

ROLE OF IRON IN CARCINOGENESIS



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ABSTRACT

Iron is abundant universally. During the evolutionary processes, humans have selected iron as a carrier of oxygen inside the body. However, iron works as a double-edged sword, and its excess is a risk for cancer, presumably via generation of reactive oxygen species. Thus far, pathologic conditions such as hemochromatosis, chronic viral hepatitis B and C, exposure to asbestos fibers as well as endometriosis have been recognized as iron overload-associated risks for human cancer. Indeed, iron is carcinogenic in animal experiments. These studies unexpectedly revealed that there are target genes in iron-induced carcinogenesis (e.g. homozygous deletion of *CDKN2A/2B*, etc.) and that iron-catalyzed oxidative DNA damage is not random *in vivo*. The data of our laboratory on asbestos-induced mesothelial carcinogenesis in rats will be presented, which disclosed that local iron overload is a critical pathogenic mechanism even for chrysotile (white asbestos). Role of iron in ovarian carcinogenesis associated with endometriosis will also be discussed. A recent epidemiological study reported that iron reduction by phlebotomy decreased cancer risk in the apparently normal population. These results warrant reconsideration of the role of iron in carcinogenesis and suggest that fine control of body iron stores would be a wise strategy for cancer prevention.

References: 1. Kobayashi H *et al.* The ferromodulatory role of ectopic endometriotic stromal cells in ovarian endometriosis. *Fertil Steril* 98: 415-22, 2012. 2. Akatsuka S *et al.* Fenton reaction induced cancer in wild type rats recapitulates genomic alterations observed in human cancer. *PLoS One* 7:e43403, 2012. 3. Jiang L *et al.* Iron overload signature in chrysotile-induced malignant mesothelioma. *J Pathol* 228: 366-77, 2012. 4. Toyokuni S. Role of iron in carcinogenesis. *Cancer Sci* 100: 9-16, 2009. 5. Yamashita Y, *et al.* Met is the most frequently amplified gene in endometriosis-associated ovarian clear cell adenocarcinoma and correlates with worsened prognosis. *PLoS One* 8::e57724, 2013.



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