Images in Lipid Research

The fatty acids from LPL-mediated processing of triglyceride-rich lipoproteins are taken up rapidly by cardiomyocytes

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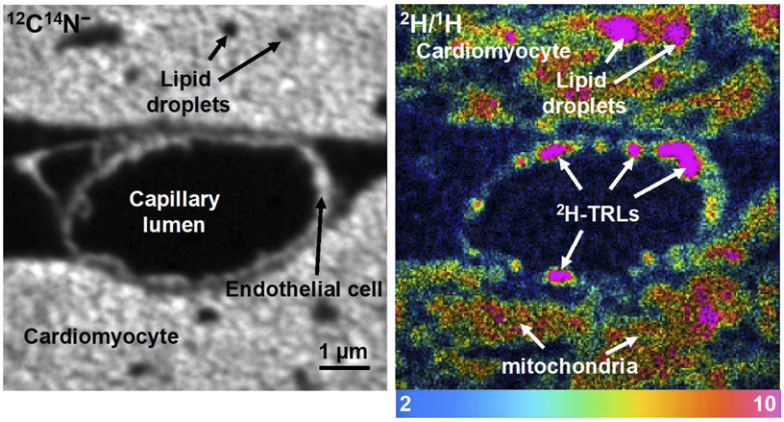

The lipolytic processing of triglyceride-rich lipoproteins (TRLs) by lipoprotein lipase has been studied at the biochemical level for >60 years (1, 2), but until recently it was not possible to image TRL processing or glean insights into the movement of lipoprotein-derived nutrients into tissues. We applied a new method, combining stable isotope labeling of TRLs and nanoscale secondary ion mass spectrometry (NanoSIMS), to visualize the movement of TRL-derived lipids across capillaries and into surrounding parenchymal cells (3, 4). The NanoSIMS instrument uses a focused Cs^+ beam to bombard the surface of a cell or a tissue section, releasing negatively charged secondary ions that are analyzed by mass spectrometry and used to generate images of tissues based solely on their isotopic content. The ability of NanoSIMS to detect and quantify secondary ions with high spatial resolution (~50 nm) and high sensitivity makes it possible to track stable isotope–labeled lipids at a subcellular level. Here, we show NanoSIMS images of a section from the left ventricle of a mouse that had been given an intravenous injection of ^2H-TRLs ([^2H] triglyceride-enriched TRLs). Two minutes after the intravenous injection, the mouse was euthanized, perfusion-fixed, and tissue sections were prepared for NanoSIMS. The NanoSIMS image on the left, generated from $^{12}C^{14}N^-$ secondary ions, reflects ^{14}N content of the tissue and is useful for morphology (e.g., visualizing a capillary endothelial cell, visualizing cytosolic lipid droplets) (arrows). The $^2H/^1H$ NanoSIMS image on the right, generated from the ratio of $^2H^-$ and $^1H^-$ secondary ions, is useful for visualizing ^2H-TRLs along the luminal surface of the capillary endothelial cell (arrows) and visualizing ^2H-labeled TRL-derived lipids in mitochondria and cytosolic lipid droplets of cardiomyocytes (arrows) (4). The $^2H/^1H$ ratio scale (multiplied by 10,000) ranges from 0.0002 to 0.001 (from slightly above ^2H natural abundance to ~7 times natural abundance). Two minutes after the intravenous injection, ^2H-labeled fatty acids had entered mitochondria of cardiomyocytes and had already been incorporated into the cytosolic triglyceride droplets of cardiomyocytes (4). The ^2H enrichment in capillary endothelial cells and cardiomyocytes was similar, implying that capillary endothelial cells do not represent a significant barrier to fatty acid movement into cardiomyocytes.

EQUIPMENT: NanoSIMS 50L (CAMECA).

REAGENTS: Mixed fatty acids (U-D, 96–98%) (Cambridge Isotope Laboratories).

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