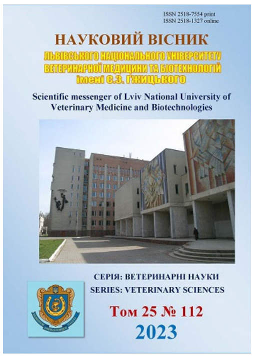

Науковий вісник Львівського національного університету ветеринарної медицини та біотехнологій імені С.З. Ґжицького. Серія: Ветеринарні науки

Scientific Messenger of Lviv National University of Veterinary Medicine and Biotechnologies. Series: Veterinary sciences

ISSN 2518–7554 print
ISSN 2518–1327 online
doi: 10.32718/nvlvet11229
https://nvlvet.com.ua/index.php/journal

UDC 619:339.9:615.453.8:636.4

Features of the functioning of the natural defense mechanisms of piglets under the influence of immunotropic substances

D. M. Masiuk✉, V. S. Nedzvetsky, A. V. Kokariev

Dnipro State Agrarian and Economic University, Dnipro, Ukraine

Article info

Received 16.10.2023
Received in revised form 16.11.2023
Accepted 17.11.2023

Dnipro State Agrarian and Economic University,
Serhiya Yefremova Str., 25,
Dnipro, 49000, Ukraine.
Tel.: +38-050-636-62-37
E-mail: dimasiuk@gmail.com

Masiuk, D. M., Nedzvetsky, V. S., & Kokariev, A. V. (2023). Features of the functioning of the natural defense mechanisms of piglets under the influence of immunotropic substances. Scientific Messenger of Lviv National University of Veterinary Medicine and Biotechnologies. Series: Veterinary sciences, 25(112), 181–192. doi: 10.32718/nvlvet11229

The number of studies related to detailed characteristics of immune system development in early stages of ontogenesis are directed to expansion of concepts of mechanisms of inherent and adaptive immunity in premature newborns. However, discrepancy in publication data and absence of clear conceptions about unique features of immune system in newborn piglets for different gestation periods have significant actuality for further investigation. The study was carried out to establish characteristics of phenotypic and functional characteristics of the immune cells and establishment of adaptive immunity in piglets. The antibody repertoire of sow has interested immunologists for decades, in part because of the ease with which large quantities of high affinity antibodies can be observed in serum, and into other fluids because of the presence of genetic variants for both light and heavy chain of all known immunoglobulin types. The integrative analysis of the cellular and humoral immunity in piglets during early ontogenesis carried out to clarify the exact mechanisms of the immune response modulation. Effectiveness and selectivity of the immunotropic chemicals application to regulate immune cell populations in piglets is presented. The progress in immune cell populations is regulated by the various cytokines production in the universal concentration-dependent manner. Furthermore, the development of the immune functions cross reacts with innate immunity mechanisms including anti-bacterial enzymes, epithelial barrier integrity in the both skin and intestine. The interaction between multiple components of innate immunity is a critic initiator of the dynamic changes in adaptive immunity. The natural resistance targets to the establishment of infection root and delays disease progression. The duration of the exposure to colostrum in important role in the dynamics of immune response as well as its efficacy. The chapter discusses the plural mechanisms so far proposed to be responsible for the modulation natural resistance.

Key words: *piglets, immune system, immunocorrection, colostral immunity, immune cells.*

Introduction

Non-specific protection of the most of animal species is represented by various proteins and peptides (Lipsit et al., 2022). They are present in the various biological fluids and circulate in the blood of animals in the significant amount to maintain the homeostasis (Law et al., 2017). These factors have antimicrobial properties or have the ability to activate other humoral and cellular immune defense mechanisms (Navarro et al., 2021).

Immunoglobulins, namely antibodies, are the group of soluble glycoproteins that persist in peripheral blood and biological fluids (Vodolazska et al., 2023). They have the ability to interact with antigens and thus cause neutralization of the latter (Du et al., 2023; Wang et al., 2023). This specific recognizing is accompanied by the antigen-antibody immune complex formation, which circulate in the blood for a while (Park et al., 2023).

The main source of immunoglobulins in newborn piglets is the colostrum (Le Floc′h et al., 2022; Innamma et al., 2023). Colostrum is the main factor in the newborn piglet protection, as it contains a large number of immune and biologically active substances that maintain piglet health beginning with the first colostrum consuming (Maciag et al., 2022). This result in the formation of both general and local colostral immunity, which level depends on the immune proteins concentration in colostrum (Merlot et al., 2019). Colostral immunity has an important impact to maintain the health, the viability, as well as the safety of piglets first week of life (Farmer & Edwards, 2022; Baxter et al., 2023). In this review, we discuss the anatomy and physiology of lactation, the immune functions of components provided to neonatal swine in mammary secretion, the importance of maternal immunity in the prevention and control of significant pathogens.

Physiological aspects of humoral immunity mechanisms mounting in early ontogenesis piglets. After birth, piglet has the potential ability for the functional restructuring of various systems and organs (Abrao Trad et al., 2023). This period is called the neonatal period. For pigs, it lasts about three weeks. Its end coincides with the ability to secrete hydrochloric acid by the glandular cells of the piglet's stomach (Vodolazska et al., 2023; Yao et al., 2023). At the same time, the newborn organism's physiological systems are in a state of unstable equilibrium. Its violation can lead to various diseases (Cheng et al., 2023). A certain dependence of piglet safety in the suckling period on the total protein and immunoglobulin levels in their blood serum has been determined (Hao et al., 2021; Chen et al., 2022).

The weight of piglets after birth is related to the mortality rate in the neonatal period (Charneca et al., 2023; Romero et al., 2023). The piglets with a body weight of 1.4 kg on average during the suckling period have a mortality rate of 8 %. Whereas the mortality rate of piglets with a body weight of 1.0 kg reaches 20 % (Harper & Bunter, 2023). This dependency is associated with differences in viability and with varying placental nutrient supply or endocrine differences in uterine conditions (Schoos et al., 2023). Therefore, the neonatal period is essential for the postnatal formation and animal development. Immediately after birth, newborn animals remain in the late fetal period for some time. During the same period, which coincides with the neonatal period and lasts 12–14-day, prenatal structures of the body, including components of the immune system, are transformed into newborns. This is indicated by dynamic changes in the haematopoiesis and immunopoiesis structures and blood components (Pieper et al., 2016; Le Huërou-Luron et al., 2018; Schlosser-Brandenburg et al., 2021). Leukocyte number, their phagocytic activity and the content of protein fractions in piglets before colostrum consumption are similar to the values of these parameters in pig fetuses of the late fetal period. In 4–6 hours after birth, the piglets' blood shows an increase of active microphages, phagocytic number, phagocytic capacity, albumin and γ-globulin content by more than 50 % (Forner et al., 2021; Inoue & Tsukahara, 2021).

Biochemical blood characteristics in piglets before colostrum consumption differ in the large range from those in animals on the first day of life (Ayala et al., 2023). The level of total protein, including the fraction of γ-globulins, glucose, bilirubin, increases, the activity of the enzymes ALT, GGT and LDH increases, and the amount of albumin, urea and alkaline phosphatase activity decreases.

Another factor indicating the immaturity of the newborn piglet immune system is the low bactericidal and lysozyme activity level in the blood serum (Huang et al., 2018; Qi et al., 2020). The early piglet development period is characterized by low natural resistance levels of the organism. Under these conditions, the blood serum bactericidal activity is in the range of 40.9 ± 1.90 %, the neutrophil phagocytic activity is 21.0 ± 0.84 %, and the phagocytic index is up to 1.0 ± 0.09 % (Kokariev & Masiuk, 2017). This is due to the haemopoietic organs immaturity. They produce young forms of leukocytes with a low phagocytosis capacity.

Physiological aspects of cellular immunity mechanisms mounting in early ontogenesis piglets. Morphological changes in the tissue structure of the spleen and thymus in early postnatal piglets are associated with their adaptive functional rate during the first three weeks of piglet life. They are characterized by an increase in the lymphoid tissue percentage (Dai et al., 2017; Ding et al., 2021). Before birth, the piglet lymph nodes only form a full range of morphological markers of immunocompetence in every tissue and cell type. Their functional development begins after birth and continues until the end of the lactation period (Zhang et al., 2019). In the late fetal and early neonatal periods, there is an increase in the absolute weight of the thymus, including its cortical zone, and an increase in the number of thymic bodies in the cerebral zone (Dai et al., 2017). At the moment of birth, the thymus cortical zone occupies about 80 % of the whole organ weight and contains about 95 % of all thymocytes. Meanwhile, in the cerebral thymus layer, single T-lymphocytes and Hassel bodies are detected. Their number increases rapidly in piglets on the second day of life. This is associated with the newborn immune system's response to antigens. Thymus involution in piglets begins during puberty (Ujčič-Vrhovnik et al., 2020). In one-day-old piglets, the number of T-lymphocytes in the thymus is about 78 %, on day 5 of life its level decreases to 55 % and remains at this level for 2 months. The newborn piglet thymus also contains B lymphocytes, but their number does not exceed 4 % (Ito et al., 2014; Dong et al., 2015). Also, many lymphoid nodules are created in the lymph nodes and spleen during proliferation immune cells. It reflects the potential to initiate the response against various antigens. This is confirmed by the intensive lymphoid tissue development in the tonsils, spleen, feather plaques, etc. In piglets of 2-week-old, secondary follicles appear in many lymph nodes. Starting from 3–4-week, plasma cells are found in the bone marrow (Sinkora & Butler, 2016).

