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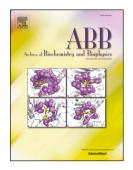
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#### ACCEPTED MANUSCRIPT

### What can flies tell us about zinc homeostasis?

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#### **Abstract**

Zinc is an essential micronutrient for all organisms. For multicellular organisms, zinc uptake, storage, distribution and export are tightly regulated at both cellular and organismal levels, to cope with the multiple requirements versus the toxicity of the metal ion. During the past decade, the fruit fly *Drosophila melanogaster* has become an important model organism for the elucidation of metazoan zinc homeostasis. This review describes our current knowledge of various zinc transporters in *Drosophila*, with an emphasis on the process of dietary zinc uptake in the fly. We also discuss how *Drosophila* was used as a model to facilitate our understanding of the role of zinc in neurodegenerative diseases.

### **Keywords**

Drosophila, zinc, homeostasis, gut, neurodegeneration

### Introduction

Zinc plays a catalytic or structural role in many enzymes and numerous proteins, and accordingly, contributes to a variety of fundamental biological processes<sup>1-3</sup>. Zinc dyshomeostasis could lead to various defects in multiple biological progresses. Although intensive study of zinc transporters at the cellular level has been performed in recent decades, their physiological functions on the maintenance of zinc homeostasis at the organismal level is less well characterized.

Our current knowledge of zinc metabolism largely comes from mammalian and microbial research. Questions at the organismal level have to be addressed properly with multi-cellular organisms. In terms of rodents, one limitation so far is that not all zinc transporters in mice have been targeted for mutagenesis and for those that have been targeted, mutations were usually generated ubiquitously rather than tissue-specifically, making it difficult to pinpoint their specific roles in a specific tissue or biological process. Another limit is likely functional redundancies among the zinc transporters, making functional analysis sometimes difficult unless various mutations are combined together, which can be time and financially costly.

As a complement to these approaches, Drosophila has been used fruitfully for

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