

Major acute phase proteins act as health status biomarker

In pigs, acute phase proteins could be used as a biomarker for animal health. Presence of these proteins in blood could point to the presence of pathogens as well. What are the options and possibilities of this method in swine production?

By Matilde Piñeiro, Joaquín Morales and Carlos Piñeiro, PigChamp Pro Europa

Acute phase proteins (APPs) are blood proteins which modify their concentration in case of tissue damage, infection or stress.

Acute phase proteins (APPs) are blood proteins which modify their concentration in case of tissue damage, infection or stress. Changes in APP levels are part of

physiological alterations taking place during a rapid, generalised reaction of an organism, directed to fight against any attack to its integrity. This phenomenon is also called an 'acute phase response' (APR). As general and unspecific markers of inflammation, APPs can help in the detection of pathological states and in the evaluation of the health status of pig herds.

Pig-MAP (Major Acute-phase Protein) is a plasma protein of relatively recent discovery, despite being one of the main acute phase proteins in pigs. It was described for the first time in 1994, as an alpha-glycoprotein that increased considerably in pigs with locally induced inflammation. Pig-MAP shows homology (around 50%) with

the heavy chains (H) of the inter-alpha trypsin inhibitor family, and is considered a new member of this group of proteins, also known as ITIH4. However, unlike the other members of the ITI family, ITIH4 is not a protease inhibitor.

The function of this pig APP has not been completely elucidated. As a member of the ITI family, Pig-MAP/ITIH4 might participate in extracellular matrix stabilisation, and might have a role in the embryonic development and in the restoration of damaged organs. It has also been suggested that ITIH4 may exert an anti-inflammatory function, because of its ability to bind actin and inhibit phagocytosis of polymorphonuclear cells.



Carlos Piñeiro: "In field conditions, Pig-MAP has shown efficacy as health status biomarker in different scenarios."

Concentration

During the acute phase response, the concentration of the acute phase protein can augment up to 10-15 times the baseline levels, however the magnitude of the increase depends on the inducing agent and the severity of the underlying condition. The behaviour of Pig-MAP has been studied in detail in different acute phase conditions, including bacterial, viral or parasite infections (see Table 1). In normal state, the APP concentration is around 0.3-1 mg/ml, reaching values of 2-12 mg/ml during the acute phase response. Maximum values are observed two to five days after the onset of the response. Then, if the animal overcomes the aggression, the concentration decreases progressively, to return to initial values after 10-20 days.

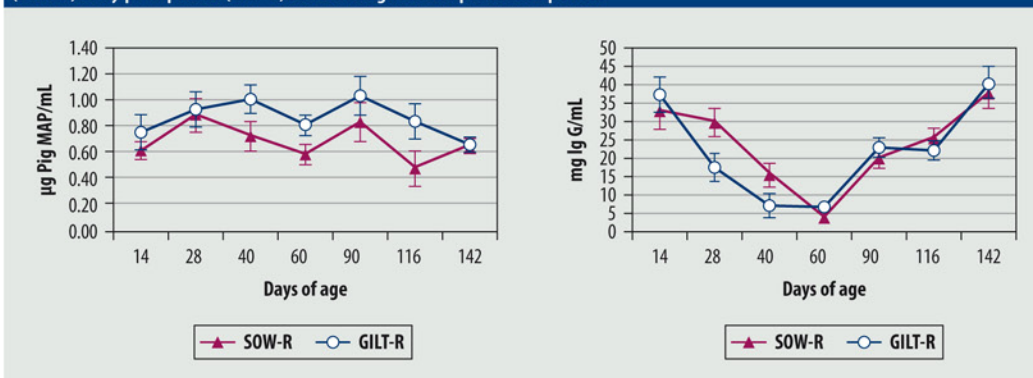
Elevated levels of the Pig-MAP can be observed also in pigs affected by stress situations compromising animal welfare, such as low space allowance, mixing with other animals, transport or inadequate handling of feed (Table 1). Pig-MAP concentration can augment after long distance transportation, the increase being related to the quality of transport conditions. A correlation between high concentration and losses of productive performance has also been reported.

Health status biomarker

In studies performed in an European shared cost project 'Acute Phase Proteins in Pigs' with participation of the main European experts in the field, Pig-MAP was selected to be included together with other acute phase proteins in an acute phase index that may be used to determine the health status of the animal. This works also showed that Pig-MAP is the most sensitive among the individual acute phase proteins studied, in the general detection of disease. As biomarker, Pig-MAP has the advantage of its low variability in normal state compared with other APPs such as haptoglobin, as it has been shown in recently published studies which aimed to establish reference ranges of these proteins for fatteners and reproductive pigs in commercial farms.

In field conditions, Pig-MAP has shown efficacy as health status biomarker in

Figure 1. Pig-MAP (left) and Ig G (right) serum concentration in pigs reared by multiparous (SOW-R) or by primiparous (GILT-R) sows throughout the productive period.



different scenarios, such as first parity progenies. It is well known that primiparous litters have lower productive performance and viability, likely related to a lower immune transmission via colostrum, which results in a higher susceptibility to pathogens and a lower health status compared with multiparous offspring. Pigs do not obtain immunoglobulins through the placenta and thus they initially depend on passive immunity derived from colostrum.