The spleen parenchyma which is represented by red and white pulp, is not clearly demarcated in newborn piglets (Wang et al., 2020). White pulp makes up about 7 % of the organ parenchyma. During 7 days of life, the organ weight increases almost 3 times. This leads to an increase in white pulp by 16 %. The white pulp is composed of lymphoid cells, including lymphocytes, lymphoblasts, reticulocytes and macrophages. The generation of all aforementioned cell types accompanied by the immune system progress in newborn piglets and they development during the first week of life. Newborn animals have an unformed immune system during the first days of life, as indicated by the lymphoid tissue development state at the fetal level (Bæk et al., 2019). This is also facilitated by the morphological structure peculiarity of the placental barrier between the sow and the fetus. The pig's placenta is of a diffuse, epithelia-choroidal type. The placenta is impervious to macromolecules, including antibodies. This leads to the creation of an immune balance between the embryo or fetus and the mother's body (Vonnahme et al., 2001).

The fetal immune system is formed in the late fetal period due to the genetic potential realization and the placental barrier functioning (Bidarimath & Tayade, 2017). The immune system's central organs in piglets are formed at the end of prenatal development. Their maturation occurs after birth, directly under the antigenic load influence (Haverson et al., 2009). It is accompanied by an increase in the number of T-lymphocytes in piglets up to 2 months of age (Maciag et al., 2022).

Piglets during first two weeks of life are typified by a decrease in the number of phagocytic cells. It is associated with the colostrum immune defense in newborns formation. At the end of the first month of life, this indicator increases, which is associated with the formation of their own immune system (Bréa et al., 2020). At the same time, during the first month of life, a gradual increase in the number of T-lymphocytes occurs in the piglet's blood (Bæk et al., 2019). By the end of the second month of life, their number in the piglet blood achieves the adult pig level. It should be noted that the number of leukocytes in the newborn piglets' blood increases by more than 50 % during the first day of life, mainly due to T-lymphocytes. Whereas the B-lymphocyte level is several times lower than in 4–6-month-old pigs, and after 4 weeks their number doubles (Ren et al., 2015; Kreuzer-Redmer et al., 2018). Antibodies are detected in the blood of piglets before birth. This reflects a placental barrier violation by antigenic structures and the physical contact fetus with antigens. This is because the first immunoglobulins synthesis is possible in pig fetuses from the early fetal period (Park et al., 2021; Rebollada-Merino et al., 2023).

The development and growth of immunocompetent structures is autonomous in accordance with the genetic potential due to the placental barrier (Wippermann et al., 2018). It is determined by their ability to respond to the antigen action entering the body immediately after birth. Colostrum proteins are such an antigen, which activate the immunocompetent newborn organs (De Carvalho et al., 2023; Wang et al., 2023).

Under the colostrum proteins influence, lymphocytes rapidly colonize the mucous membranes and lymph nodes. As a result, prenatal lymphoid structures change into competent ones. This is confirmed by the inhibition of the immunocompetent structure’s formation for 20–30 days with late colostrum feeding. Thus, at the time of birth, piglets form a complex of immunocompetence morphological markers at the tissue and cellular levels. After birth, their functional development is activated (Wu et al., 2021; Jiang et al., 2022).

The immune components activity in piglets during the first weeks of life has a downward trend. At the end of the suckling period, immunity changes to an upward trend due to the activation and intensification of their own immune system components (Martins Soto et al., 2008; Holda et al., 2020).

Postnatal developmental physiological processes in mammals modulated with immunotropic chemicals. Immunoglobulins can’t cross the placenta in pregnant sow. Therefore, neonatal piglets are agammaglobulinemic at birth. However, this limiting for immune protection accompanied by weak growth of immunocompetent cells, they cannot mount rapid immune responses at systemic and mucosal sites (Salmon et al., 2009). The piglet survival depends directly on the acquisition of maternal immunity via colostrum and milk. Protection by maternal immunity is mediated by a number of factors, including specific systemic humoral immunity, involving mostly maternal IgG transferred from blood to colostrum and typically absorbed within the first 36 h of life (Yao et al., 2023). Passive mucosal immunity involves local humoral immunity, including the production of secretory IgA (sIgA), which is transferred principally via milk until weaning (Quesnel et al., 2023). The mammary gland (MG) produces sIgA, which is, then secreted into the milk via the poly-Ig receptor (pIgR) of epithelial cells (Jiang et al., 2016). These antibodies are produced in response to intestinal and respiratory antigens, including pathogens and commensal organisms. Protection is also mediated by cellular immunity, which is transferred via maternal cells present in mammary secretions (Yuan et al., 2022). The mechanisms underlying the various immunological links between MG and the mucosal surfaces involve hormonally regulated addressins and chemokines specific to these compartments. The enhancement of colostrogenic immunity depends on the stimulation of systemic immunity, whereas the enhancement of lactogenic immunity depends on appropriate stimulation at induction sites, an increase in cell trafficking from the gut and upper respiratory tract to the MG and, possibly, enhanced immunoglobulin production at the effector site and secretion in milk (Quesnel, 2011). In addition, mammary secretions provide factors other than immunoglobulins that protect the neonate and regulate the development of mucosal immunity-a key element of postnatal adaptation to environmental antigens (Yuan et al., 2022).

Maternal immunity plays a pivotal role in swine health and production because piglets are born agammaglobulinemic and with limited cell-mediated immunity, i.e. few peripheral lymphoid cells, immature lymphoid tissues, and no effector and memory T-lymphocytes (Suzuki et al., 2014; Poonsuk & Zimmerman, 2018). Swine do not become fully immunologically competent until about 4 weeks of age, which means that their compromised ability to respond to infectious agents during the first month of life must be supplemented by maternal immune components: circulating antibodies derived from colostrum; mucosal antibodies from colostrum and milk; and immune cells provided in mammary secretions (Kurihara et al., 2019; Masiuk et al., 2022). Because maternal immunity is highly effective at protecting piglets against specific pathogens, strengthening sow herd immunity against certain diseases through exposure or vaccination is a useful management tool for ameliorating clinical effects in piglets and delaying infection until the piglets' immune system is better prepared to respond (Grześkowiak et al., 2020; Zheng et al., 2021).

The immunological state of newborn animals’ issue and its changes in the neonatal period have been sufficiently studied. There are certain neonatal developmental periods that are critical in postnatal ontogeny and are associated with the immunodeficiencies development (Navarro Alvarez et al., 2015; Hervé et al., 2022). This is indicated by the cortisol level, which changes in the healthy piglets' blood during 7 months of life (Quesnel et al., 2023). Thus, in piglets of 1–3 day old, the level of this hormone is the highest, and ranges from 55.8–78.2 nmol/l. At the end of the first week of life, its concentration decreased to 34.15–46.00 nmol/l, and the lowest level of the hormone was recorded in piglets of 25 day old and in pigs of 2 and 3 months old – 19.9–30.6 nmol/l. This indicates that during the first 2 week of life, piglets are in a constant stress state, which occurs in animals at birth and is associated with changes in environmental conditions, activation of adaptation processes to the environment, etc. (Cheng et al., 2023) Also, an increase in cortisol levels is detected in piglets of 1, 5 and 6 months old, which in the first case is associated with the stress development due to weaning and a change in the feeding type, and at an older age – the effect of feed toxins and pathogens (Maskal et al., 2021).

Age-related immunodeficiencies are mainly detected in young pigs during the neonatal period and after weaning. The first immunodeficiency state can develop in piglets in the absence or insufficient colostrum consumption in the first days of life, after a disruption of intestinal absorption mechanisms, or at low immunobiological components of colostrum levels, against the background of stress experienced by the body after birth (Quesnel et al., 2023). Currently, piglets are the most sensitive to environmental influences (Fardisi et al., 2023).

The analysis of the piglets' mortality causes from birth to 5 months old shows that the piglets' mortality on the 1st day after birth is 13.5 %, including stillbirths, 3 % – on the 2nd and 3rd day, 1.9 % – on the 4th day (McPeek et al., 2023). Subsequently, piglet mortality gradually decreases to 0.02 % in the period from 4 to 22 weeks after birth. Such mortality rates are directly related to the functioning of piglets' immune defence mechanisms level (Bahrenthien et al., 2020). Newborns that do not receive colostrum in the first 4–6 hours after birth die within the first few days of life (Cheng et al., 2023). This is due to a sudden change in the immunoglobulin's concentration in colostrum, which is characterised by a 50 % decrease in the immune proteins level in colostrum 4–6 hours after the first piglet is born, since the main piglet immune defence mechanisms are colostral immunoglobulins of two main classes – IgG and IgA (Wang et al., 2023). In this regard, there are several critical periods in the first month of life: the first day, when newborns should receive colostral antibodies, and the end of the first week of life, when the colostral antibody concentration in the neonatal piglet's blood reaches the lowest concentration (Martínez-Boixaderas et al., 2022).

