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Editorial

Integrated Antioxidant Defence Network in Animals

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For the last 3 decades it has become clear that over-production of free radicals leading to oxidative stress and redox disbalance is involved in the development of different human/animal diseases at various stages of their development. Therefore, during evolution an integrated antioxidant defence network was developed to provide effective protection of biological molecules against damaging effects of reactive oxygen and nitrogen species (RONS) and toxic products of their metabolism. Previously we suggested vitamin E and coenzyme Q to be called "head quarter" of the antioxidant system, while carotenoids, comprising a group of pigments accounting for more than 1000 compounds to be called "communicating services" of the antioxidant defence. A group of polyphenols combining more than 8,000 various natural compounds can be called "antioxidant police", while Se regulating activity of 25 selenoproteins we suggested to be considered as "chief executive" of the antioxidant defence network [1]. Recently vitagene concept of stress adaptation has been developed [2] and successfully tasted in animal/poultry production [3]. Taking into account recent information on essential roles of transcription factors, including Nrf2 [4] and NF-κB [5] in redox homeostasis maintenance, an update on the vitagene-regulated antioxidant defense mechanisms and their involvement in stress adaptation can be presented as follows (Figure 1). Mitochondria and phagocyte cells are major sources of RONS. There are also various stress conditions in poultry production increasing RONS production. It is well appreciated that RONS play important roles as signaling molecules; however, when their concentration is above threshold level, they can cause damage to main biological molecules, including lipids, proteins, and DNA/RNA. As a result of RONS excess, a stress response program (Oxidative stress response, OSR) is activated [3,6].

Since oxidative stress can cause a range of damages to various molecules, in addition to OSR, other stress response programs, including heat shock response (HSR), unfolded protein response (UPR), hypoxia-induced response (HIR), and DNA damage response, are also activated. This leads to activation of various transcription factors, including HSF1, Nrf2, NF-κB, FOXO, HIF, p53, and others. As a result of the upregulation of transcription factors, various genes, including vitagenes, are activated. In fact, activation of HSF increased production of HSP70, Nrf2 activation increased synthesis of SOD, HO-1, elements of thioredoxin and glutathione systems; and FOXO activation would affect expression of sirtuins. There is a complex system of interplay between vitagenes and transcription factors. In fact, some vitagenes, like SOD, are affected by several transcription factors including Nrf2, NF-κB, p53, etc. Since SOD is responsible for production of H_2O_2, major

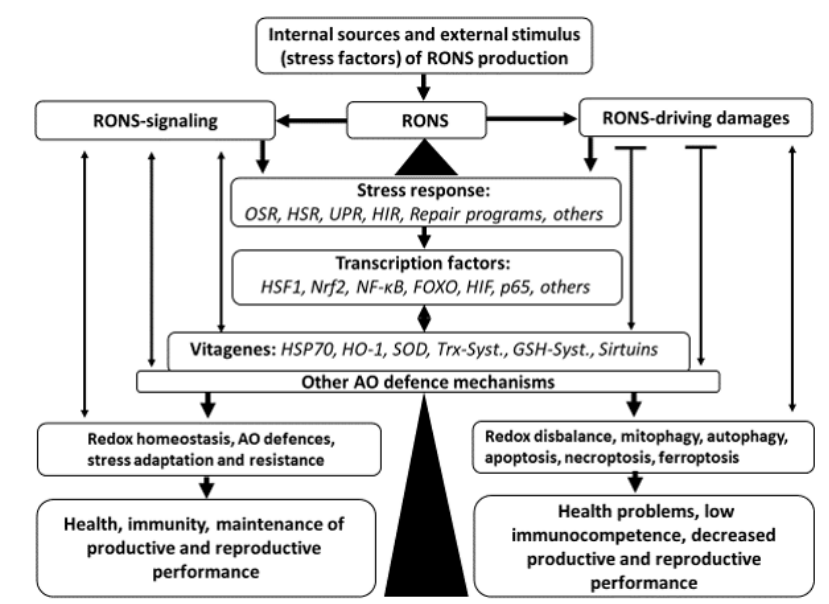

Figure 1: *Antioxidant defense network in animals (Adapted from 3, 6).*

signaling RONS, control of its concentration is of paramount importance. Furthermore, products of vitagene activation, e.g. sirtuins, would affect expression and activity of some transcription factors, including Nrf2, NF-κB, FOXO, etc. Some vitagenes can be activated directly without transcription factor involvement. This includes transcriptional regulation of SOD in response to RONS as well as activation of sirtuins by changes in NAD+/NADH ratio. In general, redox homeostasis plays an important role in the regulation of antioxidant defences. RONS are also responsible for adaptive production/activation of other antioxidants, which are not included into vitagene family (e.g. CoQ, catalase, various selenoproteins, etc.) and they all responsible for redox balance maintenance, stress resistance and adaptation leading to good health, high immunocompetence, high productive and reproductive performance of poultry. However, when the antioxidant defense system, together with the vitagene network, are not able to prevent or repair damages imposed by RONS to biological molecules, other protective mechanisms including mitophagy, autophagy, apoptosis, necroptosis, and ferroptosis are dealing with terminally damaged molecules, organelles or cells. As a result of disrupted redox balance and accumulation of damages in cells/tissues, health-related problems, including low immunocompetence, appear. In addition, decreased productive and reproductive performance can cause heavy economic losses for poultry industry [3].

It is important to note that there is a range of nutrients able to affect various transcription factors and activate vitagenes, including vitamin E [7], selenium [8,9], taurine [10,11], carnitine [12,13], various polyphenolics, including silymarin [6,14,15]. Therefore, recent research is devoted to finding/design effective nutrient mixtures to be used as practical tools in stress management in animal production [3]. The same approach can be used in medical sciences where stress management and redox homeostasis maintenance is of a paramount importance in various neurogenerative and other diseases [6].

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