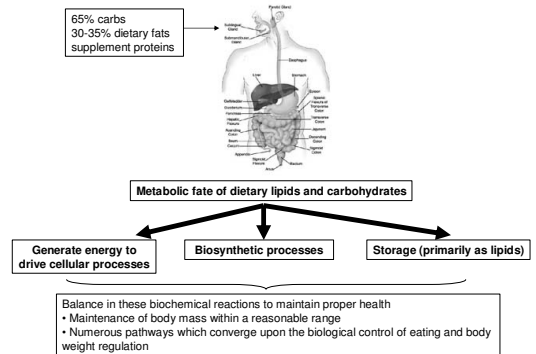


Aluminum toxicity leads to fat accumulation in human liver cells: a link to obesity

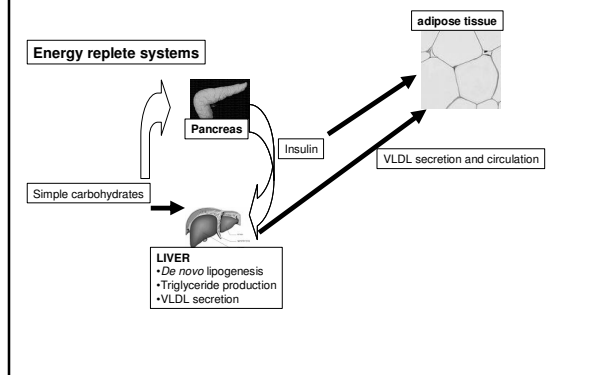
Presented by: Ryan Mailloux, PhD candidate at Laurentian University

Contact: ri_mailloux@laurentian.ca
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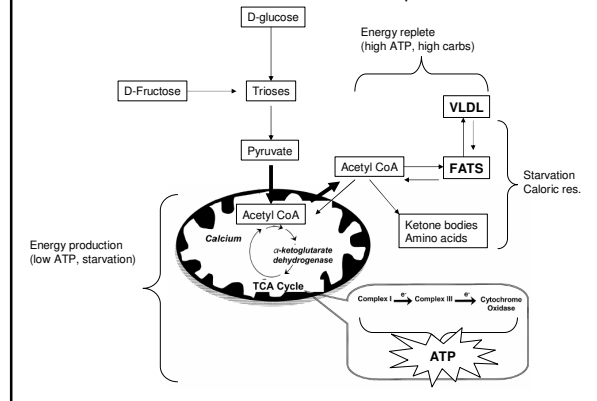
Energy balance and adipose tissue mass



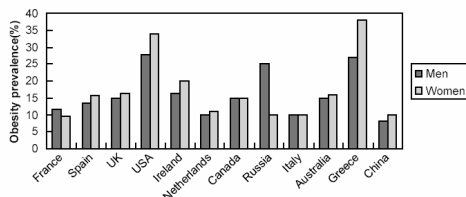
The liver is central to the production of fats



Functional mitochondria is central to lipid metabolism

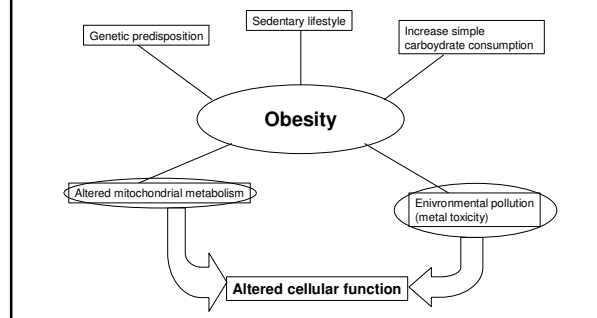


Obesity as a world wide health concern

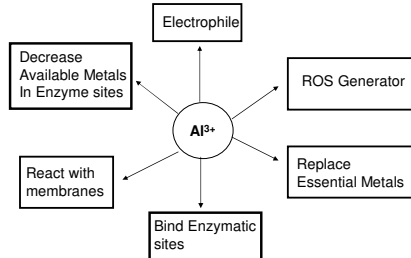


The most simplistic level of obesity is the net accumulation of fat in adipose tissue (positive energy balance). Thus the simplest question to be asked is what is the origin of this fat and what controls the flux of energy to these storage depots?