Within 2–3 weeks of birth, another critical neonatal period is identified, which is associated with a decrease in the colostral protective components level, mainly due to immunoglobulins, against the background of an unformed own immune system (Corsaut et al., 2021; Miguel et al., 2021). The next critical period associated with the piglet's immunodeficiency state is detected after weaning. At this time, there is a sudden change in the feeding type – a transition from dairy to concentrate feed. Against the background of the feed stress development, piglets have liver function disorders, immune defence mechanisms are depleted, resulting in secretory immunoglobulin synthesis disruption and reduced phagocytic cell activity (Saladrigas-García et al., 2022; Sampath et al., 2022; Scollo et al., 2023).

The immune system deficiencies development in mammals necessitates the search for a set of measures that would help prevent the pathology occurrence under such conditions. One of these measures is the use of drugs that directly or indirectly affect the body's immune system mechanisms, or selectively, certain components (Storino et al., 2023; Cull et al., 2023).

There are three groups of immunotropic drugs including immunostimulants, immunosuppressants and immunomodulators. Immunomodulators are drugs that restore the immune system function in therapeutic doses. That is why the immunological effect of immunomodulatory substances depends on the initial body immunity status: these substances reduce elevated and, conversely, increase decreased immunity indicators (Sepiashvili, 2015). Meanwhile, immunostimulants enhance immune responses, bringing reduced indicators to normal values, and immunosuppressants, on the contrary, suppress the body's immune response (Khonina et al., 2017; Arefieva et al., 2018).

There are 7 main groups of substances that have immunotropic properties: microbial, thymic, bone marrow, cytokine, nucleotide, plant and chemical (Hadden, 1993). Each group is divided into organic and chemical, except for the latter, which is divided into high and low molecular weight substances. Their essence is based on the basic immune system principles, the main activators of which in the mammalian body are foreign organic substances of a protein nature, accordingly, drugs based on this basis are classified as exogenous substances. The immune response development is driven by numerous immunoregulatory substances, the use of which also affects the immune response. Drugs based on these substances are classified as endogenous (Desbois et al., 2016; Kim et al., 2023).

The most pronounced immunomodulatory effect is provided by muramyldipeptide (MDP), a minimal bacterial wall peptidoglycan component (Grudyanov et al., 2021). Preparations based on it belong to the immunomodulator's third generation. TIR is found in the peptidoglycan of all known gram-positive and gram-negative bacteria. The main purpose of such drugs is to restore haemopoiesis, leukopoiesis, and immunity (Ushkalova et al., 2019). These drugs are widely used in medicine. In the form of a lactobacillus cell wall hydrolysation, they are used to correct the body's resistance and immune system in patients with burns, cancer and respiratory diseases (Jakopinv et al., 2012; Matsui et al., 2014).

The use of these drugs leads to an increase in haemopoiesis, with a particularly pronounced effect on leukocyte synthesis. Under the TIR effect, phagocytic cells are activated, the number of lymphocytes is normalised, cytokine synthesis is enhanced, etc. (Kalyuzhin et al., 2015). Thus, in order to correct the mammalian immune system state during immunosuppressive periods of organism development, it is necessary to use immunotropic drugs that directly or indirectly affect the resistance mechanisms and allow to ensure their optimally high level, and thus reduce the risk of infectious diseases in animals (Srinivasan & Babensee, 2020).

In spite of the fact that the use of immunotropic, probiotic and biologically active substance-based drugs to prevent the immunodeficiency development in animals has been sufficiently studied, a number of unresolved issues remain regarding their effect on newborn animals in the first days of life (Choudhury et al., 2023). One of the effective schemes for the use of immunotropic substances to address these issues is the use of corrective substances in the mother-fetus-newborn organism complex. This complex should be considered as a single system, which components are closely interconnected, and functional changes in each component affect the others (Kokarev & Masyuk, 2016; Kokarev & Masyuk, 2017).

Influencing the newborn immune system indirectly, through the mother's colostrum, by stimulating the sows' immunity is an extremely effective way of using immunocorrective drugs. In most cases, these are substances that are introduced into the sow's body with feed or parenterally (Alijotas-Reig et al., 2014; Maciag et al., 2022; Yuan et al., 2022).

Correction of the sows' and piglets' adaptive capacity is possible with the use of ascorbic acid. Feeding the latter to sows 10 day before farrowing can increase the newborn piglets' stress resistance during critical neonatal development periods (Gaykwad et al., 2019; Zhang et al., 2023). Biological metal compounds also affect the sows' immunity. For example, feeding inorganic chromium compounds to sows a week before farrowing results in a change in antioxidant defence during piglet development's critical periods, which contributes to the prooxidant processes inhibition in their body (Liu et al., 2023). All these feeding various substances to gestating sow schemes determine the antioxidants effect on preventing the stress and immunosuppression development in piglets, against which an increase in animal productivity is established (Wang et al., 2022; Li et al., 2023).

The application of immunotropic substances in the mother-fetus-newborn axis leads not only to an improvement in piglets and their mother natural resistance, but also improves their productive performance by increasing young animal safety, increasing average daily weight gain and reducing biological costs of adaptation and immunoreactivity (Jang et al., 2020). A good example is the use of Echinacea purpurea extract in gestating sow. This helps to increase immunity in piglets born from them. Such changes occur due to the intake of biologically active substances in the mother's milk and colostrum (Maass et al., 2005).

Feed additives are also used to correct the immunosuppressive state of piglets after weaning. For this purpose, starting from 3–5 day after birth, piglets are fed a peat-based biologically active feed additive. As a result, the piglets' safety has increased and their weight has increased during the suckling period. This contributes to increased stress resistance during weaning. Such changes are associated with the hematopoiesis processes activation against the background of a decrease in the immunosuppressive compounds functional load on the liver (Yefimov et al., 2016). These compounds are formed in the intestine during stress due to their absorption (Suwan et al., 2023).

There are reports on parenteral drugs administered to piglets in the first days of life for immunobiological correction of their body's defensive reactions to influence critical periods that may occur in postnatal ontogeny. One of the most common substance groups used for this purpose is tissue drugs (Papakonstantinou et al., 2023). It has been established that biologically active substances contained in thymus tissues can stimulate the T-cell component of piglet immunity (Farmer et al., 2022). A much more significant effect was observed after using an extract of thymic tissues in piglets at 20 day old (Ruedas-Torres et al., 2021).

The biogenic substances positive effect on the piglet immune system is accompanied by an increase in haemopoiesis, which was marked by a significant increase in the number of red blood cells, T- and B-lymphocytes and an increase in the phagocytic activity of leukocytes in piglets' blood (Brown et al., 2006). It should be noted that cellular immunity in newborn piglets can also be stimulated with fat-soluble vitamins and interferon, which promotes the reorganisation of the lymphocyte membrane receptor part and leads to increased plasma membrane receptor expression (Langel et al., 2019).

The combination of tissue preparations from the thymus and bone marrow used in piglets of the first days of life promotes an increase in bactericidal and lysozyme activity in the animal serum on day 5 (Benzoni et al., 2013). Studies have shown that strengthening the immune system in piglets is also possible with the use of a porcine immunoglobulins injectable solution. Their parenteral injection a week before weaning stimulates the level of nonspecific resistance in piglets by activating factors (Li et al., 2023).

Recent report evidence that the treatment with organic acid preparations during critical periods showed a positive effect on the state of natural piglet resistance (Jang et al., 2020). It was confirmed by an increase in the animal viability and productivity against the background of a decrease in piglet mortality by 2.5–3 times. An increase in immune defence was found in piglets fed sodium humate in combination with succinic acid and trace elements after weaning. This was reflected in an increase in the number of T-lymphocytes in the blood, which is associated with the succinic acid's ability to activate the phagocytic cells' oxygenation, which promotes their proliferation. Also, under the peat preparations influence, there is an increase in the T- and B-lymphocyte differentiation against the background of an increase in the number of red blood cells and a decrease in the lymphocyte index (Yefimov et al., 2016).

Current concepts and application of promising strategies for modulating the immune response in newborn piglets. Natural resistance in pigs is provided by a number of cellular and humoral mechanisms that are closely interconnected. All of them are dynamic indicators that are determined by both the pigs' genetic characteristics and adaptive changes to the various anthropogenic and natural factors (Tang et al., 2022).

Sows are particularly sensitive to environmental changes, as the pregnancy period causes a decrease in the level of their immune defence mechanisms both at the general and local levels, which affects the physiological adaptation reactions of both their organism and newborn young animals, and correlates with the animal safety and productivity level (Tuchscherer et al., 2012).

