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Permalink
https://escholarship.org/uc/item/5g87t4jt

Journal
Biophysical Journal, 104(2)

ISSN
0006-3495

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Publication Date
2013

DOI
10.1016/j.bpj.2012.11.1902

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Metabolic Imaging of Colon Cancer Tumors In Vivo by Phasor Fluorescence Lifetime Microscopy of NADH

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Here we use a non-invasive method to measure the metabolic phenotype of single colon cancer cells in vivo. By using NADH as optical biomarker and the phasor approach to Fluorescence Lifetime microscopy (FLIM) we identify cancer metabolism related to different rates of glycolysis, cell growth and proliferation of cells. We perform label-free Phasor FLIM on living and actively perfused xenograft tumors. Colon cancer cells are injected subcutaneously into immune deficient (NSG) mice and tumors are allowed to grow for three weeks. The tumor vasculature is labeled by injecting TRITC Dextran into the tail vein and xenografts are exposed via a skin flap, still perfused by their feeder vessels.

FLIM distinguishes collagen fibers, the tumor stroma, adipocytes, blood vessels and single cancer cells within the living tumor. By measuring NADH lifetime, we quantify the relative concentration of free and bound NADH in single cancer cells, which reflects the cellular redox NADH/NADþ ratio and balance of oxidative phosphorylation and glycolysis. We investigate the tumor microenvironment by characterizing the distribution of the metabolic fingerprint of single colon cancer cells and by mapping the three-dimensional metabolic heterogeneity of the tumor at different distances from blood vessels.

Our method permits a non-invasive measurement of single cancer cell metabolism in a living intact tumor microenvironment. It allows monitoring of spatial and temporal dynamic changes of tumor metabolism upon different physiological conditions such as blood flow, tissue oxygenation levels, nutrient availability and drug delivery.

Work supported by NIH-P41 P41-