

## David Y. Hui, PhD

Professor

Department of Pathology and Laboratory Medicine

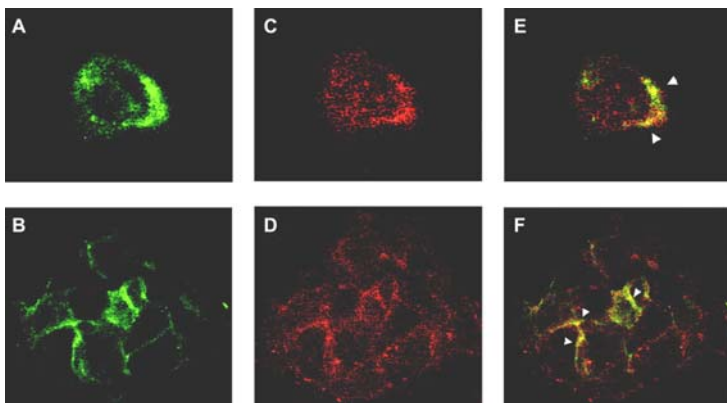
### Description of Research:

Dr. Hui investigates the role of pancreatic lipolytic enzymes in dietary lipid absorption, metabolism, and impact on metabolic diseases including obesity, diabetes, and atherosclerosis. He uses gene targeting approach to produce mice with defective expression of each of the pancreatic lipolytic enzymes, namely carboxyl ester lipase (CEL), pancreatic phospholipase A2 (PLA2), and pancreatic triglyceride lipase (PTL), and then test their efficiency in lipid absorption and transport. Results indicate that the CEL plays an important role in chylomicron assembly and secretion. Mice lacking this enzyme absorb lipid and cholesterol efficiently, but intestinal lipoproteins produced from the CEL-null mice are smaller in size than the normal chylomicrons. In contrast, mice lacking PTL displayed reduced cholesterol absorption efficiency and delayed fat absorption and metabolism, whereas the PLA2-defective mice have normal lipid absorption and transport mechanisms but are resistant to diet-induced obesity and diabetes. Current research is being undertaken to determine the mechanism by which CEL influences chylomicron production, the mechanism by which PTL affects cholesterol absorption, and the mechanism by which observation of the PLA2 lipolytic product lysophosphatidylcholine directly suppresses insulin signaling and thereby contributing to postprandial hyperlipidemia and hyperglycemia. Dr. Hui has also initiated a project to identify the role of the putative cholesterol transporter NPC1-L1 in cholesterol transport and absorption and impact on lipoprotein metabolism. Specific attention is paid to the mechanism by which the cholesterol absorption inhibitor ezetimibe influences intracellular cholesterol trafficking as well as its systemic effect on lipoprotein metabolism.

### Collaborations:

Dr. Hui collaborates with Drs. Aronow in the **Bioinformatics Core**, Martin, Tschop, and Tso to investigate lipid metabolism. He also works with Dr. Heubi investigating the molecular mechanism of cholesterol absorption.

### Representative Figure:



HepG2 cells grown on glass coverslips were incubated for 30 min with carboxyl ester lipase (CEL) (30  $\mu\text{g/ml}$ ) then rinsed with PBS, fixed, and permeabilized. CEL was immunostained with Texas Red, class B, type I scavenger receptor (SR BI) was immunostained with fluorescein isothiocyanate and cells were examined with a confocal microscope. *Panels A and B* show only fluorescein isothiocyanate-stained SR BI, whereas *panels C and D* show only Texas Red-stained CEL. *Panels E and F* show the merged fluorescein isothiocyanate and Texas Red images. The *yellow color* represents the coincidence of red and green pixels, indicating colocalization of CEL and SR BI. The *arrowheads* in *panels E and F* indicate specific areas of apparent SR BI and CEL concentration and colocalization in plasma membranes. From JBC 2004 279:26, 27599-27606