At the same time, newborn piglets, due to a number of biological characteristics, are prone to the immunodeficiency states development during the neonatal period of life, which contribute to the occurrence of infectious diseases and economic losses (Gava et al., 2017).

Due to the mechanisms of neonatal pathology development in piglets and the sow's immune system peculiarities, the use of immunotropic substances has become widespread. They are used according to various schemes both for sows during the farrowing period and directly to newborn piglets (Jang et al., 2020). The latter option does not allow to influence the newborn period immunodeficiency, so it is more effective to correct the piglets' natural resistance mechanisms indirectly, through the mother's body. The sows' immunobiological natural resistance mechanisms are in close contact and, owing to the factors of humoral and cellular defence mechanisms, provide immunotolerance to fetal antigens. Therefore, an active immunosuppressive or immunostimulatory effect on sows' resistance mechanisms can lead to fetal developmental disorders or fetal rejection (Wang et al., 2019).

Conclusion

Thus, at the time of birth, piglets form a complex of immunocompetence morphological markers at the tissue and cellular levels. After birth, their functional development is activated. The immune components activity in piglets during the first weeks of life has a downward trend. At the end of the suckling period, it changes to an upward trend due to the activation and intensification of their own immune system components.

Thus, the critical piglet developmental periods during the suckling period are based on immunodeficiency states, which are caused by a decrease in the natural resistance level and an increase in the animals' susceptibility to environmental pathogens. These conditions contribute to the piglets' death in the first days of life. To prevent the occurrence of immunosuppression in piglets, it is effective to use immunotropic substances in the mother-colustrum-newborn system, which purposefully or selectively affect the protective mechanisms of both mother and fetus, limitation the risk of developing an immunodeficiency state of the newborn or, if it occurs, reducing its degree, increasing the piglets' resistance capacity during postnatal ontogeny.

Prevent the immunodeficiency states development and correct the immune protective mechanisms of both newborns and their mothers, it is necessary to use drugs with immunomodulatory effects. Their use does not cause an imbalance in the mother-colostrum-newborn immune system and provides a less expressed but more effective impact on their body. However, the literature does not present exact data on the natural resistance efficacy in sow during the second half of pregnancy. Furthermore, the colostrum immunobiological parameters as well as functional immune system characteristics remains unclear for various molecular tools including new generation of immunotropic chemicals to correct the mother-colostrum-newborn axis functioning.

Conflict of interest

The authors declare that there is no conflict of interest.

References

Abrao Trad, A. T., Buddington, R., Enninga, E., Duncan, J., Schenone, C. V., Mari, G., Buddington, K., & Schenone, M. (2023). Report of an experiment with a fetal ex-utero support system in piglets. Cureus, 15(4), e38223. DOI: 10.7759/cureus.38223.

Alijotas-Reig, J., Llurba, E., & Gris, J. M. (2014). Potentiating maternal immune tolerance in pregnancy: a new challenging role for regulatory T cells. Placenta, 35(4), 241–248. DOI: 10.1016/j.placenta.2014.02.004.

Arefieva, T. I., Filatova, A. Y., Potekhina, A. V., & Shchinova, A. M. (2018). Immunotropic effects and proposed mechanism of action for 3-hydroxy-3-methylglutaryl-coenzyme a reductase inhibitors (Statins). Biochemistry. Biokhimiia, 83(8), 874–889. DOI: 10.1134/S0006297918080023.

Ayala, L., Sánchez, C. J., Hernández, F., Madrid, J., López, M. J., & Martínez-Miró, S. (2023). A comparison of haematological and biochemical profiles between intrauterine growth restriction and normal piglets at 72 hours postpartum. Animals, 13(22), 3540. DOI: 10.3390/ani13223540.

Bæk, O., Sangild, P. T., Thymann, T., & Nguyen, D. N. (2019). Growth restriction and systemic immune development in preterm piglets. Frontiers in immunology, 10, 2402. DOI: 10.3389/fimmu.2019.02402.

Bahrenthien, L., Kluess, J., Berk, A., Kersten, S., Saltzmann, J., Hüther, L., Schatzmayr, D., Schwartz-Zimmermann, H. E., Zeyner, A., & Dänicke, S. (2020). Detoxifying deoxynivalenol (DON)-contaminated feedstuff: consequences of sodium sulphite (SoS) treatment on performance and blood parameters in fattening pigs. Mycotoxin research, 36(2), 213–223. DOI: 10.1007/s12550-019-00385-5.

Baxter, E. M., Hall, S. A., Farish, M., Donbavand, J., Brims, M., Jack, M., Lawrence, A. B., & Camerlink, I. (2023). Piglets' behaviour and performance in relation to sow characteristics. Animal, 17(2), 100699. DOI: 10.1016/j.animal.2022.100699.

Benzoni, G., Foresti, F., Archetti, I. L., Coceva, G., Guyonvarch, A., & Alborali, L. (2013). Specific and non-specific immunity of piglets from sows fed diets containing specific fatty acids in field conditions. Journal of animal physiology and animal nutrition, 97(5), 996–1005. DOI: 10.1111/jpn.12014.

Bidarimath, M., & Tayade, C. (2017). Pregnancy and spontaneous fetal loss: A pig perspective. Molecular reproduction and development, 84(9), 856–869. DOI: 10.1002/mrd.22847.

Bréa, D., Soler, L., Fleurot, I., Melo, S., Chevaleyre, C., Berri, M., Labas, V., Teixeira-Gomes, A. P., Pujo, J., Cenac, N., Bähr, A., Klymiuk, N., Guillon, A., Si-Tahar, M., & Caballero, I. (2020). Intrinsic alterations in peripheral neutrophils from cystic fibrosis newborn piglets. Journal of cystic fibrosis: official journal of the European Cystic Fibrosis Society, 19(5), 830–836. DOI: 10.1016/j.jcf.2020.02.016.

Brown, D. C., Maxwell, C. V., Erf, G. F., Davis, M. E., Singh, S., & Johnson, Z. B. (2006). Ontogeny of T lymphocytes and intestinal morphological characteristics in neonatal pigs at different ages in the postnatal period. Journal of animal science, 84(3), 567–578. DOI: 10.2527/2006.843567x.

Charneca, R., Freitas, A., Nunes, J., & Le Dividich, J. (2023). Effects of the mean weight of uniform litters on sows and offspring performance. Animals, 13(19), 3100. DOI: 10.3390/ani13193100.

Chen, Y., Tibbs-Cortes, L. E., Ashley, C., Putz, A. M., Lim, K. S., Dyck, M. K., Fortin, F., Plastow, G. S., Dekkers, J. C. M., Harding, J. C. S., & PigGen Canada (2020). The genetic basis of natural antibody titers of young healthy pigs and relationships with disease resilience. BMC genomics, 21(1), 648. DOI: 10.1186/s12864-020-06994-0.

Cheng, Y., Azad, M. A. K., Ding, S., Liu, Y., Blachier, F., Ye, T., & Kong, X. (2023). Metabolomics analysis reveals the potential relationship between sow colostrum and neonatal serum metabolites in different pig breeds. Molecular nutrition & food research, 67(16), e2200677. DOI: 10.1002/mnfr.202200677.

Cheng, Z., Zhou, S. T., Zhang, X. H., Fu, Q., Yang, Y., Ji, W. B., & Liu, H. G. (2023). Effects of early intermittent maternal separation on behavior, physiological, and growth performance in piglets. Journal of animal science, 101, skad122. DOI: 10.1093/jas/skad122.

Choudhury, R., Gu, Y., Bolhuis, J. E., & Kleerebezem, M. (2023). Early feeding leads to molecular maturation of the gut mucosal immune system in suckling piglets. Frontiers in immunology, 14, 1208891. DOI: 10.3389/fimmu.2023.1208891.

Corsaut, L., Martelet, L., Goyette-Desjardins, G., Beauchamp, G., Denicourt, M., Gottschalk, M., & Segura, M. (2021). Immunogenicity study of a Streptococcus suis autogenous vaccine in preparturient sows and evaluation of passive maternal immunity in piglets. BMC veterinary research, 17(1), 72. DOI: 10.1186/s12917-021-02774-4.

Cull, C. A., Singu, V. K., Bromm, J. J., Lechtenberg, K. F., Amachawadi, R. G., & Cull, B. J. (2023). Effects of core antigen bacterin with an immunostimulant on piglet health and performance outcomes when challenged with enteric and respiratory pathogens. Antibiotics (Basel, Switzerland), 12(3), 599. DOI: 10.3390/antibiotics12030599.

Dai, C. H., Wu, J. Y., Zhao, C. X., Yu, L. H., Bao, W. B., & Wu, S. L. (2017). Nramp1 gene expression in different tissues of Meishan piglets from newborn to weaning. Genetics and molecular research: GMR, 16(1), DOI: 10.4238/gmr16019288.

De Carvalho, R. H., Callegari, M. A., Dias, C. P., Kirwan, S., da Costa, M. C. R., & da Silva, C. A. (2023). Euglena gracilis β-Glucans (1,3): Enriching Colostrum of Sow for Enhanced Piglet Immunity. Animals, 13(22), 3490. DOI: 10.3390/ani13223490.

