

Iron metabolism is a tightly regulated intracellular network consisting of numerous regulatory feedback loops. Changes in this network have been observed in connection with cancers in breast and other tissues. Because of the network's complexity and apparent importance in cancer biology, we simulated intracellular iron metabolism using a discrete logical mathematical model. This model included the main regulatory elements of the network as well as the proteins involved in heme synthesis. By adjusting the logical model, we simulated many different experiments with little extra computational effort. This use of mathematics allows us to gain insight as to which species are crucial to cancer cell survival without the expense of laboratory time and materials. To verify the model, it was used to accurately predict the result of overexpressing the ferroportin gene. We again verified the model by showing that it could accurately reproduce the results of a series of iron regulatory protein knockout experiments. Simulations of a neoplastic cell showed that an increase of the iron import protein transferrin receptor 1 and a decrease of the iron export protein ferroportin were necessary to stabilize the network in the face of high iron demand. Without these modifications, cyclic patterns of iron availability were observed. These results suggest that misregulation of the iron regulatory network is necessary to meet the increased iron demand of a neoplastic cell.