Long-term survival

Long-term survival of pigs is related to the amount of immunoglobulins acquired immediately after birth and primiparous sows may confer less nutrients and immune competence to their litter than multiparous sows do due to differences in colostrums and milk composition. In 2006, Carlos Piñeiro and others demonstrated the relationship between poorer productive performance throughout the whole productive period of pigs reared by primiparous sows than pigs reared by multiparous (88.3 kg vs 81.6 kg body weight in primiparous and in multiparous reared pigs, at 144 days of age) and health status. In the overall growing-finishing period, the percentage of mortality tended to be higher in primiparous-reared than in multiparous-reared pigs (6.9% vs 5.5%).

Associated with this result, Pig-MAP serum concentration was also higher in pigs reared by primiparous, confirming this is a good biomarker of health status. On the other hand, IgG serum concentration (Figure 1) was higher in

multiparous-reared than in primiparous-reared pigs at weaning (30.0 vs 17.8 mg/ml) and in nursery period, suggesting higher immune transmission by multiparous sows. No differences were observed thereafter.

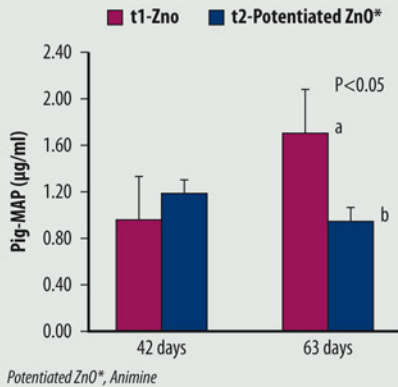
As a second example, Pig-MAP serum concentration has also been effective to evidence postweaning diarrhoea syndrome, a multi-factorial problem where management, feed composition, hygiene and other factors play an important role in the expression of the disease. Pig-MAP serum concentration, as unspecific biomarker, will be increased independently of the causal agent.

In an own experimental trial by Joaquín Morales last year, two dietary treatments against this post-weaning

Table 1. Factors inducing a Pig-MAP response.

Factor	Examples
Bacterial infection	<i>Actinobacillus pleuropneumoniae</i> <i>Streptococcus suis</i> <i>Haemophilus parasuis</i> (Glässer's disease) <i>Pasteurella multocida</i> (Atrophic rhinitis)
Viral infection	PCV2 E. Aujeszky African Swine Fever PRRS
Parasitic infection	<i>Toxoplasma gondii</i>
Lesions/inflammation	Sterile inflammation Surgery Inflammatory states
Stressors	Transport Crowding Mixing Disorderly feeding

Figure 2. PigMAP serum concentration (mg/ml) throughout the starter phase (42 to 63 days of age) in pigs fed with potentiated zinc oxide* (150 ppm) or Zn oxide (3,000 ppm).



diarrhoea syndrome were compared in the starter phase (42 to 63 days of age): Zinc oxide at pharmacological dosage (3,000 ppm of Zn) and a new potentiated form of zinc oxide (HiZox, Animine) administered at nutritional level (150 ppm). Piglets fed with the potentiated form of zinc oxide had improved average daily weight gain (424 vs 359 g/d), final bodyweight (17.9 vs 16.5 kg) and feed conversion ratio (1.44 vs 1.71 g/g) compared with

piglets fed with zinc oxide. Associated with these productive performance results, Pig-MAP serum concentration was lower in the potentiated form of zinc oxide than in Zn oxide group (see Figure 2). In conclusion, better productive performance obtained by the potentiated zinc oxide group could be explained by a better health of pigs expressed by a lower level of inflammatory protein Pig-MAP.

Today's pig production is increasingly focused on quality, security and welfare topics. In this context the introduction of new tools that may contribute to the evaluation of the quality of the processes, to the detection of critical points in the productive system, as well as to warrant as much as possible the absence of risks, have become increasingly important. In this sense, acute phase proteins may have an important role in the near future. Pig-MAP assay has applications in the pig industry for the evaluation of animal health and welfare in an objective way, as well as for the detection of failures in the productive system, and might be incorporated in certification programmes for the meat industry. Pig-MAP assay can be used to evaluate the general sanitary status of the farms, or the health

of new animals arriving at the farm. It might also be used to assure the health of the animals sent to the slaughterhouse or that transport is performed in adequate conditions.

In addition, some authors have proposed that analysis with this acute phase protein might have a role in the end point inspection at the slaughterhouse, to evaluate the quality of the animals for consumption, particularly in the case of wasting pigs. A good correlation exists between Pig-MAP levels in serum and meat juice, which suggest that this could be an alternative matrix for the evaluation of this acute phase protein concentration. Recent studies have reported elevated concentration values in slaughter pigs with pleuritis and other pulmonary lesions, being this APP the one having higher sensitivity to discriminate between the presence or not in the pig of different types of lesions, as well as to differentiate between affected or not affected farms, after the analysis of a sample of the slaughtered pigs from this farm. In summary, Pig-MAP has been confirmed as an effective biomarker of health and welfare in pigs. **PP**

References available on request.

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