Desbois, M., Le Vu, P., Coutzac, C., Marcheteau, E., Béal, C., Terme, M., Gey, A., Morisseau, S., Teppaz, G., Boselli, L., Jacques, Y., Béchard, D., Tartour, E., Cassard, L., & Chaput, N. (2016). IL-15 Trans-Signaling with the Superagonist RLI Promotes Effector/Memory CD8+ T Cell Responses and Enhances Antitumor Activity of PD-1 Antagonists. Journal of immunology (Baltimore, Md.: 1950), 197(1), 168–178. DOI: 10.4049/jimmunol.1600019.

Ding, D., Mou, D., Zhao, L., Jiang, X., Che, L., Fang, Z., Xu, S., Lin, Y., Zhuo, Y., Li, J., Huang, C., Zou, Y., Li, L., Wu, D., & Feng, B. (2021). Maternal organic selenium supplementation alleviates LPS induced inflammation, autophagy and ER stress in the thymus and spleen of offspring piglets by improving the expression of selenoproteins. Food & function, 12(22), 11214–11228. DOI: 10.1039/D1FO01653A.

Dong, L., Zhong, X., Zhang, L., Kong, L., Kong, Y., Kou, T., & Wang, T. (2015). Impaired intestinal mucosal immunity is associated with the imbalance of T lymphocyte sub-populations in intrauterine growth-restricted neonatal piglets. Immunobiology, 220(6), 775–781. DOI: 10.1016/j.imbio.2014.12.017.

Du, P., Yan, Q., Zhang, X. A., Zeng, W., Xie, K., Yuan, Z., Liu, X., Liu, X., Zhang, L., Wu, K., Li, X., Fan, S., Zhao, M., & Chen, J. (2023). Virus-like particle vaccines with epitopes from porcine epidemic virus and transmissible gastroenteritis virus incorporated into self-assembling ADDomer platform provide clinical immune responses in piglets. Frontiers in immunology, 14, 1251001. DOI: 10.3389/fimmu.2023.1251001.

Fardisi, M., Thelen, K., Groenendal, A., Rajput, M., Sebastian, K., Contreras, G. A., & Moeser, A. J. (2023). Early weaning and biological sex shape long-term immune and metabolic responses in pigs. Scientific reports, 13(1), 15907. DOI: 10.1038/s41598-023-42553-9.

Farmer, C., & Edwards, S. A. (2022). Review: Improving the performance of neonatal piglets. Animal: an international journal of animal bioscience, 16(2), 100350. DOI: 10.1016/j.animal.2021.100350.

Forner, R., Bombassaro, G., Bellaver, F. V., Maciag, S., Fonseca, F. N., Gava, D., Lopes, L., Marques, M. G., & Bastos, A. P. (2021). Distribution difference of colostrum-derived B and T cells subsets in gilts and sows. PloS one, 16(5), e0249366. DOI: 10.1371/journal.pone.0249366.

Gava, D., Souza, C. K., Mores, T. J., Argenti, L. E., Streck, A. F., Canal, C. W., Bortolozzo, F. P., & Wentz, I. (2017). Dynamics of vanishing of maternally derived antibodies of Ungulate protoparvovirus 1 suggests an optimal age for gilts vaccination. Tropical animal health and production, 49(5), 1085–1088. DOI: 10.1007/s11250-017-1301-0.

Gaykwad, C. K., De, U. K., Jadhav, S. E., Chethan, G. E., Akhilesh, Sahoo, N. R., Mondal, D. B., Gaur, G. K., Verma, M. R., & Chaudhuri, P. (2019). Adding α-tocopherol-selenium and ascorbic acid to periparturient sow diets influences hemogram, lipid profile, leptin, oxidant/antioxidant imbalance, performance and neonatal piglet mortality. Research in veterinary science, 125, 360–369. DOI: 10.1016/j.rvsc.2019.07.014.

Grudyanov, A. I., Fomenko, E. V., & Kalyuzhin, O. V. (2021). Antibakterial'nyi effekt immunomodulyatora na osnove kompozitsii muramilpeptidov pri khronicheskom generalizovannom parodontite. Stomatologiia, 100(4), 16–19 (in Ukrainian).

Grześkowiak, Ł., Pieper, R., Kröger, S., Martínez-Vallespín, B., Hauser, A. E., Niesner, R., Vahjen, W., & Zentek, J. (2020). Porcine Colostrum Protects the IPEC-J2 Cells and Piglet Colon Epithelium against Clostridioides (syn. Clostridium) difficile Toxin-Induced Effects. Microorganisms, 8(1), 142. DOI: 10.3390/microorganisms8010142.

Hadden, J. W. (1993). Immunostimulants. Trends in Immunology, 14(5), 169–174. DOI: 10.1016/0165-6147(93)90203-v.

Hao, Y., Wang, J., Teng, D., Wang, X., Mao, R., Yang, N., & Ma, X. (2021). A prospective on multiple biological activities of lactoferrin contributing to piglet welfare. Biochemistry and cell biology = Biochimie et biologie cellulaire, 99(1), 66–72. DOI: 10.1139/bcb-2020-0078.

Harper, J., & Bunter, K. L. (2023). Review: Improving pig survival with a focus on birthweight: a practical breeding perspective. Animal: an international journal of animal bioscience, 100914. DOI: 10.1016/j.animal.2023.100914.

Haverson, K., Corfield, G., Jones, P. H., Kenny, M., Fowler, J., Bailey, M., Stokes, C. R., & Miller, B. G. (2009). Effect of oral antigen and antibody exposure at birth on subsequent immune status. A study in neonatal pigs. International archives of allergy and immunology, 150(2), 192–204. DOI: 10.1159/000218123.

Hervé, J., Haurogné, K., Buchet, A., Bacou, E., Mignot, G., Allard, M., Leblanc-Maridor, M., Gavaud, S., Lehébel, A., Terenina, E., Mormède, P., Merlot, E., Belloc, C., Bach, J. M., & Lieubeau, B. (2022). Pathogen exposure influences immune parameters around weaning in pigs reared in commercial farms. BMC immunology, 23(1), 61. DOI: 10.1186/s12865-022-00534-z.

Holda, K. O., Masiuk, D. M., Kokariev, A. V., & Vasilenko, T. O. (2020). Colostral immunity of piglets to the virus of Aujeszky's disease with active sows' immunization. Theoretical and Applied Veterinary Medicine, 8(4), 257–260. DOI: 10.32819/2020.84037.

Huang, G., Li, X., Lu, D., Liu, S., Suo, X., Li, Q., & Li, N. (2018). Lysozyme improves gut performance and protects against enterotoxigenic Escherichia coli infection in neonatal piglets. Veterinary research, 49(1), 20. DOI: 10.1186/s13567-018-0511-4.

Innamma, N., Ngamwongsatit, N., & Kaeoket, K. (2023). The effects of using multi-species probiotics in late-pregnant and lactating sows on milk quality and quantity, fecal microflora, and performance of their offspring. Veterinary world, 16(10), 2055–2062. DOI: 10.14202/vetworld.2023.2055-2062.

Inoue, R., & Tsukahara, T. (2021). Composition and physiological functions of the porcine colostrum. Animal science journal = Nihon chikusan Gakkaiho, 92(1), e13618. DOI: 10.1111/asj.13618.

Ito, T., Sendai, Y., Yamazaki, S., Seki-Soma, M., Hirose, K., Watanabe, M., Fukawa, K., & Nakauchi, H. (2014). Generation of recombination activating gene-1-deficient neonatal piglets: a model of T and B cell deficient severe combined immune deficiency. PloS one, 9(12), e113833. DOI: 10.1371/journal.pone.0113833.

Jakopin, Ž., Gobec, M., Mlinarič-Raščan, I., & Sollner Dolenc, M. (2012). Immunomodulatory properties of novel nucleotide oligomerization domain 2 (nod2) agonistic desmuramyldipeptides. Journal of medicinal chemistry, 55(14), 6478–6488. DOI: 10.1021/jm300503b.

Jang, K. B., Kim, J. H., Purvis, J. M., Chen, J., Ren, P., Vazquez-Anon, M., & Kim, S. W. (2020). Effects of mineral methionine hydroxy analog chelate in sow diets on epigenetic modification and growth of progeny. Journal of animal science, 98(9), skaa271. DOI: 10.1093/jas/skaa271.

Jang, K. B., Purvis, J. M., & Kim, S. W. (2020). Supplemental effects of dietary lysophospholipids in lactation diets on sow performance, milk composition, gut health, and gut-associated microbiome of offspring. Journal of animal science, 98(8), skaa227. DOI: 10.1093/jas/skaa227.

Jiang, X., Hu, J., Thirumalai, D., & Zhang, X. (2016). Immunoglobulin Transporting Receptors Are Potential Targets for the Immunity Enhancement and Generation of Mammary Gland Bioreactor. Frontiers in immunology, 7, 214. DOI: 10.3389/fimmu.2016.00214.

