

Phenotypic and Behavioral Defects Induced by Iron Exposure Can Be Transferred to Progeny in *Caenorhabditis elegans*¹

YA-OU HU^{#,+}, YANG WANG[#], BO-PING YE⁺, AND DA-YONG WANG^{#,2}

[#]Key Laboratory of Developmental Genes and Human Disease of Ministry of Education, Department of Genetics and Developmental Biology, Southeast University, Nanjing 210009, Jiangsu, China; ⁺School of Life Science & Technology, China Pharmaceutical University, Nanjing 210009, Jiangsu, China

Objective Previous work has showed that excess iron accumulation is harmful to reproduction and even promotes death; however, whether the multiple biological toxicity of iron (Fe) exposure could be transferred to progeny remains unknown. The present study used *Caenorhabditis elegans* to analyze the multiple toxicities of iron exposure and their possible transferable properties. **Methods** Three concentrations of iron sulfate solution (2.5 μmol/L, 75 μmol/L, and 200 μmol/L) were used. The endpoints of lifespan, body size, generation time, brood size, head thrash and body bend frequencies, and chemotaxis plasticity were selected to investigate Fe toxicity and its effect on progeny in *Caenorhabditis elegans*. **Results** The Fe toxicity could cause multiple biological defects in a dose-dependent manner by affecting different endpoints in nematodes. Most of the multiple biological defects and behavior toxicities could be transferred from Fe-exposed *Caenorhabditis elegans* to their progeny. Compared to the parents, no recovery phenotypes were observed for some of the defects in the progeny, such as body bend frequency and life span. We further summarized the defects caused by Fe exposure into 2 groups according to their transferable properties. **Conclusion** Our results suggest that Fe exposure could cause multiple biological defects, and most of these severe defects could be transferred from Fe exposed nematodes to their progeny.

Key words: Iron toxicosis; Transferable; Phenotype; Behavior; *C. elegans*

REFERENCES

1. Fraga C G, Oteiza P I (2002). Iron toxicity and antioxidant nutrients. *Toxicology* **180**, 23-32.
2. Chatterjee C, Gopal R, Dube, B K (2006). Impact of iron stress on biomass, yield, metabolism and quality of potato. *Scientia Horticulturae* **108**, 1-6.
3. Aisen P, Enns C, Wessling-Resnick M (2001). Chemistry and biology of eukaryotic iron metabolism. *Int J Biochem Cell Biol* **33**, 940-959.
4. Petrini M, Pelosi-Testa E, Sposi N M, *et al.* (1989). Constitutive expression and abnormal glycosylation of transferrin receptor in acute T-cell leukemia. *Cancer Res* **49**, 6989-6996.
5. Angelucci E, Brittenham G M, McLaren C E, *et al.* (2000). Hepatic iron concentration and total body iron stores in thalassemia major. *N Engl J Med* **343**, 327-331.
6. Lu J P, Hayashi K, Awai M (1989). Transferrin receptor expression in normal, iron-deficient and iron-overloaded rats. *Acta Pathol Jpn* **39**, 759-764.
7. Han H J, Park S H, Park H J, *et al.* (2002). Effect of various oestrogens on cell injury and alteration of apical transporters induced by tert-butyl hydroperoxide in renal proximal tubule cells. *Clin Exp Pharmacol Physiol* **29**, 60-67.
8. Zhang Y, Li H, Zhao Y, *et al.* (2006). Dietary supplementation of baicalin and quercetin attenuates iron overload induced mouse liver injury. *Eur J Pharmacol* **535**, 263-269.
9. Rauen U, Petrat F, Sustmann R, *et al.* (2004). Iron-induced mitochondrial permeability transition in cultured hepatocytes. *J Hepatol* **40**, 607-615.
10. Ferrante M, Geubel A P, Fevery J, *et al.* (2005). Hereditary hyperferritinaemia-cataract syndrome: a challenging diagnosis for the hepatogastroenterologist. *Eur J Gastroenterol Hepatol* **17**, 1247-1253.
11. Riddle D L, Blumenthal T, Meyer B J, *et al.* (eds.) (1997). *C. ELEGANS II* Cold Spring Harbor Laboratory Press, Plainview, New York.
12. Swain S C, Keusekotten K, Baumeister B, *et al.* (2004). *C. elegans* metallothioneins: new insights into the phenotypic effects of cadmium toxicosis. *J Mol Biol* **341**, 951-959.
13. Peredney C L, Williams P L (2000). Utility of *Caenorhabditis elegans* for assessing heavy metal contamination in artificial soil. *Arch Environ Contam Toxicol* **39**, 113-118.
14. Graves A L, Boyd W A, Williams P L (2005). Using transgenic *Caenorhabditis elegans* in soil toxicity testing. *Arch Environ Contam Toxicol* **48**, 490-494.
15. Traunspurger W, Haitzer M, Höss S, *et al.* (1997). Ecotoxicological assessment of aquatic sediments with *Caenorhabditis elegans* (nematode)—a method testing liquid medium and whole-sediment samples. *Environ Toxicol Chem* **16**, 245-250.
16. Mutwakil M H A Z, Reader J P, Holdich D M, *et al.* (1997). Use

