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Evaluating heme flux and function in lung cancer

Li Zhang
The University of Texas at Dallas, USA

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. 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 heme biosynthesis and uptake, like inhibiting mitochondrial respiration, effectively reduced oxygen consumption, cancer cell proliferation, migration and colony formation. To further ascertain the importance of elevated heme flux and function in lung tumorigenesis, we use multiple experimental approaches to detect the levels of heme synthesis, uptake, and degradation in an array of NSCLC cell lines and in *de novo* tumors in genetically engineered mouse models for lung cancer. We also measure oxygen consumption and ATP generation in these cell lines and tumors. These experiments should reveal the degree to which elevated heme flux—heme synthesis, uptake, and degradation—contribute to lung tumorigenesis and how heterogeneity in heme flux contributes to metabolic and bioenergetics heterogeneity in lung tumors.

Biography

Li Zhang completed her PhD from UCLA and Post-doctoral studies from MIT Department of Biology. She is the Cecil H and Ida Green Distinguished Chair in Systems Biology Science at 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”. Her research work has also made important contributions in understanding the roles of molecular chaperones in cellular signaling, molecular mechanisms of oxygen signaling, and the actions of neurotoxicants. Recently, her work focuses on investigating heme function in lung cancer. She and colleagues have provided a unifying view of cancer bioenergetics in a review article entitled “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.*

li.zhang@utdallas.edu

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