Jiang, Z., Su, W., Li, W., Wen, C., Du, S., He, H., Zhang, Y., Gong, T., Wang, X., Wang, Y., Jin, M., & Lu, Z. (2022). Bacillus amyloliquefaciens 40 regulates piglet performance, antioxidant capacity, immune status and gut microbiota. Animal nutrition (Zhongguo xu mu shou yi xue hui), 12, 116–127. DOI: 10.1016/j.aninu.2022.09.006.

Kalyuzhin, O. V., Artem'eva, K. A., Boltovskaya, M. N., Bunyatyan, K. A., Inviyayeva, E. V., Vinnitskii, L. I., & Karaulov, A. V. (2015). Intraperitoneal Administration of Muramyl Dipeptide β-Heptylglycoside to Pregnant and Non-Pregnant Female Mice Modulates Production of Th1/Th2/Th17/Tr1 Cytokines by Splenocytes Ex Vivo. Bulletin of experimental biology and medicine, 159(1), 53–57. DOI: 10.1007/s10517-015-2888-7.

Khonina, T. G., Ivanenko, M. V., Chupakhin, O. N., Safronov, A. P., Bogdanova, E. A., Karabanalov, M. S., Permikin, V. V., Larionov, L. P., & Drozdova, L. I. (2017). Silicon-zinc-glycerol hydrogel, a potential immunotropic agent for topical application. European journal of pharmaceutical sciences: official journal of the European Federation for Pharmaceutical Sciences, 107, 197–202. DOI: 10.1016/j.ejps.2017.07.012.

Kim, S., Park, C. I., Lee, S., Choi, H. R., & Kim, C. H. (2023). Reprogramming of IL-12 secretion in the PDCD1 locus improves the anti-tumor activity of NY-ESO-1 TCR-T cells. Frontiers in immunology, 14, 1062365. DOI: 10.3389/fimmu.2023.1062365.

Kokarev, A., & Masiuk, D. (2016). The natural resistance's condition of sows under the influence of the preparation «imunolac». Scientific Messenger of LNU of Veterinary Medicine and Biotechnologies. Series: Veterinary Sciences, 18(4(72), 32–36. URL: https://nvlvet.com.ua/index.php/journal/article/view/980.

Kokarev, A., & Masiuk, D. (2017). Formation mechanisms of immune cells protection in pigs under the influence of «Imunolak». Scientific Messenger of LNU of Veterinary Medicine and Biotechnologies. Series: Veterinary Sciences, 19(77), 214–219. URL: https://nvlvet.com.ua/index.php/journal/article/view/1211.

Kreuzer-Redmer, S., Arends, D., Schulte, J. N., Karweina, D., Korkuc, P., Wöltje, N., Hesse, D., Pieper, R., Gerdts, V., Zentek, J., Meurens, F., & Brockmann, G. A. (2018). High dosage of zinc modulates T-cells in a time-dependent manner within porcine gut-associated lymphatic tissue. The British journal of nutrition, 120(12), 1349–1358. DOI: 10.1017/S0007114518002908.

Kurihara, T., Matsuda, S., Nakamura, Y., Suzuki, S., Fuchimoto, D., Onishi, A., Saeki, K., Nakagawa, T., Fujiwara, R., Kamata, M., Kuramoto, J., Kameyama, K., Sekino, M., Kusakabe, M., Hayashida, T., Jinno, H., & Kitagawa, Y. (2019). Establishment of a model of sentinel lymph node metastasis using immunodeficient swine. Scientific reports, 9(1), 7923. DOI: 10.1038/s41598-019-44171-w.

Langel, S. N., Paim, F. C., Alhamo, M. A., Lager, K. M., Vlasova, A. N., & Saif, L. J. (2019). Oral vitamin A supplementation of porcine epidemic diarrhea virus infected gilts enhances IgA and lactogenic immune protection of nursing piglets. Veterinary research, 50(1), 101. DOI: 10.1186/s13567-019-0719-y.

Law, J., UCVM Class of 2015, McCorkell, R., Muench, G., Wynne-Edwards, K., Schaetzl, H. M., Solis, C., Nourozieh, N., Waeckerlin, R., Eschbaumer, M., Horsman, S., & Czub, M. (2017). Induction of humoral immune response in piglets after perinatal or post-weaning immunization against porcine circovirus type-2 or keyhole limpet hemocyanin. Canadian journal of veterinary research = Revue canadienne de recherche veterinaire, 81(1), 5–11. URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5220598.

Le Floc'h, N., Achard, C. S., Eugenio, F. A., Apper, E., Combes, S., & Quesnel, H. (2022). Effect of live yeast supplementation in sow diet during gestation and lactation on sow and piglet fecal microbiota, health, and performance. Journal of animal science, 100(8), skac209. DOI: 10.1093/jas/skac209.

Le Huërou-Luron, I., Bouzerzour, K., Ferret-Bernard, S., Ménard, O., Le Normand, L., Perrier, C., Le Bourgot, C., Jardin, J., Bourlieu, C., Carton, T., Le Ruyet, P., Cuinet, I., Bonhomme, C., & Dupont, D. (2018). A mixture of milk and vegetable lipids in infant formula changes gut digestion, mucosal immunity and microbiota composition in neonatal piglets. European journal of nutrition, 57(2), 463–476. DOI: 10.1007/s00394-016-1329-3.

Li, L., Wang, H., Dong, S., & Ma, Y. (2023). Supplementation with alpha-glycerol monolaurate during late gestation and lactation enhances sow performance, ameliorates milk composition, and improves growth of suckling piglets. Journal of animal science and biotechnology, 14(1), 47. DOI: 10.1186/s40104-023-00848-x.

Li, Y., Xu, L., Jiao, D., Zheng, Z., Chen, Z., Jing, Y., Li, Z., Ma, Z., Feng, Y., Guo, X., Wang, Y., He, Y., Zheng, H., & Xiao, S. (2023). Genomic similarity and antibody-dependent enhancement of immune serum potentially affect the protective efficacy of commercial MLV vaccines against NADC30-like PRRSV. Virologica Sinica, 38(5), 813–826. DOI: 10.1016/j.virs.2023.08.010.

Lipsit, S., Facciuolo, A., Scruten, E., Griebel, P., & Napper, S. (2022). Plasma Cytokines and Birth Weight as Biomarkers of Vaccine-Induced Humoral Responses in Piglets. Frontiers in veterinary science, 9, 922992. DOI: 10.3389/fvets.2022.922992.

Liu, H. W., Gao, L. M., Liu, G. Y., Tai, W. J., Xie, C. Y., & Wu, X. (2023). Effects of Maternal Dietary Enteromorpha prolifera Polysaccharide Iron Supplement on Mineral Elements and Iron Level of Neonatal Piglets. Biological trace element research. DOI: 10.1007/s12011-023-03874-y.

Maass, N., Bauer, J., Paulicks, B. R., Böhmer, B. M., & Roth-Maier, D. A. (2005). Efficiency of Echinacea purpurea on performance and immune status in pigs. Journal of animal physiology and animal nutrition, 89(7-8), 244–252. DOI: 10.1111/j.1439-0396.2005.00501.x.

Maciag, S. S., Bellaver, F. V., Bombassaro, G., Haach, V., Morés, M. A. Z., Baron, L. F., Coldebella, A., & Bastos, A. P. (2022). On the influence of the source of porcine colostrum in the development of early immune ontogeny in piglets. Scientific reports, 12(1), 15630. DOI: 10.1038/s41598-022-20082-1.

Maciag, S., Volpato, F., Bombassaro, G., Forner, R., Oliveira, K. P. V., Bovolato, A. L. C., Lopes, L., & Bastos, A. P. (2022). Effects of freezing storage on the stability of maternal cellular and humoral immune components in porcine colostrum. Veterinary immunology and immunopathology, 254, 110520. DOI: 10.1016/j.vetimm.2022.110520.

Martínez-Boixaderas, N., Garza-Moreno, L., Sibila, M., & Segalés, J. (2022). Impact of maternally derived immunity on immune responses elicited by piglet early vaccination against the most common pathogens involved in porcine respiratory disease complex. Porcine health management, 8(1), 11. DOI: 10.1186/s40813-022-00252-3.

Martins Soto, F. R., Regina Pinheiro, S., Honma Ito, F., Maria Moraes, Z., Paldes Gonçales, A., Santos de Azevedo, S., Bernardi, F., Rodrigues Camargo, S., & Arruda Vasconcellos, S. (2008). Evaluation of colostral immunity in swine with commercial anti-leptospira polyvalent whole-bacteria vaccine. Comparative immunology, microbiology and infectious diseases, 31(4), 327–335. DOI: 10.1016/j.cimid.2007.03.002.

Masiuk, D., Tamchuk, L. M., Nedzvetsky, V., & Kokariev, A. (2022). Study of the monoglycerides features as a promising alternative to antibiotics in feeding broiler chickens. Scientific Messenger of LNU of Veterinary Medicine and Biotechnologies. Series: Veterinary Sciences, 24(107), 110–118. DOI: 10.32718/nvlvet10718.