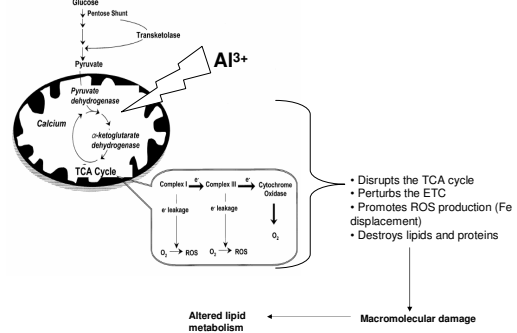
Major contributors to obesity



Aluminum; an environmental pollutant with toxic implications



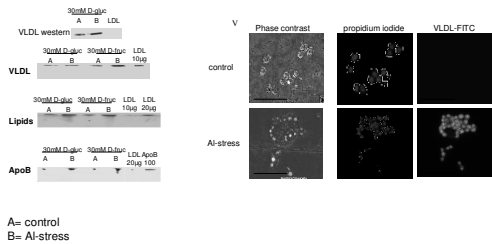
Aluminum toxicity and mitochondrial dysfunction



MallouxFJ and Appanna VD (2006) Aluminum toxicity elicits a dysfunctional TCA cycle and succinate accumulation in hepatocytes. *J Biochem Mol Toxicol* 20(4): 198-208.
 MallouxFJ and Appanna VD (2006) In-gel activity staining of oxidized nicotinamide adenine dinucleotide kinase by blue native polyacrylamide gel electrophoresis. *Anal Biochem* 350(2): 210-5.
 MallouxFJ and Appanna V. (2007) Aluminum toxicity leads to enhanced lipogenesis in human hepatocytes; a link to obesity. *Cell. Phys and Biochem* IN PRESS.
 MallouxFJ and Appanna VD (2007) The Tricarboxylic acid cycle, an ancient metabolic network with a novel twist. *PLoS ONE*, SUBMITTED

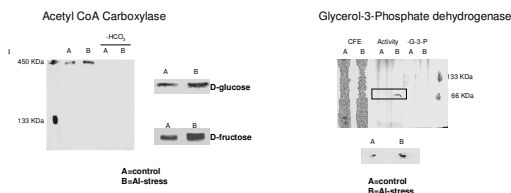
Aluminum toxicity promotes fat production in liver cells

Aluminum increases VLDL production



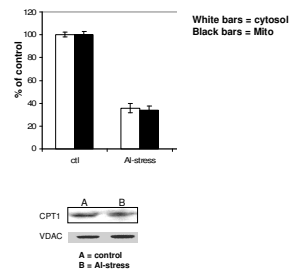
MallouxF and Appanna V. (2007) Aluminum toxicity leads to enhanced lipogenesis in human hepatocytes; a link to obesity. *Cell. Phys and Biochem* IN PRESS

Al enhances the activity of fat producing enzymes

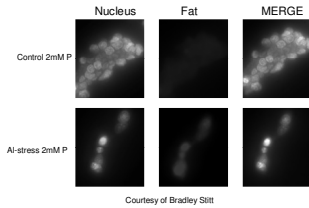


MallouxF and Appanna V. (2007) Aluminum toxicity leads to enhanced lipogenesis in human hepatocytes; a link to obesity. *Cell. Phys and Biochem* IN PRESS

Al diminishes the availability of L-carnitine and CPT action

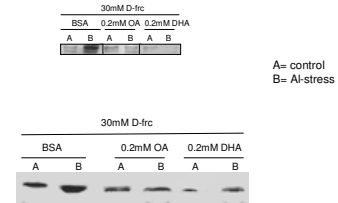


Al prevents lipid consumption

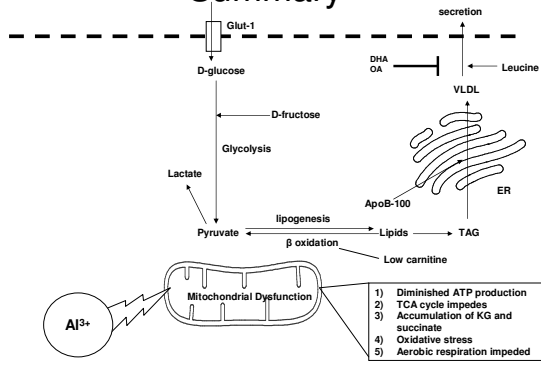


NOTE these observations were confirmed by HPLC

Omega-3 fats attenuate Al-mediated VLDL production



Summary



Conclusions

- Al promotes mitochondrial dysfunction in human liver cells
- This event alters lipid flux (enhanced fat production and reduced fat oxidation)
- The accumulation of fat in liver cells encourages VLDL production and secretion
- VLDL accumulates in the extracellular environment
- These events were circumvented by omega-3
- These observations may allow for the development of therapeutic and preventative medicines.

THIS IS THE FIRST STUDY THAT IMPLICATES MITOCHONDRIAL DYSFUNCTION AND ENVIRONMENTAL POLLUTION IN AN INCREASE IN THE EXTRACELLULAR LIPID MOLECULES, EVENTS WHICH WOULD CONTRIBUTE TO THE PATHOGENESIS OF OBESITY

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