Copper and other heavy metals: from insects to mammals

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The "metal-responsive transcription factor-1"(MTF-1), a zinc finger protein, regulates target genes in response to heavy metal load and other stress (1). MTF-1 is also an essential protein: disruption of the gene in the mouse causes embryonic lethality due to liver degeneration around E13.5-E14.5. When MTF-1 is provided during a critical window of embryonic development, mice are thereafter viable but sensitive to cadmium, in support of a critical role of MTF-1 in coping with heavy metal stress (2). In Drosophila, knockout of MTF-1 yields viable flies which are however highly sensitive not only to heavy metal load but also to copper depletion (3). The reason for this is latter phenomenon is a failure to activate Ctr1B, a copper importer (in collaboration with the lab of Dennis J. Thiele, Duke University, NC). Thus MTF-1 can handle not only metal load but also copper depletion, by activating different genes (4). In Drosophila we have also eliminated, by targeted gene disruption, the genes for all four metallothioneins and some metal transporters, as a prerequisite to elucidate their role in heavy metal homeostasis and heavy metal stress response.

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