

Doxorubicin-associated mitochondrial iron accumulation promotes cardiotoxicity

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Doxorubicin is a widely used as a component of chemotherapy regimes; however, the use of doxorubicin is associated with severe cardiotoxicity. It is unclear exactly how doxorubicin promotes cardiotoxicity, but it has been proposed that doxorubicin-associated cardiomyopathy develops as the result of reactive oxygen species (ROS) production and iron accumulation.

In this issue of the *Journal of Clinical Investigation*, Hossein Ardehali and colleagues at Northwestern University determined that doxorubicin accumulates within the mitochondria of cardiomyocytes and this accumulation promotes mitochondrial ROS production and iron accumulation.

In a mouse model of doxorubicin-associated cardiotoxicity, overexpression of a protein that enhances mitochondrial iron transport reduced mitochondrial iron, ROS, and protected animals from doxorubicin-induced cardiomyopathy. Treatment of animals with dexrazoxane, which attenuates doxorubicin-induced cardiotoxicity, decreased mitochondrial iron levels and reversed doxorubicin-induced cardiac damage. Furthermore, heart samples from patients undergoing doxorubicin therapy revealed higher levels of mitochondrial iron in patients with cardiomyopathies compared to patients without [cardiac complications](#).

These data suggest that therapies that limit mitochondrial iron accumulation have potential to limit [doxorubicin](#)-associated

cardiotoxicity.

More information: *J Clin Invest.* [DOI: 10.1172/JCI72931](https://doi.org/10.1172/JCI72931)

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