New insights into disruption of iron homeostasis by environmental pollutants

Xiang Wang, Tian Xia*  
Department of Medicine, Division of NanoMedicine, University of California, Los Angeles, CA 90095, USA  
California NanoSystems Institute, University of California, Los Angeles, CA 90095, USA

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ABSTRACT  
Among the numerous health conditions environmental pollutants can cause, chronic exposure to pollutants including persistent organic pollutants (POPs) and heavy metals has been shown to disturb a specific biological homeostatic process, the iron metabolism in human body. Disorders of iron metabolism are among the common diseases of humans and encompass a broad spectrum of diseases with different clinical manifestations, ranging from anemia to iron overload, and possibly to neurodegenerative diseases and cancer. 

Hepcidin–ferroportin (FPN) signaling is one of the key mechanisms responsible for iron supply, utilization, recycling, and storage, and recent studies demonstrated that exposure to environmental pollutants including POPs and heavy metals could lead to disruption of the hepcidin–FPN axis along with disordered systemic iron homeostasis and diseases. This article introduces and highlights the accompanying review article by Drs. Xu and Liu in this journal, which elaborates in detail the adverse effects of environmental pollutants on iron metabolism, and the mechanisms responsible for these toxicological outcomes. It also points out the knowledge gaps still existing in this subject matter. Research that will fill these gaps will improve our understanding of the issue and provide useful information to prevent or treat diseases induced by environmental pollutants.

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The World Health Organization estimates that 24% of the global disease burden and 23% of all deaths can be attributed to environmental factors. The situation gets worse for children, and the proportion of deaths attributed to the environment was as high as 36% (WHO, 2006). Among the numerous health conditions environmental pollutants can cause, chronic exposure to pollutants including persistent organic pollutants (POPs) and heavy metals have shown to disturb a specific biological homeostatic process, the iron metabolism in human body.

Iron is an essential element for all forms of life, from bacteria to mammals. Its importance lies in its ability to mediate electron transfer (Duce et al., 2010). In the ferrous state, iron acts as an electron donor, while in the ferric state it acts as an acceptor. Thus, iron plays a vital role in the catalysis of enzymatic reactions that involve electron transfer (reduction and oxidation). Many proteins contain iron as part of different cofactors, such as iron-containing heme groups in oxygen-transport hemoglobin, and iron–sulfur clusters (Fe–S) containing mitochondrial complexes in the respiratory chain (Torti and Torti, 2013). Iron homeostasis is concertedly governed under physiological conditions. Disorders of iron metabolism are among common diseases of humans and encompass a broad spectrum of diseases with different clinical manifestations, ranging from anemia to iron overload, and possibly to neurodegenerative diseases and cancer. 

Hepcidin–ferroportin (FPN) signaling is one of the key mechanisms responsible for iron supply, utilization, recycling, and storage, and recent studies demonstrated that exposure to environmental pollutants including POPs and heavy metals could lead to disruption of the hepcidin–FPN axis along with disordered systemic iron homeostasis and diseases. This article introduces and highlights the accompanying review article by Drs. Xu and Liu in this journal, which elaborates in detail the adverse effects of environmental pollutants on iron metabolism, and the mechanisms responsible for these toxicological outcomes. It also points out the knowledge gaps still existing in this subject matter. Research that will fill these gaps will improve our understanding of the issue and provide useful information to prevent or treat diseases induced by environmental pollutants.

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clinical manifestations, ranging from anemia to iron overload, and possibly to neurodegenerative diseases and cancer (Lieu et al., 2001).

To balance the absorption, transport, storage and utilization of iron in the body, systemic iron homeostasis is fine-tuned through various signaling pathways. Hepcidin–ferroportin (FPN) signaling is one of the key mechanisms responsible for iron supply, utilization, recycling and storage (Fig. 1). Hepcidin, a 25 amino acid peptide, is the central regulator of iron absorption and mainly derived from hepatocytes. It fundamentally equilibrates systemic iron homeostasis. The expression of hepcidin is primarily regulated by iron status, anemia, hypoxia and inflammation, and now environmental pollutants. FPN is the only known iron exporter in mammals, and its concentration is mainly controlled by the binding of hepcidin (Ganz, 2013). Recent studies demonstrated that, following exposure to environmental pollutants, the hepcidin–FPN axis is misregulated in administrated animals along with disordered systemic iron homeostasis.

Environmental pollutants discussed in the accompanying Review article by Drs. Xu and Liu reviewed in detail the potential adverse effects of environmental pollutants on iron metabolism, and also highlighted the corresponding mechanisms responsible for cellular responses (Guo et al., 2015). It needs to be noted that although substantial progress has been made in understanding the mechanisms of disruption in iron metabolism by these environmental pollutants, there are still many knowledge gaps existed that demand future studies, e.g., detailed molecular mechanisms involved in environmental pollutant-induced disturbance of iron homeostasis, especially the hepcidin–ferroportin signaling pathway; synergistic effects of multiple environmental pollutants on the disturbance of iron homeostasis; and the role of the environmental pollutant-induced disruption of iron homeostasis in carcinogenesis. Providing answers for these questions will not only improve our understanding to this subject matter, but also provide information to prevent or treat diseases induced by environmental pollutants.

REFERENCES