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Evaluating the association of heme and heme metabolites with lung cancer energetics and progression

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Emerging experimental data increasingly show that despite the enhanced glycolytic flux, many types of cancer cells exhibit intensified oxygen consumption or mitochondrial respiration. Even under hypoxia, cancer cells can maintain oxidative phosphorylation at a substantial rate. Heme is a central factor in oxygen utilization and oxidative phosphorylation. It serves as a prosthetic group in many proteins and enzymes involved in mitochondrial respiration. Notably, our recent work showed that non-small-cell lung cancer (NSCLC) cells and xenograft tumors exhibit substantially increased levels in an array of proteins promoting heme synthesis, uptake and function. These proteins include the rate-limiting heme biosynthetic enzyme ALAS, transporter proteins, and various types of oxygen-utilizing hemoproteins such as cytoglobin and cytochromes. In contrast, lowering hemebiosynthesis and uptake, like lowering mitochondrial respiration, effectively reduced oxygen consumption, cancer cell proliferation, migration and colony formation. Therefore, elevated heme function and flux are likely key features of NSCLC cells and tumors. Based on this observation, we decided to further ascertain the relationship between heme and lung cancer. We extracted heme and its metabolites from various NSCLC cancer cells and tumors. We then performed LCmass spectrometry to quantify the amounts of heme and its metabolites. We also measured the rates of oxygen consumption in various cancer cells and compare them to the levels of heme in these cells. We expected that these experimental results will enable us to determine the extent to which heme and heme metabolites impact cancer cell bioenergetics and progression.

Biography

Li Zhang completed her PhD from UCLA and Postdoctoral studies from MIT Department of Biology. She is Cecil H. and Ida Green Distinguished Chair in Systems Biology Science at the University of Texas at Dallas. She 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.

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