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Target Organ Toxicology in *Caenorhabditis elegans*

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Preface

Nematode *Caenorhabditis elegans* is a classic model animal widely used in the study of life sciences. Meanwhile, it has been further frequently used for toxicity assessment and toxicological study of various environmental toxicants or stresses. One of the important reasons is the sensitivity of nematodes to various environmental exposures. The second reason is the conserved property for most of the molecular events and the signaling pathways between nematodes and mammals or human beings. The third reason is from the classic model animal properties of *C. elegans* with well-described genetic and developmental backgrounds and rich and available genetic and molecular resources. In nematodes, once exposed to environmental toxicants, the toxicants can enter the primary targeted organs (such as intestinal cells) and even be translocated into secondary targeted organs (such as reproductive organs and neurons).

Structurally, *C. elegans* do not have some important organs (such as the heart, liver, lung, and kidney) due to the lack of the mesoderm during the development. Nevertheless, the *C. elegans* has epidermal system, nervous system, excretory system, muscle system, coelomocyte system, alimentary system, and reproductive system. Especially, the development and the corresponding molecular control of these systems in *C. elegans* can reflect the processes in mammals to a great degree. These backgrounds provide important developmental basis for the study of target organ toxicology in nematodes.

In this book, we have raised these four important concerns:

1. What are the protective responses of different organs and the neuronal and molecular basis of avoidance behavior of nematodes to environmental toxicants or stresses?
2. What's the molecular basis of primary biological barriers for nematodes against the toxicity of environmental toxicants or stresses?
3. What are the toxic effects of environmental toxicants or stresses on different organs in nematodes?
4. How the molecular signaling pathways in different organs of nematodes regulate the toxicity of environmental toxicants or stresses?

Based on these concerns, in Chaps. 1 and 2, we first introduced the protective responses of different organs and avoidance behavior of nematodes to environmental toxicants or stresses. In Chaps. 3 and 4, we introduced the molecular basis of intestinal and epidermal barriers for nematodes against the toxicity of environmental toxicants or stresses. In Chaps. 5, 6 and 7, we introduced the toxicity induction in the intestine, epidermis, neurons, muscle, and reproductive organs in nematodes exposed to environmental toxicants or stresses. Finally, in Chaps. 8, 9, 10 and 11, we introduced the intestinal, epidermal, neuronal, and germline signaling pathways required for the regulation of toxicity of environmental toxicants or stresses.

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Contents

Chapter 1
Protective Responses of Different Organs to Environmental Toxicants or Stresses

Abstract Environmental toxicants or stresses at low doses or for short-term duration will induce various protective responses in organisms. We here introduced and discussed the different protective responses activated in different organs (intestine, epidermis, neurons, and muscle) in nematodes exposed to environmental toxicants or stresses. The protective responses activated in different organs will provide the first defense line for nematodes against the environmental toxicants or stresses.

Keywords Protective response · Intestine · Epidermis · Neurons · Muscle · Environmental exposure · *Caenorhabditis elegans*

1.1 Introduction

In nematode *Caenorhabditis elegans*, exposure to various environmental toxicants or stresses can cause the toxicity at multiple aspects on animals [1–6]. Meanwhile, it is found that environmental toxicants or stresses at low doses or for short-term duration can induce different forms of protective response. These responses provide important mechanisms for nematodes against the adverse effects from environmental toxicants or stresses. In nematodes, different protective responses may be activated in different organs after exposure to environmental toxicants or stresses. In this chapter, we introduced the protective responses of nematodes to environmental toxicants or stresses in intestine, in epidermis, in neurons, and in muscle.

1.2 Protective Responses to Environmental Toxicants or Stresses in the Intestine

Intestine barrier is one of the primary biological barriers for nematodes against the toxicity of environmental toxicants or stresses [1, 2].

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1.2.1 Superoxide Dismutase (SOD) Proteins

SODs are well-known proteins with the function in defending against the oxidative stress in organisms. In nematodes, there are five SODs, SOD-1, SOD-2, SOD-3, SOD-4, and SOD-5. SOD-3, a mitochondrial iron/manganese SOD, is expressed constitutively in intestinal cells [7]. Engineered nanomaterials (ENMs), such as titanium oxide nanoparticles (TiO_2-NPs) and nanopolystyrene particles, could induce the toxicity on the function of both primary targeted organs (such as intestine) and secondary targeted organs (such as reproductive organs) in nematodes [8–14]. We here selected SOD-3::GFP as an example to explain the SOD-mediated intestinal protective response of nematodes to environmental toxicants. In nematodes, it was observed that prolonged exposure to TiO_2-NPs (1 μg/L) could significantly increase the expressions of *sod-2* and *sod-3* and the expression of SOD-3::GFP (Fig. 1.1)

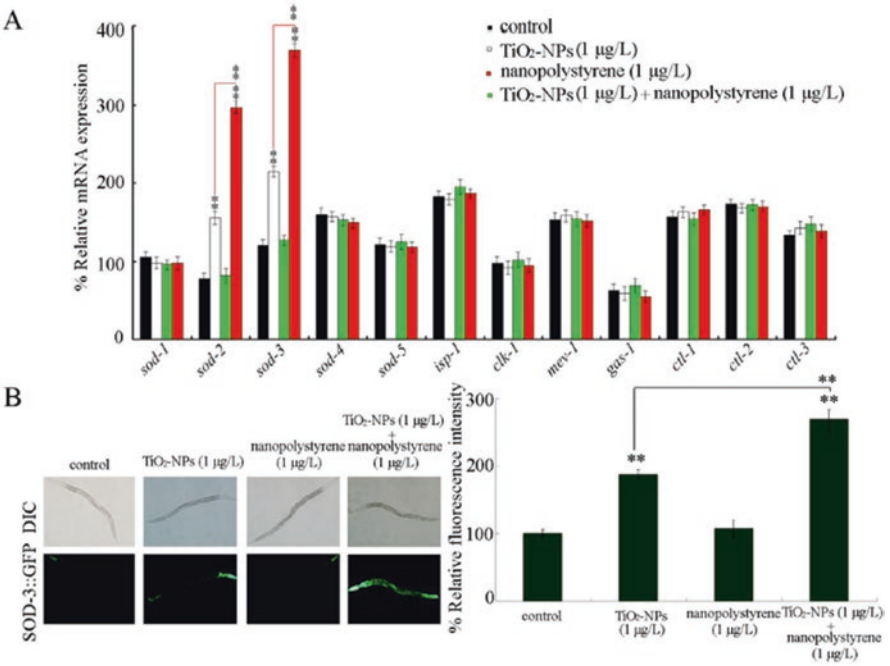

Fig. 1.1 Combinational exposure to TiO_2-NPs and nanopolystyrene particles altered the molecular basis for oxidative stress in wild-type nematodes [15]. (**a**) Combinational exposure to TiO_2-NPs and nanopolystyrene particles altered transcriptional expressions of genes required for the control of oxidative stress. (**b**) Combinational exposure to TiO_2-NPs and nanopolystyrene particles affected the expression of SOD-3::GFP. (**c**) Combinational exposure to TiO_2-NPs and nanopolystyrene particles affected the expression of SKN-1::GFP. Arrowheads indicate the signal of SKN-1::GFP in the nucleus. Prolonged exposure was performed from L1-larvae to adult day 1. Control, without TiO_2-NPs and nanopolystyrene particles exposure. Bars represent means ± SD. $^{**}P < 0.01$ vs. control (if not specially indicated)