¹This work was supported by the Southeast University Foundation for Excellent Young Scholars (No. 4023001013).

²Correspondence should be addressed to Da-Yong WANG. Tel: 86-25-83272314-817. E-mail: dayongw@seu.edu.cn

Biographical note of the first author: Ya-Ou HU, female, born in 1982, master fellow, majoring in genetics and developmental biology.

- of stress-inducible transgenic nematodes as biomarkers of heavy metal pollution in water samples from an English river system. *Arch Environ Contam Toxicol* **32**, 146-153.
17. American Society for Testing and Materials (2002). Standard guide for conducting laboratory soil toxicity tests with the nematode *Caenorhabditis elegans*. In: Annual book of ASTM standard. Philadelphia, PA, 11.05, pp. 1606-1616.
18. Brenner S (1974). The genetics of *Caenorhabditis elegans*. *Genetics* **77**, 71-94.
19. Donkin S, Williams P L (1995). Influence of developmental stage, salts and food presence on various end points using *Caenorhabditis elegans* for aquatic toxicity testing. *Environ Toxicol Chem* **14**, 2139-2147.
20. Tsalik E L, Hobert O (2003). Functional mapping of neurons that control locomotory behavior in *Caenorhabditis elegans*. *J Neurobiol* **56**, 178-197.
21. Saeki A, Yamamoto M, Iino Y (2001). Plasticity of chemotaxis revealed by paired presentation of a chemoattractant and starvation in the nematode *Caenorhabditis elegans*. *J Exp Biol* **204**, 1757-1764.
22. Lucesoli F, Fraga C G (1995). Oxidative damage to lipids and DNA concurrent with decrease of antioxidants in rat testes after acute iron intoxication. *Arch Biochem Biophys* **316**, 567-571.
23. Lucesoli F, Caligiuri M, Roberti M F, et al. (1999). Dose-dependent increase of oxidative damage in the testes of rats subjected to acute iron overload. *Arch Biochem Biophys* **372**, 37-43.
24. Loria P M, Hodgkin J, Hobert O A (2004). Conserved Postsynaptic Transmembrane Protein Affecting Neuromuscular Signaling in *Caenorhabditis elegans*. *J Neurosci* **24**, 2191-2201.
25. Harley A, Cooper J M, Schapira A H (1993). Iron induced oxidative stress and mitochondrial dysfunction: relevance to Parkinson's disease. *Brain Res* **627**, 349-353.
26. Quintana C, Bellefqih S, Laval J Y, et al. (2006). Study of the localization of iron, ferritin, and hemosiderin in Alzheimer's disease hippocampus by analytical microscopy at the subcellular level. *J Struct Biol* **153**, 42-54.
27. Murakami H, Bessinger K, Hellman J, et al. (2005). Aging-dependent and -independent modulation of associative learning behavior by insulin/insulin-like growth factor-1 signal in *Caenorhabditis elegans*. *J Neurosci* **25**, 10894-10904.
28. Rachmilewitz E A, Weizer-Stern O, Adamsky K, et al. (2005). Role of iron in inducing oxidative stress in thalassemia: can it be prevented by inhibition of absorption and by antioxidants. *Ann NY Acad Sci* **1054**, 118-123.

(Received February 17, 2007 Accepted December 20, 2007)