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Molecular actions of heme, an important molecule impacting fungal virulence and drug resistance

Statement of the Problem: Heme, iron protoporphyrin IX, is a crucial metallonutrient and a major source of iron for living organisms ranging from bacteria to humans. In humans, 95% of functional iron is in the form of heme. Heme is a central molecule in oxygen metabolism and utilization. It serves as a prosthetic group or cofactor for many proteins and enzymes involved in oxygen utilization and metabolism. The utilization of heme as an iron source strongly impacts the virulence of most pathogenic bacteria and some pathogenic fungi. For example, *Candida albicans* secretes a hemolytic factor and uses heme and hemoglobin as an iron source. *Cryptococcus neoformans* can subsist on solely heme- and hemoglobin-sourced iron. Further, *Histoplasma capsulatum* can only utilize iron in the form of heme. Consequently, disrupting heme uptake may be a viable approach to inhibit fungal infection. Additionally, understanding how heme acts to control various cellular processes should provide novel insights into how pathogenic fungi can be suppressed. Particularly, our lab has extensively investigated the molecular mechanisms underlying heme regulation of two yeast regulators, the heme activator protein Hap1 and the important regulator of nutrient sensing and signaling, Gis1. Heme directly controls the transcriptional activity of Hap1, while it controls the transcriptional and demethylase activities of Gis1. I will describe our latest studies to design heme-sequestering agents and to study the molecular mechanism by which heme controls Gis1 activity.

Biography

Li Zhang has completed her PhD from UCLA and postdoctoral studies from MIT department of Biology. She is the Cecil H and Ida Green Distinguished Chair in Systems Biology Science at the University of Texas at Dallas. Her laboratory has worked on studying heme signaling and function for 20+ years. She has published many original research articles and a book entitled heme biology: The secret life of heme in regulating diverse biological processes on this subject. Her recent representative publications include heme, an essential nutrient from dietary proteins, critically impacts diverse physiological and pathological processes, published in *Nutrients*, and a holistic view of cancer bioenergetics: Mitochondrial function and respiration play fundamental roles in the development and progression of diverse tumors, published in the journal *Clinical and Translational Medicine*.

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