from maternal blood (Bourne and Curtis, 1973), therefore increasing concentration of IgG in maternal blood may improve the acquisition of passive immunity by piglets (Quesnel at al., 2012). RAC, a novel dietary product, typically comprises resin acids (active ingredients ~8%) and free fatty acids (~90%), and 2 to 3% neutral components. RAC has been used in broiler feed as a gut microbiota-modulating ingredient to improve performance (Kettunen et al., 2017; Vienola et al., 2018). The mechanism of action of resin as a functional feed additive has recently been defined as anti-inflammatory by Aguirre et al. (2019). In traditional human medicine RAC has been used to enhance immunity and regulate inflammation and wound healing (Kang et al., 2008; Park et al., 2017). In our study III, however, RAC supplementation significantly increased some beneficial and fermentative gut bacteria (*Romboutsia* and *Clostridium sensu stricto*) while some opportunistic pathogens, like *Barnesiella*, *Sporobacter*, *Intestinimonas*, *Campylobacter*, and the dysbiotic Proteobacteria, were suppressed.

Sows are considered to be the primary source of microbiota that colonize the newborn piglets immediately after birth (Tan et al., 2015; Li et al., 2017). Therefore, feeding gestating sows with specific functional ingredients can modulate sow gut microbiota, and may reduce the spread of pathogenic and dysbiotic bacteria to piglets. As it was mentioned by Kyriakis et al. (1999), supplementing the sow diet with probiotics can

reduce the shedding of pathogenic *E. coli* within the pens and thereby reduce the risk of spread as an environmental source. In our study II, suckling piglets at one week of age had unique microbiota acquired from the mother. This is in accordance with the results of many studies reporting that the maternal dietary treatment affected the composition of the gut microbiota in piglets, feeding sows with inulin, prebiotics, probiotics or soluble fibers (Tan et al., 2015; Li et al., 2017; Cheng et al., 2018).

5.5 Piglets' early gut microbiota development and weaning weight

We established that piglets at one week of age had a specific gut microbiota, similar to that of their mothers fed a YD. This specific gut microbiota significantly improved their ADG and their weaning weight. Researchers have shown that gut microbiota, acquired in early life, play multiple roles in host growth and health, including energy extraction from the diet, gut barrier function, immune system maturation, and growth performance (Martin et al., 2010; Cheng et al., 2019). However, alteration in this microbial acquisition may have permanent metabolic consequences (Nowland et al., 2019). Therefore, development of an optimal gut microbiota population during the early life period is of crucial importance for growth and metabolic health in neonatal piglets. Furthermore, besides a fecal transfer, also the chemical and microbial composition of colostrum and milk can influence the intestinal microbiota of the progeny (Mach et al., 2015). Although, dietary supplementation and alteration of gut microbiota have been extensively studied, the more indirect effects of maternal nutrition during pregnancy on the development of the neonatal intestine after birth, have until now largely remained unexplored and merit further investigation.

5.6 Practical implications

All the studies included in this thesis were carried in commercial piggeries using an experimental setup. We believed that such studies would reflect the realistic situation in pig production and help farmers build successful strategies accordingly.

Successful weaning should start with successful farrowing. With large litters, farrowing lasts longer, and more piglets are born smaller. Therefore, good and efficacious management of colostrum has to be practiced at the beginning of farrowing to maximize the output at weaning. Piglets are born devoid of gammaglobulins, they depend on sow colostrum in order to achieve the best protective passive immunity. On the other hand, the immunoglobulin content of colostrum is at its maximum only during the first 6 hours from the beginning of parturition, and declines rapidly thereafter. We demonstrated that a farmer can easily and inexpensively collect a drop of colostrum and estimate its IgG content using a Brix refractometer. Farmers will have sufficient time, in the first three hours after the start of farrowing, to assess the colostrum quality, according to Table 2, and optimize the appropriate supportive colostrum intake strategies, especially in hyper-prolific sows.

Farmers have to ensure a sufficient CI for the piglets to reduce pre-weaning mortality. We confirmed that a minimum average amount of 250 g colostrum intake per piglet is recommended to achieve good growth before weaning. A prolonged duration of farrowing and low Hp in sow plasma decreased sow CY. Therefore, easing the process of farrowing can reduce farrowing duration and pain/inflammation for the sow, improving colostrum production and allowing greater colostrum intake for the piglets. We found that the average progesterone levels were numerically lowest in the herds where sows had unlimited access to nest building materials and sows were loosely housed in pens. Therefore, it is strongly suggested that sufficient nesting materials are provided to the sow and proper maternal behavior is allowed to be expressed, which results in a consequent increase in the prolactin-to-progesterone ratio.