Maskal, J. M., Brito, L. F., Duttlinger, A. W., Kpodo, K. R., McConn, B. R., Byrd, C. J., Richert, B. T., Marchant, J. N., Lay, D. C., Jr, Perry, S. D., Lucy, M. C., Safranski, T. J., & Johnson, J. S. (2021). Characterizing the postnatal hypothalamic-pituitary-adrenal axis response of in utero heat stressed pigs at 10 and 15 weeks of age. Scientific reports, 11(1), 22527. DOI: 10.1038/s41598-021-01889-w.

Matsui, K., & Ikeda, R. (2014). Peptidoglycan in combination with muramyldipeptide synergistically induces an interleukin-10-dependent T helper 2-dominant immune response. Microbiology and immunology, 58(4), 260–265. DOI: 10.1111/1348-0421.12139.

McPeek, A. C., Patton, B., Columbus, D. A., Olver, T. D., Rodrigues, L. A., Sands, J. M., Weber, L. P., & Ferguson, D. P. (2023). Low birth weight and reduced postnatal nutrition lead to cardiac dysfunction in piglets. Journal of animal science, 101, skad364. DOI: 10.1093/jas/skad364.

Merlot, E., Pastorelli, H., Prunier, A., Père, M. C., Louveau, I., Lefaucheur, L., Perruchot, M. H., Meunier-Salaün, M. C., Gardan-Salmon, D., Gondret, F., & Quesnel, H. (2019). Sow environment during gestation: part I. Influence on maternal physiology and lacteal secretions in relation with neonatal survival. Animal: an international journal of animal bioscience, 13(7), 1432–1439. DOI: 10.1017/S1751731118002987.

Miguel, J., Mitjana, O., Tejedor, M. T., Martínez, A., & Falceto, M. V. (2021). Supplementing Colostrum from Multiparous Sows: Effects on Performance and Health in Piglets from Gilts in Farm Conditions. Animals: an open access journal from MDPI, 11(9), 2563. DOI: 10.3390/ani11092563.

Navarro Alvarez, N., Zhu, A., Arellano, R. S., Randolph, M. A., Duggan, M., Scott Arn, J., Huang, C. A., Sachs, D. H., & Vagefi, P. A. (2015). Postnatal xenogeneic B-cell tolerance in swine following in utero intraportal antigen exposure. Xenotransplantation, 22(5), 368–378. DOI: 10.1111/xen.12186.

Navarro, E., Mainau, E., de Miguel, R., Temple, D., Salas, M., & Manteca, X. (2021). Oral Meloxicam Administration in Sows at Farrowing and Its Effects on Piglet Immunity Transfer and Growth. Frontiers in veterinary science, 8, 574250. DOI: 10.3389/fvets.2021.574250.

Papakonstantinou, G. I., Gougoulis, D. A., Voulgarakis, N., Maragkakis, G., Galamatis, D., Athanasiou, L. V., & Papatsiros, V. G. (2023). Effects of Injectable Administration of Dexamethasone Alone or in Combination with Vitamin E/Se in Newborn Low Birth Weight Piglets. Veterinary sciences, 10(2), 135. DOI: 10.3390/vetsci10020135.

Park, H. J., Choi, E. A., Choi, S. M., Choi, Y. K., Lee, J. I., & Jung, K. C. (2023). IL-4/IL-4 Ab complex enhances the accumulation of both antigen-specific and bystander CD8 T cells in mouse lungs infected with influenza A virus. Laboratory animal research, 39(1), 32. DOI: 10.1186/s42826-023-00183-2.

Park, Y., Oh, Y., Wang, M., Ganges, L., Bohórquez, J. A., Park, S., Gu, S., Park, J., Lee, S., Kim, J., & Sohn, E. (2021). A Novel E2 Glycoprotein Subunit Marker Vaccine Produced in Plant Is Able to Prevent Classical Swine Fever Virus Vertical Transmission after Double Vaccination. Vaccines, 9(5), 418. DOI: 10.3390/vaccines9050418.

Pieper, R., Scharek-Tedin, L., Zetzsche, A., Röhe, I., Kröger, S., Vahjen, W., & Zentek, J. (2016). Bovine milk-based formula leads to early maturation-like morphological, immunological, and functional changes in the jejunum of neonatal piglets. Journal of animal science, 94(3), 989–999. DOI: 10.2527/jas.2015-9942.

Poonsuk, K., & Zimmerman, J. (2018). Historical and contemporary aspects of maternal immunity in swine. Animal health research reviews, 19(1), 31–45. DOI: 10.1017/S1466252317000123.

Qi, M., Tan, B., Wang, J., Liao, S., Li, J., Cui, Z., Shao, Y., Ji, P., & Yin, Y. (2021). Postnatal growth retardation is associated with deteriorated intestinal mucosal barrier function using a porcine model. Journal of cellular physiology, 236(4), 2631–2648. DOI: 10.1002/jcp.30028.

Quesnel, H. (2011). Colostrum production by sows: variability of colostrum yield and immunoglobulin G concentrations. Animal: an international journal of animal bioscience, 5(10), 1546–1553. DOI: 10.1017/S175173111100070X.

Quesnel, H., Resmond, R., Merlot, E., Père, M. C., Gondret, F., & Louveau, I. (2023). Physiological traits of newborn piglets associated with colostrum intake, neonatal survival and preweaning growth. Animal: an international journal of animal bioscience, 17(6), 100843. DOI: 10.1016/j.animal.2023.100843.

Rebollada-Merino, A., García-Seco, T., Pérez-Sancho, M., Domínguez, L., & Rodríguez-Bertos, A. (2023). Histopathologic and immunohistochemical findings in the placentas and fetuses of domestic swine naturally infected with Brucella suis biovar 2. Journal of veterinary diagnostic investigation: official publication of the American Association of Veterinary Laboratory Diagnosticians, Inc, 35(3), 258–265. DOI: 10.1177/10406387231163867.

Ren, Z. H., Yuan, W., Deng, H. D., Deng, J. L., Dan, Q. X., Jin, H. T., Tian, C. L., Peng, X., Liang, Z., Gao, S., Xu, S. H., Li, G., & Hu, Y. (2015). Effects of antibacterial peptide on cellular immunity in weaned piglets. Journal of animal science, 93(1), 127–134. DOI: 10.2527/jas.2014-7933.

Romero, M., Calvo, L., Morales, J. I., Magro, A., Rodríguez, A. I., Segura, J., Escudero, R., López-Bote, C., & Olivares, Á. (2023). Short- and Long-Term Effects of Split-Suckling in Pigs According to Birth Weight. Animals: an open access journal from MDPI, 13(22), 3521. DOI: 10.3390/ani13223521.

Ruedas-Torres, I., Gómez-Laguna, J., Sánchez-Carvajal, J. M., Larenas-Muñoz, F., Barranco, I., Pallarés, F. J., Carrasco, L., & Rodríguez-Gómez, I. M. (2021). Activation of T-bet, FOXP3, and EOMES in Target Organs From Piglets Infected With the Virulent PRRSV-1 Lena Strain. Frontiers in immunology, 12, 773146. DOI: 10.3389/fimmu.2021.773146.

Saladrigas-García, M., Durán, M., D'Angelo, M., Coma, J., Pérez, J. F., & Martín-Orúe, S. M. (2022). An insight into the commercial piglet's microbial gut colonization: from birth towards weaning. Animal microbiome, 4(1), 68. DOI: 10.1186/s42523-022-00221-9.

Salmon, H., Berri, M., Gerdts, V., & Meurens, F. (2009). Humoral and cellular factors of maternal immunity in swine. Developmental and comparative immunology, 33(3), 384–393. DOI: 10.1016/j.dci.2008.07.007.

Sampath, V., Song, J. H., Jeong, J., Mun, S., Han, K., & Kim, I. H. (2022). Nourishing neonatal piglets with synthetic milk and Lactobacillus sp. at birth highly modifies the gut microbial communities at the post-weaning stage. Frontiers in microbiology, 13, 1044256. DOI: 10.3389/fmicb.2022.1044256.

Schlosser-Brandenburg, J., Ebner, F., Klopfleisch, R., Kühl, A. A., Zentek, J., Pieper, R., & Hartmann, S. (2021). Influence of Nutrition and Maternal Bonding on Postnatal Lung Development in the Newborn Pig. Frontiers in immunology, 12, 734153. DOI: 10.3389/fimmu.2021.734153.

Schoos, A., Muro, B. B. D., Carnevale, R. F., Chantziaras, I., Biebaut, E., Janssens, G. P. J., & Maes, D. (2023). Relationship between piglets' survivability and farrowing kinetics in hyper-prolific sows. Porcine health management, 9(1), 37. DOI: 10.1186/s40813-023-00332-y.

