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# Trace elements in nutrition and health: a deep dive into essentiality and mechanism of their biological roles

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Although trace elements are present in various organisms at levels lower than 1/10,000 of their mass, they are essential for survival and health of animals. They play crucial roles in a variety of biological processes, including DNA replication, transcription, cell growth, and cofactors of various enzymes. In animals, trace elements such as iron (Fe), copper (Cu), zinc (Zn), manganese (Mn), and selenium (Se) are mainly ingested from commercial feeds and functional feed additives. Once ingested, these elements are released into the stomach and absorbed in the proximal small intestine. Subsequently, they enter systemic circulation through the portal vein and are transported to other tissues. The distribution of trace elements and their functions, particularly with respect to the intestinal and gut microbiota, are of vital importance. Thus, we are publishing this special issue to highlight novel scientific findings and field applications of trace element nutrition in China.

In recent years, the precise quantification of trace elements has predominantly relied on inductively coupled plasma optical emission spectroscopy (ICP-OES) or inductively coupled plasma mass spectrometry (ICP-MS). Among the advances of analytical techniques, ionomics has emerged as a method to reveal the distribution of trace elements in animals in relation to their requirements. In this issue, Li et al. (2023) report this method to quantify the evolution of 35 elements and their isotopes across 8 organs in laying hens of various ages. Their comprehensive study illustrates the elemental composition, interactions, and utilization patterns of these organs and their correlation with egg white quality. The use of ionomics provides a wide-reaching perspective on the selection of the ionome, showing significant promise and applicability for studying the absorption and distribution of trace elements in animals.

The integrity and function of small intestine, which is the main site of nutrient absorption, directly affect the economic outcomes of animal husbandry. We can help animals resist infection elicited by harmful microorganisms through dietary manipulations of trace elements, either by deprivation or excess (Sousa Gerós et al., 2020). In this issue, we are publishing studies exploring the role of Fe on intestinal epithelium development and function in both farm and laboratory animals. These studies reveal that an administration of deferoxamine to porcine intestinal organoids resulted in non-significant difference in epithelial maturation markers (Yin et al., 2023), while in mouse intestinal organoids, ferric ammonium citrate (FAC) directly induced mucin expression and promoted goblet cell proliferation in both the ileum and colon (Liu et al., 2023). However, adding FAC to Caco-2 cells revealed that plasma Fe might lead to intestinal injury and dysbiosis of intestinal flora, potentially mediated by ZIP14 (Zhang et al., 2023). Thus, excessively low or high Fe levels can cause adverse impact on intestinal regeneration and barrier function. In contrast, the appropriate enhance-

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ment of host Fe intake can support intestinal mucosal growth and immune regulation, which may outweigh the risks of altered gut microbiota (Dong et al., 2023; Liu et al., 2023).

Trace elements influence the composition of the gut microbiota and foster the production of beneficial secondary metabolites like bacteriocins and antimicrobial peptides, thereby strengthen host immunity (Duan et al., 2023; Squizani et al., 2022). Functional alterations in symbiotic microorganisms can impact the host's metabolism of trace elements, contributing to the interactions between the host and intestinal microorganisms. Both excessive and deficient levels of trace elements can disturb the ecological balance between host and microorganisms, leading to metabolic disorders in the host and structural alterations in intestinal bacteria. Iron, which is necessary for both mammals and bacteria, has a close relationship with gut microbiota. For instance, the oral or parenteral administration of Fe to anemic piglets resulted in similar bacterial structural changes. These changes included an increase in *Proteobacteria*, *Escherichia-Shigella*, and *Fusobacterium*, as well as a decrease in *Christensenellaceae_R-7_group* in the colon, which were positively correlated with iron status (Dong et al., 2023). The host's Fe homeostasis affects the composition of the gut microbiota and the interaction between host and gut microbiota through various mechanisms such as nutrient-gene interaction and homeostasis, intestinal permeability, gut immunity, and oxidative stress. Therefore, understanding the relationship between gut microbes and host Fe homeostasis is significant not only for host health but also for providing preventative and therapeutic strategies to cope for a wild range of disorders affecting both host and microbiota (Xiao et al., 2023).

As China progressively disallows the use of antibiotics in farming and agriculture, there is a growing concern regarding the potential consequences of both deficiency and excessive use of trace elements on intestinal health. Nutritional immunity associated with trace elements is a critical aspect of this dynamic. Trace elements play vital roles in the function and differentiation of immune cells, and most immune activation processes affect the metabolism of trace elements (Ma et al., 2023). Concentrations of metals in macrophages and neutrophils contribute to regulating the homeostasis between the gut microbiota and the host. Certain pathogens have developed storage mechanisms for trace elements, allowing them to secure nutrients without competing for the host's trace elements, thus bypassing the host's nutritional immunity (Ben-Eghan et al., 2020). In mammals, trace elements are essential for the development of the immune system, specifically for T-cell proliferation and differentiation (Jin et al., 2023). Selenium, for instance, serves as an antioxidant, immunity booster, anticancer agent, and has detoxification functions. Se deficiency can lead to multiple tissue damage, such as the dysregulation of immune and redox homeostasis in broilers (Zhao et al., 2023). A novel Se source, Se-enriched *Cardamine violifolia* (SEC), can mitigate sepsis-induced intestinal injury, which is associated with modulating mitochondrial fusion (Wang et al., 2023).

At present, our understanding of the roles of trace elements in animal nutrition remains partial. Only a handful of studies have explored transporters and roles of trace elements in the immune systems of pigs, particularly those infected with pathogens. A comprehensive analysis of trace elements in individualized animals is necessary to understand their requirements at different stages of life. The development of novel methods providing high-throughput analysis is critically important. Moreover, further investigation into the yet-discovered functions of trace elements in animals is required, especially concerning their role in regulating gastrointestinal development, aiding in the recovery of intestinal injuries, and influencing lipid metabolism and immune responses. More studies are needed to explore the mechanisms through which trace metal elements target externally-infected bacteria, clarify the link between changes in the composition and levels of trace elements and the functions of T cells, and develop more effective trace element products.

The advances in the field of animal nutrition of trace elements in China have greatly benefited from the rapid progress of new technologies and the steadily increasing funding for basic research in recent years. With these achievements, we are optimistic and confident that the successful trend of trace elements research will continue in the future. This is expected for not only basic research but also for the development of products and techniques, which will substantially enhance economic growth and animal welfare. Finally, as guest editors, we would like to express our sincere appreciation to all the authors, reviewers, and the editorial staff of *Science China Life Sciences* for their invaluable contributions that have made this special issue published. We hope that this specific issue will attract considerable attention from the fields and will promote research of trace elements in animal nutrition and human health in many years to come.

**Compliance and ethics** *The author(s) declare that they have no conflict of interest.*

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