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Elevated heme synthesis and uptake underpin intensified oxidative metabolism and tumorigenic functions in non-small cell lung cancer cells

Tumors of human non-small cell lung cancer (NSCLC) are heterogeneous but exhibit elevated glycolysis and glucose oxidation relative to the benign lung. Heme is a central molecule of oxidative metabolism and ATP generation via mitochondrial oxidative phosphorylation (OXPHOS). Heme is an essential iron source and metallonutrient for organisms ranging from pathogenic bacteria to humans. Heme is also a versatile signaling molecule regulating diverse molecular and cellular processes. Heme constitutes 95% of functional iron in humans. As a prosthetic group and cofactor, heme is required for the proper functioning of mitochondrial respiratory chain complexes and many proteins and enzymes involved in oxygen metabolism, such as cytochromes. We found that the levels of heme synthesis and uptake, mitochondrial heme, oxygen-utilizing hemoproteins, oxygen consumption, ATP generation and key mitochondrial biogenesis regulators are enhanced in NSCLC cells relative to non-tumorigenic cells. Likewise, proteins and enzymes relating to heme and mitochondrial functions are upregulated in human NSCLC tissues relative to normal control tissues. Our data show that elevated heme flux and function increase the levels of proteins and enzymes relating to oxygen consumption and potentiate tumorigenic functions in NSCLC cells. Conversely, decreased heme availability effectively suppresses tumorigenic functions and delay NSCLC tumor growth.

Biography

Li Zhang completed her PhD at UCLA and postdoctoral studies at the 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 studied heme signaling and function for 20+ years and 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 research interest is to elucidate the metabolic and signaling network coordinating the functions of heme and mitochondria to promote lung tumorigenesis.

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