Scollo, A., Borello, I., Ghilardi, M., & Cavagnini, A. (2023). The Administration of Inactivated and Stabilized Whole-Cells of Saccharomyces cerevisiae to Gestating Sows Improves Lactation Efficiency and Post-Weaning Antimicrobial Use. Veterinary sciences, 10(9), 576. DOI: 10.3390/vetsci10090576.

Sepiashvili, R. (2015). Basic principles and methods to the use immunomodulating preparations in clinical practice: classification, indications and contraindications. Georgian medical news, (243), 7–14. URL: https://pubmed.ncbi.nlm.nih.gov/26087723.

Sinkora, M., & Butler, J. E. (2016). Progress in the use of swine in developmental immunology of B and T lymphocytes. Developmental and comparative immunology, 58, 1–17. DOI: 10.1016/j.dci.2015.12.003.

Srinivasan, S., & Babensee, J. E. (2020). Controlled Delivery of Immunomodulators from a Biomaterial Scaffold Niche to Induce a Tolerogenic Phenotype in Human Dendritic Cells. ACS biomaterials science & engineering, 6(7), 4062–4076. DOI: 10.1021/acsbiomaterials.0c00439.

Storino, G. Y., Petri, F. A. M., Mechler-Dreibi, M. L., Aguiar, G. A., Toledo, L. T., Arruda, L. P., Malcher, C. S., Martins, T. S., Montassier, H. J., Sant'Anna, O. A., Fantini, M. C. A., & de Oliveira, L. G. (2023). Use of Nanostructured Silica SBA-15 as an Oral Vaccine Adjuvant to Control Mycoplasma hyopneumoniae in Swine Production. International journal of molecular sciences, 24(7), 6591. DOI: 10.3390/ijms24076591.

Suwan, P., Boonsoongnern, A., Phuttapatimok, S., Sukmak, M., Jirawattanapong, P., Chumsing, W., Boodde, O., Woramahatthanon, K., & Woonwong, Y. (2023). Effectiveness of gilt acclimatization - improvement procedures in a farm with recurrent outbreaks of porcine epidemic diarrhea. Veterinary world, 16(8), 1695–1701. DOI: 10.14202/vetworld.2023.1695-1701.

Suzuki, S., Suzuki, M., Nakai, M., Sembon, S., Fuchimoto, D., & Onishi, A. (2014). Transcriptional and histological analyses of the thymic developmental process in the fetal pig. Experimental animals, 63(2), 215–225. DOI: 10.1538/expanim.63.215.

Tang, S., Li, M., Sun, Y., Liao, Y., Wu, X., Zhong, R., Chen, L., & Zhang, H. (2022). Effects of chronic heat stress on the immunophenotyping of lymphocytes in immune organs of growing pigs. Journal of animal science, 100(11), skac317. DOI: 10.1093/jas/skac317.

Tuchscherer, M., Otten, W., Kanitz, E., Gräbner, M., Tuchscherer, A., Bellmann, O., Rehfeldt, C., & Metges, C. C. (2012). Effects of inadequate maternal dietary protein:carbohydrate ratios during pregnancy on offspring immunity in pigs. BMC veterinary research, 8, 232. DOI: 10.1186/1746-6148-8-232.

Ujčič-Vrhovnik, I., Švara, T., Malovrh, T., & Jakovac-Strajn, B. (2020). The effects of feed naturally contaminated with Fusarium mycotoxins on the thymus in suckling piglets. Acta veterinaria Hungarica, 68(2), 186–192. DOI: 10.1556/004.2020.00030.

Ushkalova, E. A., Zyryanov, S. K., & Zatolochina, K. E. (2019). Muramyldipeptide - based compounds in current medicine: focus on glucosaminylmuramyl dipeptide. Terapevticheskii arkhiv, 91(12), 122–127. DOI: 10.26442/00403660.2019.12.000471.

Vodolazska, D., Feyera, T., & Lauridsen, C. (2023). The impact of birth weight, birth order, birth asphyxia, and colostrum intake per se on growth and immunity of the suckling piglets. Scientific reports, 13(1), 8057. DOI: 10.1038/s41598-023-35277-3

Vonnahme, K. A., Wilson, M. E., & Ford, S. P. (2001). Relationship between placental vascular endothelial growth factor expression and placental/endometrial vascularity in the pig. Biology of reproduction, 64(6), 1821–1825. DOI: 10.1095/biolreprod64.6.1821.

Wang, L., Huo, B., Huang, L., Che, L., Feng, B., Lin, Y., Xu, S., Wu, D., & Fang, Z. (2022). Dietary supplementation with a mixture of herbal extracts during late gestation and lactation improves performance of sows and nursing piglets through regulation of maternal metabolism and transmission of antibodies. Frontiers in veterinary science, 9, 1026088. DOI: 10.3389/fvets.2022.1026088.

Wang, M., Huang, H., Hu, Y., Liu, Y., Zeng, X., Zhuang, Y., Yang, H., Wang, L., Chen, S., Yin, L., He, S., Zhang, S., Li, X., & He, S. (2020). Effects of dietary supplementation with herbal extract mixture on growth performance, organ weight and intestinal morphology in weaning piglets. Journal of animal physiology and animal nutrition, 104(5), 1462–1470. DOI: 10.1111/jpn.13422.

Wang, S., Wang, Z., Li, Y., Tu, S., Zou, J., Cheng, Y., Zhang, H., Suolang, S., & Zhou, H. (2023). Generation of whole-porcine neutralizing antibodies of an alphacoronavirus by single B cell antibody technology. Antiviral research, 220, 105754. DOI: 10.1016/j.antiviral.2023.105754.

Wang, T., Yao, W., Liu, X., Bao, Z., Lv, C., & Huang, F. (2023). Dietary embelin supplementation during mid-to-late gestation improves performance and maternal-fetal glucose metabolism of pigs. Journal of animal science, 101, skad010. URL: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10079812.

Wang, T., Yao, W., Xia, J., Li, J., Shao, Y., & Huang, F. (2019). Dietary supplementation with garcinol during late gestation and lactation facilitates acid-base balance and improves the performance of sows and newborn piglets1. Journal of animal science, 97(11), 4557–4566. DOI: 10.1093/jas/skz292.

Wippermann, W., Heckmann, A., Jäger, K., Dänicke, S., & Schoon, H. A. (2018). Exposure of pregnant sows to deoxynivalenol during 35-70 days of gestation does not affect pathomorphological and immunohistochemical properties of fetal organs. Mycotoxin research, 34(2), 99–106. DOI: 10.1007/s12550-017-0304-z.

Wu, Y., Zhang, X., Pi, Y., Han, D., Feng, C., Zhao, J., Chen, L., Che, D., Bao, H., Xie, Z., & Wang, J. (2021). Maternal galactooligosaccharides supplementation programmed immune defense, microbial colonization and intestinal development in piglets. Food & function, 12(16), 7260–7270. DOI: 10.1039/D1FO00084E.

Yao, R., Cools, A., Matthijs, A., Deyn, P. P., Maes, D., & Janssens, G. P. J. (2023). Peculiarities in the Amino Acid Composition of Sow Colostrum and Milk, and Their Potential Relevance to Piglet Development. Veterinary sciences, 10(4), 298. DOI: 10.3390/vetsci10040298.

Yefimov, V., Kostiushkevych, K., Rakytianskyi, V. (2016). Effect of feeding treated peat as a supplement on the parameters of cellular immunity, antioxidant status and performance of piglets in early post-weaning period. HVM Bioflux, 8(3), 133–136. URL: https://dspace.dsau.dp.ua/bitstream/123456789/591/1/1.pdf.

Yuan, C., Zhang, P., Liu, P., Li, Y., Li, J., Zhang, E., Jin, Y., & Yang, Q. (2022). A Novel Pathway for Porcine Epidemic Diarrhea Virus Transmission from Sows to Neonatal Piglets Mediated by Colostrum. Journal of virology, 96(14), e0047722. DOI: 10.1128/jvi.00477-22.

Zhang, L., Li, Z., Deng, X., Li, J., Li, T., & Lv, Y. (2019). Tylvalosin administration in pregnant sows attenuates the enlargement and bluish coloration of inguinal lymph nodes in newborn piglets. Research in veterinary science, 125, 148–152. DOI: 10.1016/j.rvsc.2019.06.006.

Zhang, P., Jiang, G., Wang, Y., Yan, E., He, L., Guo, J., Yin, J., & Zhang, X. (2023). Maternal consumption of l-malic acid enriched diets improves antioxidant capacity and glucose metabolism in offspring by regulating the gut microbiota. Redox biology, 67, 102889. DOI: 10.1016/j.redox.2023.102889.

Zheng, D., Wang, X., Ju, N., Wang, Z., Sui, L., Wang, L., Qiao, X., Cui, W., Jiang, Y., Zhou, H., Li, Y., & Tang, L. (2021). Immune Responses in Pregnant Sows Induced by Recombinant Lactobacillus johnsonii Expressing the COE Protein of Porcine Epidemic Diarrhea Virus Provide Protection for Piglets against PEDV Infection. Viruses, 14(1), 7. DOI: 10.3390/v14010007.