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Anna Konstorum*, akonsto@super.org, and **Suzy V. Torti, Frank M. Torti** and **Reinhard C. Laubenbacher**. *Identifying critical pathways for ferroptosis using a systems approach*.

Ferroptosis is a newly recognized form of regulated cell death that has the potential to be employed for cancer treatment. Sensitivity to ferroptosis has a critical dependence on lipid peroxidation events, but there does not exist a framework to predict ferroptosis sensitivity that encompasses systems-level information in a quantitative manner. We utilize a stochastic multistate discrete framework to model ferroptosis sensitivity, and incorporate an asynchronous update scheme and continuity constraints into the model to improve consistency with biological data. We simulate all possible combinations of input variables to explore the space of ferroptosis sensitivity. The model results show that ferroptosis is an outcome of a balance between pro- and anti-oxidant mechanisms acting on lipid peroxidation substrates. The model captures known ferroptosis results, as well as provides novel predictions for combinatorial input parameter settings. We show experimental validation for a subset of these predictions using a primary ovarian cell culture model. (Received September 03, 2019)