In addition, sow body condition and age are important factors that influence colostrum quality. We demonstrated that a sow with thicker back fat at farrowing had more IgA in its colostrum. However, Decaluwé et al. (2013) reported that late gestation back fat reductions were negatively associated with sow CY. Therefore, it appears essential that sows improve their body condition gradually during the whole pregnancy, arriving at farrowing in good body condition to allow protein turnover and promote sufficient colostrum yield. Moreover, colostrum of older sows (parity over 5) contains more IgG and IgA. In this case, we would suggest considering also these issues when planning early culling of sows.

Studies II and III suggested that gestation feeding of sows is of key importance to improve CY and quality. Feeding YD to sows during pregnancy decreased farrowing duration, and lowered plasma progesterone around farrowing. Moreover, providing sow YD throughout the gestation can increase the CY, allowing for greater colostrum intake of the litter. Feeding including YD increased more beneficial and fermentative gut microbiota in sows. Alternatively, we found that supplementing RAC in the late gestation diet of sows significantly improved IgG concentration in colostrum and also the beneficial gut microbiota population. Colostrum is mostly produced during the last week of gestation, as a result the mammary gland requires large amount of nutrients during this period. These factors can be considered when planning strategies to improve CY and colostrum quality. Improvement of the gut microbiota by dietary manipulation not only improves the production performance of a sow, it also helps to transfer beneficial microbiota to the piglets. These are key points that need to be considered for successful weaning of piglets. Those piglets growing faster and being heavier at four weeks of age had greater abundances of different bacteria like *Lactobacillus*, *Eubacterium* and *Clostridium sensu stricto* at one week of age, which were maternally derived.

5.7 Future research and new directions

From the present study it appears that the sow is the main limiting factor for CY, and approximately 36% of piglets did not get sufficient colostrum (study IV). Therefore, more research should be directed towards CY and the connections with gestation feeding, improvement of sow farrowing conditions, like sow free movement, maternal behavior expression, and supplementation of nest building materials.

Although the exact mechanism was not clear, the CY and colostrum IgG concentration can be influenced by late gestation feeding of a sow with YD and RAC. We also noted that sow body condition around parturition influenced colostrum IgA. It might be useful to investigate other specific feed ingredients that can help sows to preserve energy and maintain better body condition during late gestation up to farrowing.

The sow gut microbiota is important for improved physiology, which can ease the farrowing process, improve colostrum yield and promote early establishment of beneficial gut microbiota in piglets. The development of early gut microbiota in piglets appears to be important for higher weaning weight and better average daily gain. This merits further investigation.

Future research can also be directed at investigating suitable probiotic candidates, studying the sow's gut microbiota, developing a powder to spray around farrowing pen during parturition or incorporating it into the piglets' early creep feed. Moreover, a mixture of probiotic strains can also be tracked and isolated from faster growing and heavier piglets. These strains could be then fed to low birth weight piglets of the litter and the performance observed.

Finally, yet importantly, current methods of CY calculation are too laborious. From my personal experience, this is one of the most important limiting factors in the area of colostrum research. Therefore, an easy, reliable and cheap method is necessary for

reliable CY measurement. Advanced medical imaging techniques could help in this regard to measure functional mammary tissues and establish a correlation with CY.

6. Conclusions

1. Brix refractometers could be used at farm level to check colostrum during the initial hours after farrowing (0 to 3 h) to identify sows with an impaired IgG concentration at early colostrogenesis. This can indicate classification of IgG content in colostrum and allow the farmer to improve the management of lactating sows and neonate piglets.

2. Longer farrowing can be detrimental for CY In large litters. Easing the farrowing process, by, for example, allowing more space and providing nesting materials, could therefore be beneficial for sow health and for piglet survival and growth.

3. Sows with more back fat at farrowing had higher levels of IgA in colostrum, and piglets from such sows were at less risk of dying and being treated with antibiotic until weaning. Moreover, we found that SAA and IgA in colostrum had a beneficial influence on reducing piglet diarrhea.

4. Dietary supplementation of YD during gestation improves sow CY, reduces farrowing duration, lowers plasma progesterone around farrowing and increases the abundance of beneficial/fermentative gut microbiota in sows and piglets after birth.

5. Late gestation dietary supplementation of RAC can improve sow gut microbiota, increase IgG concentration of colostrum, and improve CY and piglet CI.

6. Dietary modulation of the gut microbiota correlates with lower progesterone level, lower farrowing duration, and improved sow physiology at farrowing and, therefore, production of more viable piglets with better gut microbiota.

7. Piglet CI was positively correlated with survivability and ADG of piglets until weaning. However, piglets having a relatively higher abundance of beneficial gut microbiota (*Lactobacillus*, *Flavonifractor*, *Barnesiella*, *Gemmiger*, *Faecalibacterium*, *Roseburia* and *Anaerophaga)* acquired from the mother at an early age, grew faster and were heavier at weaning.

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