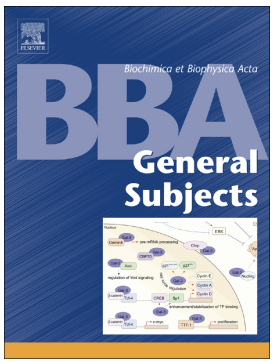

Drosophila multicopper oxidase 3 is a potential ferroxidase involved in Iron homeostasis

Xudong Wang, Sai Yin, Zhihao Yang, Bing Zhou

PII: S0304-4165(18)30110-7
DOI: doi:10.1016/j.bbagen.2018.04.017
Reference: BBAGEN 29099

To appear in:

Received date: 24 February 2018
Revised date: 29 March 2018
Accepted date: 17 April 2018

Please cite this article as: Xudong Wang, Sai Yin, Zhihao Yang, Bing Zhou , Drosophila multicopper oxidase 3 is a potential ferroxidase involved in Iron homeostasis. The address for the corresponding author was captured as affiliation for all authors. Please check if appropriate. Bbagen(2018), doi:10.1016/j.bbagen.2018.04.017

Drosophila Multicopper Oxidase 3 is a Potential Ferroxidase Involved in Iron Homeostasis

Xudong Wang, Sai Yin, Zhihao Yang[2], Bing Zhou[1,3]*

1. State Key Laboratory Membrane Biology, School of Life Sciences, Tsinghua University, Beijing, 100084, China

2. School of Medicine, Tsinghua University, Beijing, 100084, China

3. Beijing Institute for Brain Disorders, Beijing, China

*Correspondence: Bing Zhou, Tel: +86-10-62795322, Fax: +86-10-62772253, E-mail: zhoubing@mail.tsinghua.edu.cn

Abstract

Multicopper oxidases(MCOs) are a specific group of enzymes that contain multiple copper centers through which different substrates are oxidized. Main members of MCO family include ferroxidases, ascorbate oxidases, and laccases. MCO type of ferroxidases are key to iron transport across the plasma membrane. In *Drosophila*, there are four potential multiple oxidases, MCO1-4. No convincing evidence has been presented so far to indicate any of these, or even any insect multicopper oxidase, to be a ferroxidase. Here we show *Drosophila* MCO3(dMCO3) is highly likely a bona fide ferroxidase. *In vitro* activity assay with insect-cell-expressed dMCO3 demonstrated it has potent ferroxidase activity. Meanwhile, the ascorbate oxidase and laccase activities of dMCO3 are much less significant. dMCO3 expression in vivo, albeit at low levels, appears mostly extracellular, reminiscent of mammalian ceruloplasmin in the serum. A null *dMCO3* mutant, generated by CRISPR/Cas9 technology, showed disrupted iron homeostasis, evidenced by increased iron level and reduced metal importer *Mvl* expression. Notably, *dMCO3*-null flies phenotypically are largely normal at normal or iron stressed-conditions. We speculate the likely existence of a similar iron efflux apparatus as the mammalian ferroportin/ferroxidase in *Drosophila*. However, its importance to fly iron homeostasis is greatly minimized, which is instead dominated by another iron efflux avenue mediated by the ZIP13-ferritin axis along the ER/Golgi secretion pathway.

Key Words： *Drosophila* melanogaster; Multicopper oxidase 3; Ferroxidase; Iron homeostasis